UNIVERSITY OF BIELEFELD
Faculty of Health Sciences
School of Public Health

BURDEN OF ILLNESS OF BULIMIA NERVOSA IN THE UNITED STATES

An evaluation of the prevalence, incidence, and treatment costs of bulimia nervosa

Dissertation
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DECLARATION

This dissertation is the result of an independent investigation. Wherever the work is indebted to the work of others, it has been acknowledged and cited.

I declare that this dissertation has not been accepted in substance for any other degree, nor is it concurrently being submitted in candidature or achievement of any other degree at any other university.

Elke Hunsche

Bielefeld, January 31st 2007

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ABSTRACT

The objective of this thesis is to assess the medical burden of bulimia nervosa in the U.S. using a prevalence-based approach, and to place this burden in a global context. To this aim, a thorough literature review of the global evidence on the epidemiology of bulimia nervosa was performed, as well as health economic analysis of the per-patient treatment costs in a large, U.S. claims database. Results of these two research approaches were combined to project the medical costs of bulimia nervosa in the U.S. Implications of findings for clinical practice and future research needs are discussed.

Estimates of the prevalence of bulimia nervosa in the adult population of Western countries have dropped from 8%–13% in surveys in the 1980s to approximately 1% in recent studies, likely because diagnostic criteria became more stringent over time. The limited data available demonstrate that bulimia nervosa also exists in non-Western and developing countries. Estimates of a lifetime prevalence of bulimia nervosa of at least 2% among women in Western countries are based on a smaller evidence base than the amount of research conducted on the point prevalence. There are currently too few well-designed studies on the incidence of bulimia nervosa to draw reliable conclusions.

In patients with private employer-sponsored healthcare plans in U.S., the total annual per-patient fee-for-service treatment cost in 2002, including inpatient, outpatient, and drug treatment of bulimia nervosa as well as its complications and comorbidities, was estimated at $3,577, of which $1,865 were directly attributable to inpatient and outpatient care of the eating disorder. Pharmaceutical services accounted for 42% of the total costs, while inpatient and outpatient care contributed 25% and 33%, respectively. Based on a multivariate regression model, only age and comorbidity were found to be significant predictors of the daily per-patient costs, with costs increasing by 1.0% with each additional year of age and by 1.6% with each additional diagnosis. For patients with partially or fully capitated healthcare plans (encounter claims), costs had to be approximated by fee-for-service equivalents, yielding estimated per-patient annual costs of $4,238, of which $2,113 were directly attributable to the outpatient and inpatient treatment of bulimia nervosa.

Following a prevalence-based approach, it was estimated that in 2002 between 0.5 and 1.0 million adults suffered from bulimia nervosa, leading to a total annual cost of $1.7 billion in patients with private employer-based health insurance, of which $0.9 billion were directly attributable to the outpatient and inpatient treatment of bulimia nervosa. However, the burden to payers would rise to $3.5 billion if all predicted sufferers, irrespective of insurance status, were diagnosed and treated. Since most cases currently go untreated, this estimate provides an indication of potential future costs. Additional research is needed to identify barriers to care and strategies to overcome them. Determining the need for additional resources will require research to quantify healthcare resources currently available for the treatment of bulimic individuals, as well as studies to identify long-term trends in the epidemiology of bulimia nervosa.

ZUSAMMENFASSUNG

Ziel dieser Dissertation ist es – basierend auf dem Prävalenzansatz – die medizinischen Kosten der Bulimie in den USA zu schätzen und in einen globalen Kontext zu stellen. Zu diesem Zweck wurde eine eingehende Literaturrecherche bezüglich der globalen epidemiologischen Evidenz zur Bulimie vorgenommen sowie - anhand einer grossen amerikanischen Krankenversicherungsdatenbank - eine gesundheitsökonomische Analyse der Behandlungskosten pro Patient. Die Ergebnisse dieser beiden Forschungsansätze wurden kombiniert, um die medizinischen Kosten der Bulimie in den USA zu projizieren. Implikationen für die klinische Praxis sowie zukünftiger Forschungsbedarf werden diskutiert.

In den 80er Jahren wurde in Erhebungen die Prävalenz der Bulimie unter Erwachsenen in westlichen Ländern auf 8%-13% geschätzt, während nach jüngsten Studien diese nur ungefähr 1% beträgt, vermutlich bedingt durch die strengeren diagnostischen Kriterien. Des Weiteren sind auch nicht westlich orientierte Länder von dieser Krankheit betroffen, wie eine begrenzte Anzahl von Studien belegt. Sehr limitierte Evidenz existiert derzeit bezüglich der Lebenszeitprävalenz, die auf mindestens 2% bei Frauen in westlichern Ländern geschätzt werden kann. Bezüglich der Inzidenz können keine verlässlichen Aussagen getroffen werden, da es zu wenige gut geplante Studien gibt.

Bei amerikanischen Patienten mit privater, vom Arbeitgeber gesponsorter Krankenversicherung wurden die jährlichen leistungsbezogenen Gesamtkosten im Jahre 2002 – einschliesslich ambulanter, hospitärer und medikamentöser Behandlung der Bulimie und ihrer Komplikationen und Komorbiditäten – auf $3.577 pro Patient geschätzt. Davon waren $1.865 direkt der ambulanten und hospitären Therapie der Bulimie zurechenbar. Von den Gesamtkosten entfielen 42% auf die medikamentöse, 25% auf die ambulante und 33% auf die stationäre Therapie. Mit Hilfe eines multivariaten Regressionsmodells wurde ermittelt, dass Alter und Komorbidität einen signifikanten Einfluss auf die Höhe der täglichen Kosten haben mit einem Kostenanstieg um 1,0% pro zusätzlichem Altersjahr und 1,6% mit jeder weiteren Diagnose. Bei Patienten mit Krankenversicherungen, die ganz oder teilweise über Kopfpauschalen abrechnen, wurden die Gesamtkosten auf der Grundlange von leistungsäquivalenten Kosten auf $4.238 pro Patient pro Jahr geschätzt, von denen $2.113 direkt der Bulimie zurechenbar waren.

Die Anzahl amerikanischer Erwachsener, die im Jahre 2002 an Bulimie litten, wurde auf 0,5 bis 1,0 Millionen geschätzt und die jährlichen Behandlungskosten für Patienten mit privater Krankenversicherung auf $1,7 Milliarden, von denen $0,9 Milliarden direkt der Bulimie zurechenbar waren. Die Gesamtkosten könnten jedoch bis auf $3,5 Milliarden ansteigen, wenn alle Betroffenen, unabhängig von ihrem Krankenversicherungsstatus, diagnostiziert und therapiert würden. Da jedoch die meisten Betroffenen in den USA nicht behandelt werden, ist dieser Schätzwert eher eine Indiz für potentielle zukünftige Kosten. Weiterer Forschungsbedarf besteht derzeit bezüglich der Identifikation von Therapiebarrieren sowie Strategien zu deren Bewältigung. Des Weiteren müssten die für die Behandlung der Bulimie verfügbaren Resourcen ermittelt werden, um den ungedeckten Bedarf bestimmen zu können. Schließlich sind Langzeitstudien erforderlich, die Aussagen über den Verlauf der Epidemiologie der Bulimie ermöglichen.

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1 Introduction

In the past, the occurrence of eating disorders was commonly characterized by the three 'Ws': western, white, and women. This perception was reinforced by the fact that in the 1980s and 1990s epidemiological studies focused predominantly on western countries and those populations assumed to be most at risk, namely white women. Eating disorders were often considered to be a culture-bound syndrome and a consequence of extreme identification with the western beauty ideals. However, recent evidence indicates that eating disorders are also prevalent in non-western countries,[1] and their prevalence in these regions is predicted to rise in the future.[2]

The clinically recognized eating disorders—anorexia nervosa, bulimia nervosa, binge eating disorder (BED), and eating disorders not otherwise specified (EDNOS)—differ not only in terms of their symptoms, but also in their short- and long-term consequences. Bulimia nervosa is characterized by frequent food binges or recurrent episodes of significant overeating, which may occur as often as several times per day. To prevent weight gain, bulimic individuals use different compensatory methods, such as vomiting, excessive exercise, or abuse of laxatives and diuretics. Their body weight is typically normal, even though patients may perceive themselves as overweight.[3]

The etiology of bulimia nervosa remains largely unknown. One of the difficulties in identifying specific risk factors is the complexity of the condition. While many potential risk factors have been studied, few have been identified as reliable predictors of bulimia nervosa, among them female gender and a history of dieting. In addition, the development of bulimia nervosa has been shown to be influenced by general risk factors for psychiatric disorders, including parental psychiatric disorder, and sexual or physical abuse, as well as by specific risk factors for dieting, such as childhood obesity and parental obesity.[4] Other potential risk factors are early menarche, perfectionism, negative self-evaluation, and critical comments by family members about body shape, weight or eating.[5]

The mean age of onset of bulimia nervosa is 18 to19 years,[6] with the eating disorder rarely affecting children under 12 years of age.[7] The syndrome generally continues until early adulthood. Although the long-term prognosis of untreated bulimia nervosa is largely unknown, evidence supports a continuum model of bulimia nervosa as a relapsing and remitting disease that remains chronic in a significant number of patients. Within 5 to 10 years of diagnosis, approximately 50% of women were found to have fully recovered without treatment, while about 20% and 30% continued to meet the full and partial diagnostic criteria for bulimia nervosa, respectively.[8] Although treatment may increase the likelihood of remission, the short-term success achieved by interventions may not guarantee a complete recovery in the long term. Treatment duration has been suggested as a critical factor for successfully preventing relapses and avoiding a chronic pattern of bulimia nervosa.[9] It is important to note that the loss of a diagnosis of bulimia nervosa does not necessarily indicate recovery, as between 19% and 32% of individuals with a diagnosis of bulimia nervosa 5 to 10 years earlier have been found to suffer from an EDNOS at follow-up.[10;11]

In addition to being a chronic disorder, bulimia nervosa has been shown to lead to physical and physiological impairments due to frequent vomiting and/or abuse of laxatives and diuretics, including, but not limited to electrolyte changes, especially hypokalaemia and hypochloremia, arrhythmias, myopathy, caries, enlarged salivary glands, gastritis/esophagitis, chronic constipation, gastroesophageal erosions, menstrual irregularities, and scarring on dorsum of the hand (Russell's sign).[12] Most of the medical complications resolve with discontinuation of the disordered behaviors, though some may remain chronic. Bulimic individuals also suffer frequently from various psychiatric comorbidities, which may be antecedents or consequences of the eating disorder, such as substance abuse (especially alcohol dependency), mood and anxiety disorders (e.g., depression, social phobia, and obsessive-compulsive disorder), and personality disorders.[7]

Evidence regarding the medical, social, and economic burden of bulimia nervosa is currently limited, which might partially be explained by the fact that since this disorder is

relatively new to the psychiatric nomenclature it has only received research attention for the past 25 to 30 years. While several articles have been published on the epidemiology of bulimia nervosa as well as its medical complications, so far only two studies have attempted to estimate its economic burden, one in the U.S. and one in Germany.[13;14] However, both studies were limited by the exclusion of certain treatment costs, notably for drugs and for treating complications of bulimia nervosa.

Since bulimia nervosa may lead to severe complications, its burden encompasses not only the direct medical costs for the treatment of the eating disorder itself, but also the costs for the prevention and treatment of short- and long-term complications. In addition, psychiatric comorbidities add to the direct burden of bulimia nervosa, so their treatment costs should be considered as part of the overall cost of illness.

In addition to its direct medical costs, the indirect costs of bulimia nervosa can be expected to be high, since bulimic individuals engage in time-consuming eating behaviors and are absorbed by thoughts related to their eating disorder, the time costs of which might have occupational and educational implications. Another component of the indirect costs is premature death, which should be considered, as an increased mortality risk has been demonstrated.[15] Also contributing to the burden of bulimia nervosa are indirect costs incurred by families and caretakers, who may need to change their work status to provide care. While one study has attempted to estimate the indirect costs incurred by patients with bulimia nervosa,[14] the published literature is currently devoid of data on the economic burden to families and friends.

Finally, the health-related quality of life impairment of affected persons and their families is an important component of the overall burden of illness. Bulimia nervosa patients have been shown to have a lower quality of life and psychological health than healthy individuals.[16] In addition, significant difficulties with activities of daily living have been reported in bulimic patients, leading to social, interpersonal, family, and work impairments.[17] Some of these impairments may continue even after improvement of the eating disorder symptoms,[18] demonstrating the long-term quality of life consequences of

bulimia nervosa. Since bulimic patients might not perceive their physical or mental health as impaired, self-reported quality of life of affected persons may be misleading, and supplemental objective measures of health status are therefore important. In addition to the quality of life detriment of bulimic individuals, the impact of the eating disorder on relatives' social relationships and leisure activities can be significant.[19] Since quality of life costs are difficult to determine, to date their burden to sufferers and caregivers has not been quantified in monetary terms.

The economic and societal burden of bulimia nervosa may be reduced by decreasing its prevalence (i.e., reducing the incidence and/or duration of cases), by minimizing or avoiding complications and comorbidities, and by developing cost-effective treatment options. However, the provision of therapy alone may be insufficient, since many sufferers do not seek treatment because they are afraid of being stigmatized or feel ashamed of their eating disorder.[20] Effective treatment also requires that physicians accurately detect and diagnose bulimia nervosa, which could be difficult given that sufferers frequently seek treatment for physical complaints associated with bulimia nervosa (e.g., gastrointestinal symptoms), rather than for the eating disorder itself.[21] Therefore, the treating physician might never diagnose the underlying disorder, or do so only long after the onset of bulimic symptoms.

A further barrier to treatment is the lack of affordable access, as even most private health insurance companies in the U.S. either do not cover therapies for bulimia nervosa or else provide coverage only with high patient copayments. The ambivalence of suffers regarding seeking treatment is therefore likely to encounter ambivalence among providers and payers to provide effective but costly treatments. In a resource-constrained environment, the temptation may be to "let sleeping dogs lie" and not be proactive in promoting and providing comprehensive treatment to those who are not vocal in demanding help.

Currently, the need for healthcare services to effectively treat and prevent bulimia nervosa, as well as the demand for treatments, are largely unknown, since there is a lack

of evidence regarding the number of people suffering from bulimia nervosa as well as the number of patients being treated.

1.1 Objective

The overall objective of this thesis is to estimate the medical burden of illness of bulimia nervosa in the U.S., based on the predicted number of prevalent cases and the estimated per-person treatment costs. While the focus of the research was on the U.S., findings will also be discussed in a global context. An assessment of indirect and health-related quality of life costs of bulimia nervosa is beyond the scope of this thesis, as is an evaluation of the cost-effectiveness of treatments.

The main objective is supported by further specific aims:

- To assess the prevalence and incidence of bulimia nervosa from a global perspective;
- To determine factors associated with the per-person treatment costs in the U.S.;
- To evaluate the currently available evidence regarding the cost of illness of bulimia nervosa as well as future research needs.

In order to answer these research questions, a thorough literature review of the evidence on the prevalence and incidence of bulimia nervosa was performed, as well as a health-economic analysis of a large, representative U.S. claims database. Results of these two research approaches were combined to estimate the medical burden of bulimia nervosa in the U.S.

1.2 Outline of thesis

The thesis is divided into five chapters, including this introduction. Chapter 2 contains the results of the comprehensive literature review, which was performed to assess and critically evaluate evidence on the global prevalence and incidence of bulimia nervosa. Chapter 3 presents results of an analysis of per-patient treatment costs in the U.S. using a

large, representative claims database. This analysis includes a multivariate regression model to assess factors that might influence treatment costs. In Chapter 4, epidemiological data from the literature review are used to predict the number of affected persons in the U.S., and this estimate is combined with the average per-person costs to project the cost of bulimia nervosa in the U.S. Since both the estimate of the number of cases as well as the costs per person are associated with uncertainty, sensitivity analyses are performed using a range of cost-of-illness estimates. Chapter 5 summarizes the existing evidence on the epidemiological and economic burden of bulimia nervosa in the U.S. and globally, and identifies data gaps and the need for future research.

2 The epidemiology of bulimia nervosa

2.1 Diagnostic criteria

Bulimia nervosa was first recognized as an eating disorder in 1979 in a publication by Russell, who described 30 cases demonstrating the following three characteristics:[22]

- An irresistible urge to overeat
- Subsequent self-induced vomiting or purging
- A morbid fear of becoming fat

However, bulimic behaviors were not new in 1979; they were practiced in the ancient Roman Empire, and syndromes of binging and vomiting were described in the 18th and 19th centuries.[23] The existence of bulimia nervosa as an eating disorder prior to its description by Russell is supported further by the fact that in the preceding decades clinicians from different countries independently proposed various descriptions for a bulimic eating disorder syndrome. A historical summary of the literature published between 1960 and 1979 can be found in Vandereycken (1994).[24]

Even though Russell reported that his 30 cases did not fulfill all the diagnostic criteria for anorexia nervosa, he did not yet propose bulimia nervosa to be a distinct diagnosis. It was one year later, in 1980, that bulimia was recognized as a distinct eating disorder and was included in the Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition (DSM-III).[25] However, the DSM-III did not use Russell's term bulimia nervosa but rather simply bulimia. According to the DSM-III, the diagnostic criteria for bulimia were:

A. Recurrent episodes of binge eating (rapid consumption of a large amount of food in a discrete period of time, usually less than 2 hours)
B. At least three of the following:
    1) Consumption of high caloric, easily digested food during a binge
    2) Inconspicuous eating during a binge
    3) Termination of such eating episodes by abdominal pain, sleep, social interruption, or self-induced vomiting

4) Repeated attempts to lose weight by severely restrictive diets, self-induced vomiting, or use of cathartics and/or diuretics
5) Frequent weight fluctuations greater than 10 pounds (>4.5kg) due to alternating binges and fasts

C. Awareness that the eating pattern is abnormal and fear of not being able to stop eating voluntarily
D. Depressed mood and self-deprecating thoughts following eating binges
E. The bulimic episodes are not due to anorexia nervosa or any known physical disorder

Unlike Russell's criteria, the DSM-III explicitly excluded cases of anorexia nervosa from the definition of bulimia. However, the initial diagnostic criteria of the DSM-III lacked any quantification in terms of the frequency of binging and purging behavior and were therefore unable to differentiate between severely disturbed cases and patients with mild eating disorder symptoms.

This weakness in the DSM-III diagnostic criteria was redressed in the revised 3rd Edition (DSM-III-R). In addition, a name change from bulimia to bulimia nervosa took place, thereby implying a psychiatric impairment of cases. According to the DSM-III-R a diagnosis of bulimia nervosa was established by:[26]

A. Recurrent episodes of binge eating (rapid consumption of a large amount of food in a discrete period of time)
B. A feeling of lack of control over eating behavior during the eating binges
C. The person regularly engages in either self-induced vomiting, use of laxatives or diuretics, strict dieting or fasting, or vigorous exercise in order to prevent weight gain
D. A minimum average of two binge eating episodes per week for at least 3 months
E. Persistent overconcern with body shape and weight

Although the DSM-III-R frequency criteria have been criticized as being arbitrary and not based on clinical experience, they remain applicable today in the absence of evidence supporting alternative criteria to identify severely disturbed cases.

Since the DSM-III-R definition still lacked some diagnostic specificity (e.g., it was also applicable in cases of anorexia nervosa with binge eating symptoms), the criteria were further refined in the 4th Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), thereby ensuring that bulimia nervosa and anorexia nervosa were mutually exclusive disorders.[27] According to the DSM-IV, a diagnosis of bulimia nervosa requires:

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
    1) Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than most people would eat during a similar period of time and under similar circumstances
    2) A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating)
B. Recurrent inappropriate compensatory behavior in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, enemas, or other medications; fasting; or excessive exercise
C. The binge eating and inappropriate compensatory behaviors both occur, on average, at least twice a week for 3 months
D. Self-evaluation is unduly influenced by body shape and weight
E. The disturbance does not occur exclusively during episodes of anorexia nervosa

The DSM-IV criteria also differentiate between two specific types of bulimia nervosa:[27]

- The purging type, characterized by self-induced vomiting or the misuse of laxatives, diuretics, or enemas during the current episode of bulimia nervosa
- The non-purging type, characterized by other inappropriate compensatory behaviors during the current episode of bulimia nervosa, such as fasting or

excessive exercise, but not self-induced vomiting or the misuse of laxatives, diuretics, or enemas

From the above description of the evolution of the diagnostic criteria for bulimia nervosa, it is evident that it would be difficult to compare studies that include patients diagnosed using different versions of the DSM. For example, individuals with anorexia nervosa may be excluded from bulimia nervosa studies that applied the DSM-IV criteria, while according to the DSM-III-R these individuals could be given both diagnoses and might be included in studies applying these criteria.

In addition to the DSM criteria, the International Classification of Diagnoses (ICD) system has defined bulimia nervosa. Epidemiological studies, especially the ones using registries or billing data, have applied the ICD criteria. According to the 10th version of the ICD (ICD-10), which was implemented by the World Health Organization (WHO) in 1992, bulimia nervosa (F50.2) is:[28]

> "A syndrome characterized by repeated bouts of overeating and an excessive preoccupation with the control of body weight, leading to a pattern of overeating followed by vomiting or use of purgatives. This disorder shares many psychological features with anorexia nervosa, including an overconcern with body shape and weight. Repeated vomiting is likely to give rise to disturbances of body electrolytes and physical complications. There is often, but not always, a history of an earlier episode of anorexia nervosa, the interval ranging from a few months to several years."

While the ICD-10 criteria are somewhat similar to the DSM-IV ones, a direct comparison of studies using the ICD-10 and DSM-IV criteria is not feasible, since the DSM-IV explicitly excludes binge eating in the context of anorexia nervosa but the ICD-10 doesn't.

The ICD-10 is the most up-to-date classification system, but the ICD Ninth Revision, Clinical Modification (ICD-9-CM), which is based on the World Health Organization's

ICD-9, is also still used, especially as the official system of assigning codes to diagnoses and procedures associated with the utilization of hospital services in the U.S. In the ICD-9-CM the disorder was referred to as bulimia; the term bulimia nervosa was introduced in the ICD-10, concurrent with the name change from the DSM-III to the DSM-III-R. According to the ICD-9-CM, bulimia (307.51) is defined as:[29] "*overeating of nonorganic origin*".

The changes and refinements to the diagnostic criteria of bulimia nervosa that have been implemented over time have made it difficult to perform longitudinal epidemiological studies of this disorder. Literature reviews of published epidemiological evidence are limited as well, since only studies applying the same criteria can reliably be compared.

Results of the literature search performed as part of this research are therefore, where possible and appropriate, categorized according to the version of the DSM and ICD criteria applied in the studies.

2.2 Literature review

The objective of this literature review was to comprehensively assess the worldwide evidence on the prevalence and incidence of bulimia nervosa since its recognition as a distinct disorder in 1980. Results of the review, together with the per-patient cost analysis (Chapter 3), served as the basis for the prediction of the cost of illness of bulimia nervosa in the U.S. (Chapter 4). In addition, the epidemiological evidence from different countries and cultures provided the context for assessing the global impact and burden of the disorder, thereby providing a global perspective for the U.S. findings (Chapter 5).

2.2.1 Methodology

A literature search of the Medline and Embase databases was performed to identify articles providing evidence on the prevalence and/or incidence of bulimia nervosa. The search was limited to manuscripts published between January 1966 and March 2006 in either English or German, which focused only on humans, and which contained the

keywords “bulimia” and “epidemiology” as either major or minor Medical Subject Heading Terms (MeSH) headings. In addition, the combined keyword “bulimia-epidemiology” was used in the major and minor MeSH headings.

To ensure inclusion of recent evidence, a further literature search was performed for the period January 2000 to March 2006, with “bulimia” and “prevalence” or “bulimia” and “incidence” or “bulimia” and “epidemiology” as search criteria in either abstract, title or keywords. Further to articles published in English or German, this additional literature search also included papers in French or Spanish, if an English abstract was available.

Abstracts of identified articles were assessed in terms of their relevance for this literature review. All potentially relevant publications were collected and reviewed. The following exclusion criteria were applied at the abstract and the publication level:

- No information regarding the prevalence or incidence of bulimia nervosa (based on accepted criteria like the ones of the DSM or the ICD)
- Editorial, letter, or case report
- Study included only children or adolescents; i.e., all study participants were 17 years or younger. Since the mean age of onset of bulimia nervosa is 18 to 19 years,[6] epidemiological studies in children and adolescents underestimate the prevalence and incidence of the disorder in the general population and therefore were excluded from the literature review.

Reference lists of identified publications were hand searched for additional evidence regarding the epidemiology of bulimia nervosa.

Findings for the point or period prevalence, lifetime prevalence, and incidence of bulimia nervosa are described in separate sections, each summarizing the results chronologically in table format as well as in the text by geographical region and country.

2.2.2 Categorization of epidemiological studies

One of the main limitations of epidemiological studies in bulimia nervosa is the subjective nature of what a respondent or interviewer considers a binge. This directly impacts the definition of bulimia nervosa and therefore the number of prevalent and incident cases reported. Further methodological limitations are imposed by the low prevalence of the disorder in the general population, requiring a large sample size to reliably calculate the prevalence or incidence, and by the tendency of sufferers to conceal their illness and avoid professional help.

Different methodological approaches have been applied to estimate the prevalence and incidence of bulimia nervosa. Results of studies are therefore not directly comparable and have to be interpreted in the context of their respective study designs.

Main differences between studies relate to the diagnostic criteria, the characteristics and size of the study population, and the method of case identification. Since the diagnostic criteria for bulimia nervosa have changed over time, between-study discrepancies in prevalence and incidence estimates may be due to differences in the definition of cases. In general, the diagnostic criteria have become more restrictive, with the most stringent being those of the DSM-IV.

The characteristics of the study population, which are determined by the inclusion and exclusion criteria as well as the selection process, are critical for the generalizability of findings. Many published studies have focused on populations in which the disorder was thought to be most common, such as Caucasian females aged 14 to 40 years, especially student samples. Results of these studies are not representative for the population as a whole and therefore provide limited evidence regarding the prevalence and incidence of bulimia nervosa. In addition, the participation rate of subjects is important, since non-response can lead to a sampling bias.

Various methods of case identification have been used for epidemiological studies of bulimia nervosa, including but not limited to:

- Registries or record-based studies
- Population-based surveys
- Clinical interviews
- Combinations of the above, specifically the 2-stage screening method, in which probable cases of bulimia nervosa are identified by a survey, which is followed by a clinical interview of potential cases

Registries or record-based studies provide an underestimate of the prevalence and incidence in the general population, since only treated cases can be accounted for; i.e., only those seeking either outpatient or inpatient treatment and being diagnosed. In addition to this sampling bias, a further limitation is that clinical records are usually not accessible for all subjects and might be incomplete with regard to the recording of diagnoses. Prevalence estimates based on clinical records are also subject to a lack of standardization of case definitions, since physicians might apply and interpret diagnostic criteria differently. Finally, record-based studies are not suitable for time-trend analyses, as the percentage of treated and untreated cases might have changed over time due to improvements in the access to health services, recognition of the disease, and diagnosis of cases. Register-based studies can therefore at best provide a minimum estimate of the number of cases, which may be useful for treatment planning purposes.

Population-based surveys, while overcoming some of the limitations of clinical record-based studies, are associated with limitations inherent to the self-reporting of symptoms and habits by subjects as well as the recruitment of participants. It can be hypothesized that individuals with bulimia nervosa are generally reluctant to either participate in a survey, respond to specific questions, or to report their symptoms accurately in terms of frequency and severity, thereby attempting to avoid stigmatization for their disorder as well as treatment by professionals. Participants' response biases as well as generally low response rates impact the generalizability of findings to the population in general.

Additionally, the representativeness of population-based surveys has often been limited due to non-random selection of subjects and the focus on convenience samples.

Since subjects' responses cannot be validated in a survey, misclassification of cases is likely to occur, especially as the diagnostic criteria for bulimia nervosa, anorexia nervosa, and binge eating disorder are very similar. In addition, respondents might interpret survey questions differently. This can partially be addressed by a proper validation of the survey instrument, including an assessment of its measurement properties. However, only a limited number of validated instruments are currently available, and many studies have used either non-validated instruments or translations of validated instruments without a cultural adaptation and respective validation.

To overcome some of the limitations inherent to population surveys, a 2-stage process of case identification has been applied in more recent surveys. While the first stage consists of screening for suspected or at-risk cases via a survey, in the second stage, probable or suspected cases (i.e., those meeting the specific cut-off criteria for bulimia nervosa of the survey instrument) are interviewed personally—usually by a clinician. The second stage also involves interviews of a random sample not at risk, to assess the psychometric properties of the screening instrument; i.e., the rate of false-negatives. Prevalence and incidence estimates are then established based on definitive cases meeting the diagnostic criteria for bulimia nervosa.

It is essential that the screening test applied in the first stage be first evaluated for its discriminative capabilities in terms of the proportion of individuals correctly classified as cases or non-cases. This implies that the test's efficiency in terms of its sensitivity, specificity, and positive predictive value needs to be determined. Validation of the screening instrument is also required for different populations (e.g., different ethnic groups).

While the inclusion of the second stage provides an improvement over population surveys, results of the 2-stage approach are still subject to limitations of the screening

instrument, the selection of the population to be surveyed, the sampling technique applied, and the response rate of the targeted population. Additional considerations are the definition of probable cases (i.e., the cut-off point chosen for the screening instrument) and factors potentially influencing participants' responses (e.g., the standardization of the interview, the setting of the interview, and training of interviewers).

Due to various methodological differences between epidemiological studies included in this literature review, it was not possible to perform a meta-analysis of the identified evidence on the prevalence and incidence of bulimia nervosa. Results are therefore summarized descriptively, while providing potential explanations for discrepancies observed between studies.

2.3 Prevalence of bulimia nervosa

2.3.1 Point and period prevalence of bulimia nervosa

Interest in the prevalence and incidence of bulimia nervosa has increased since 1979, when the disorder was first recognized by Russell.[22] To date, few review articles of the epidemiological evidence on bulimia nervosa have been published,[30-33] but none of them reported on all studies, irrespective of the applied methodology and selected target population.

The most recent review, which was performed by Hoek and van Hoeken, focused on prevalence data published between 1990 and 2002, primarily those derived from 2-stage surveys.[31] Based on the identified literature, the authors estimated 1-year prevalence rates at different levels of care: 1.5% in the community, 0.17% in primary care, and 0.078% in mental healthcare. These results suggest that only few subjects with bulimia nervosa can be expected to receive mental healthcare. Hsu (1996) reported findings from individual 2-stage studies, excluding those relying on telephone surveys.[30] He stressed that studies in college or high school students cannot be generalized to the overall population. In an earlier literature review, Fairburn and Beglin assessed the impact of diagnostic criteria

and the method of case detection.[32] The mean prevalence rate was found to be 0.9% when applying the DSM-III-R criteria with a sophisticated 2-stage method of case detection compared to 9.0% if the less stringent DSM-III criteria and self-reported questionnaires were used. The first review article published was by Szmukler (1985), who summarized the limited evidence available in the early 1980s and stressed the limitations of results derived from non-validated questionnaires and the need for a validation of the diagnosis against an independent criterion.[33]

These and other factors relevant for the interpretation of epidemiological findings, which might explain differences between study results (e.g., response rate of participants), were abstracted from all studies identified during the literature review. Results of studies providing evidence on the point or period prevalence of bulimia nervosa are summarized in Table 1 in chronological order (date of publication).

Table 1: Studies providing evidence on the prevalence of bulimia nervosa

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Kugu et al (2006) [34]	Turkey, rural area, representative sample of university students, year NR	18–24 (∅ 20) F & M	951 F: 492 M: 459 (95%)	2-stage: - Self-reported questionnaire (EAT) - Interview of at-risk group	DSM-IV	F: 1.6 M: 0.0
Cotrufo et al (2005) [35]	Italy, Naples, high school students, year NR	17–20 F	259 (1st stage 100%, 2nd stage 92%)	2-stage: - Self-reported questionnaire (EDI) - Interview of high-risk cases	DSM-IV	F: 0.8
Fichter et al (2005) [36]	Greece, adolescents in Greece and migrant Greek adolescents in Germany,[1] 1998	Germany: 13–21 Greece: 12–21 (∅ 16) F & M	Germany: 881 F: 445 M: 436 Greece: 2,920 F: 1,506 M: 1,414 (90%)	2-stage: - Self-reported questionnaire (ANIS) - Interview (SIAB-EX) of random sample of high-risk cases	DSM-IV	Germany: 1.0 F: 1.9 M: 0.0 Greece: 0.9 F: 1.2 M: 0.7
Hach et al (2005) [37]	Germany, Dresden, prospective sample T1: 1996/1997 T2: 1997–1999	18–24 F	2,064 (59%)	Psychological interview	DSM-IV	F - T1: 0.5 F - T2: 0.7
Hay et al (2005) [38]	Australia, random sample of general practice attendees, 2001	19–64 (∅ 41) M	1st stage: 383 (77%) 2nd stage: 50 (67%)	2-stage: - Self-reported questionnaire (mail) - Interview of at-risk cases	DSM-IV	M: 0.2[2]

[1] Participants attended private or public schools in Veria, or schools of the Greek Republic for Greek students in Munich.
[2] The prevalence of 0.2% was calculated based on one reported case of bulimia nervosa and a targeted sample of 500 men.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Keel et al (2005) [39]	US, university freshmen and seniors, 1982, 1992, 2002	∅ 20 F & M	1982: F: 624 (78%) M: 276 (69%) 1992: F: 564 (71%) M: 235 (59%) 2002: F: 548 (69%) M: 244 (61%)	Self-reported questionnaire (mail & web-based, EDI)	DSM-III-R	1982: F: 4.2 M: 1.1 1992: F: 1.3 M: 0.4 2002: F: 1.7 M: 0.0
Szumska et al (2005) [40]	Hungary, national cross-sectional sample, 1998	15–24 (∅ 18 students, ∅ 22 non-students) F	3,386 - 1,903 students - 1,483 non-students (88%)	Self-reported questionnaire (EDI and Eating Disorder Symptom Severity Scale)	DSM-IV[3]	F: 0.4 Students: 0.5 Non-students: 0.3
Toelgyes & Nemessury (2004) [41]	Hungary, secondary school and college students, 1996/1997	10–29 F & M	580 F: 332 M: 248 (73%)	2-stage: - Self-reported questionnaire (EAT, BITE) - Interview of at-risk cases	Simulated bulimia nervosa[4] (1st stage) DSM-IV (2nd stage)	F: 3.6 M: 0.4 F: 0.6 M: 0.0
Blesa et al (2003) [42]	Spain, sample of primary care attendees, year NR	≥ 14 (∅ 46) F	175 (response rate NA)	Semi-structured interview	DSM-IV	F: 5.3 (2.4–9.7)

[3] Criteria for bulimia nervosa were: binge eating at least twice weekly, at least one compensatory behavior per week, minimum of 14 points on the EDI drive for thinness scale.

[4] Simulated bulimia nervosa diagnosis: (i) BITE score above 25, (ii) binge eating at least twice weekly, (iii) compensating behavior at least weekly.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Favaro et al (2003) [43]	Italy, city of Padova, year NR	18–25 F	934 (78%)	Interview (ED section of the structured clinical interview)	DSM-IV	F: 1.8 (0.9–2.6)
Medina-Mora et al (2003) [44]	Mexico, National Survey of Psychiatric Epidemiology (random sample), 2001–2002	18–65 (41%: 18–29 years) F & M	2,432 F: 1,306 M: 1,126 (response rate NR)	Interview (Diagnostic Interview Schedule, WHO)	ICD-10	0.3 F: 0.5 M: 0.0
Miotto et al (2003) [45;46]	Italy, high school attendees, 1999	15–19 (∅ 16.5) F & M	930 (97%)	Self-reported questionnaire	BITE score ≥ 20	F: 4.0 M: 0.3
Quintero-Párraga et al (2003) [47]	Venezuela, random sample of high school students, year NR	12–18 F & M	1,363 F: 719 M: 644 (91%)	Self-reported questionnaire (checklist of symptoms)	DSM-IV	1.5[5] F: 1.5 M: 1.6
Ryu et al (2003) [48]	Korea, Seoul, university and high school students, year NR	18–29 F	533 (81% college, 99% high school)	Self-reported questionnaires (EDI, BULIT)	BULIT (cut-off score for bulimia NR)	F- College: 4.6 F- High school: 1.5
Al-Adawi et al (2002) [49]	Oman, sample of adults (university and residents), year NR[6]	≥ 18 F & M	100 (response rate NR)	Self-reported questionnaires (EAT, BITE)	BITE score ≥ 25	1.0

[5] Prevalence rates were calculated based on the data provided in the publication.
[6] The study also included samples of teenagers. However, only results for adults are reported here.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Augestad & Fonders (2002) [50]	Norway, students at 4 universities, 1997	18–50 F	878 (approx. 79%)	Self-reported questionnaire (EDI, Survey of Eating Disorders)	DSM-IV	F: 5.1 (0.3–1.1) Physical activity level: < 5 h/day: 4.2 ≥ 5 h/day: 7.3
Carta et al (2002) [51]	Italy, Sardinia, community samples of Sardinian immigrants in Paris, Sardinian residents, Parisian residents, 1994–96	≥ 18 F & M	153 immi-grants (85%) 2,260 Pari-sians (79%) 1,040 Sardi-nians (79%)	Interview (CIDIS)[7]	ICD-10	Immigrants: 2.0 (0.5–6.1) Parisians: NR Sardinians: 0.4 (0.1–1.1)
Lameiras Fernández et al (2002) [52]	Spain, Galicia, students year NR	17–44 (∅ 20) F & M	482 F: 325 M: 157	Self-reported questionnaire (EDI)	DSM-IV[8]	2.9 F: 4.3 M: 0.0
Gual et al (2002) [53-55]	Spain, Navarre, representative sample of schoolgirls, 1997	12–21 F	2,862 (82%)	2-stage: - Self-reported questionnaire (EAT) - Clinical interview of at-risk cases	DSM-IV	F: 0.8 (0.5–1.2)
Huon et al (2002) [56]	Republic of China, 6 cities, schoolgirls, year NR	12–19 (∅ 15.8) F	1,246 (90%)	Self-reported questionnaire	DSM-IV	F: 0.0
Klaplow et al (2002) [57]	US, patients in primary care (62 physicians), 1997/1998	<65: ∅ 40 ≥65: ∅ 73 F & M	< 65: 2,466 ≥ 65: 534 (77%)	Self-reported Patient Health Questionnaire	DSM-IV	Age < 65 y: 1.0 Age ≥ 65 y: 0.0

[7] CIDIS is a simplified version of the Composite International Diagnostic Interview (WHO).

[8] Bulimia nervosa was defined as ≥ 2 binges per week, ≥ 2 times compensatory behavior per week, and a BMI above 17.5.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Backe (2001) [58]	Germany, patients of a primary care gynecologist, 2000	14–76 (∅ 34) F	486 (97%)	Self-reported questionnaire (BITE)	DSM-IV (simulated)[9]	F: 1.9
Ghaderi & Scott (2001) [59]	Sweden, random sample of population, 1999	20–32 F	826 (74%)	Self-reported questionnaire (Survey of Eating Disorders)	DSM-IV	F: 1.3
Ghazal et al (2001) [60]	Morocco, Casablanca, random samples of secondary school students,[10] 1996	15–24 (∅ 18) F & M	2,044 - Moroccan school: 1,887 - French school: 157 (76%)	Self-reported questionnaire (BITE)	BITE score ≥ 25	Moroccan school: 0.8 F: 1.2, M: 0.1 French school: 1.9 F: 3.4 M: 0.0
Johnson et al (2001) [61]	US, patients in primary care and obstetric gynecology clinics, 1997–1999	18–99 (∅ 37) F	4,651 (response rate NR)	Self-reported questionnaire, reviewed by physician with patient	DSM-IV	F: 0.9 Age 18–25 y: 0.9 Age 26–35 y: 1.3 Age 36–45 y: 1.0 Age 46–55 y: 0.9 Age 56–99 y: 0.3
Kotler et al (2001) [62]	US, state of New York, sample of children and their mothers, 1983, 1985, 1992[11]	∅ age: 1983: 14 1985: 16 1992: 22 F & M	1983: 771 1985: 772 1992: 776 (response rate NR)	Interviews 1983/1985: Mother and Child 1992: Child	1983/1985: DSM-III-R 1992: DSM-IV	1983: F-1.2, M-0.2 1985: F-3.2, M-0.5 1992: F-1.1, M-1.1

[9] DSM-IV diagnosis of bulimia nervosa defined as BITE score of at least 20 and at least a score of 5 on the seriousness scale.
[10] Two groups of secondary school students were selected, one from a Moroccan and one from a French school.
[11] The study also included a sample of children assessed in 1975. However, only results for adolescents and adults are reported here.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Mulholland et al (2001) [63]	US, Midwest, African American college women, year NR	17–35 (∅ 20) F	403 (67%)	Self-reported questionnaire (mail)	DSM-IV	F: 0.0
Rivas et al (2001) [64]	Spain, Malaga, public and private school students, 1998/1999	12–21 F & M	1,555 F: 930 M: 625 (89%)	Self-reported questionnaire, completed by students & parents	DSM-IV (binging & purging ≥ 2/week for 3 months)	Student answers: 0.5 F: 0.6 M: 0.2 Parent answers: 0[12]
Westenhoefer (2001) [65]	West and East Germany, representative population samples, 1997, 1990	≥ 18 (∅ 46) F & M	1997 (65%) West: 2,130 East: 2,155 1990 (69%), West: 1,773	Self-reported questionnaire	≥ 2/week binging ≥ 1/week purging	1997: F: 1.1, M: 1.1 1990: F: 2.4, M: 2.1
Bhugra et al (2000) [66]	Northern India, industrial town, sample of private college students, year NR	15–23 F (Interview 14–17)	504 (response rate NR) (Sample of 50 interviewed)	Self-reported questionnaire (BITE) Clinical interview (sample)	BITE score ≥ 20 DSM-III-R	F: 0.4 F: 0.0
Lewinsohn et al (2000) [67]	US, random sample, participants in Oregon Adolescent Depression Project T1: 1987/1988 T2: 1-year follow-up T3: age 24 years[13]	Age NR for T1/T2 T3: 24 F	T1: 891 T2: 810 T3: 538 (response rate NR)	T1: In-person interview T2: In-person interview T3: Telephone interview	DSM-IV	F, T1: 0.3 F, T2: 0.5 F, T3: 0.4 (weighted 0.3)[14]

[12] Responses by parents were available for 166 male and 333 female students.
[13] T3 consisted of all participants with a history of major depressive disorder or a non-mood disorder at T2 and a randomly selected subset of those with no psychiatric disorder at T3. Study years for T2 and T3 were not reported.
[14] Weighted for the unequal stratified sampling of participants, who did not have a history of psychopathology at T2.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Nakamura et al (2000) [68]	Japan, Niigata, primary care patients (130 hospitals & 1,326 clinics), 1997	All ages F & M	Population of 2.4 million (94% of clinics & hospitals)	Clinical interview of patients with suspected eating disorder	DSM-IV DSM-III	0.001[15] (0.000–0.001) Age 15–29 y: 0.006 (0.005–0.007) 0.003 (0.003–0.004) Age 15–29 y: 0.015 (0.012–0.018)
Thiels et al (2000) [69]	Germany, Bielefeld, social work students, 1993–1995	Age NR F & M	507 F: 394 M: 113 (response rate NR)	Self-reported questionnaire (BITE)	DSM-IV DSM-III (BITE score ≥ 20)	0.6 (0.1–1.7) F: 0.8 (0.2–2.2) M: 0.0 (0.0–3.2) 5.3 F: 6.6 M: 0.9
Nakamura et al (1999) [70]	Japan, computer factory workers, 1995	20–39 F	406 (87%)	Self-reported questionnaire	EAT ≥ 20	F: 1.5
Kinzl et al (1999) [71] Kinzl et al (1998a) [72]	Austria, Tyrol, random sample, 1997	15–85 ∅ 40 F	1,000 (93%)	Phone interview (by dieticians)	DSM-IV	F: 1.5 Age 15–25 y: 6.2 Age 25–34 y: 1.5 Age 35–44 y: 1.2 Age 34–54 y: 0.0 Age 55–64 y: 0.8 Age 65–85 y: 0.0
Kinzl et al (1998b) [73] Kinzl et al (1999) [74]	Austria, Tyrol, random sample, 1997	18–88 (∅ 43) M	1,000 (92%)	Phone interview (by dieticians)	DSM-IV	M: 0.5 Age 18–25 y: 0.0 Age 25–34 y: 1.7 Age 35–44 y: 0.0 Age 45–54 y: 0.6 Age 55–88 y: 0.0

[15] The point prevalence was estimated by the 5-day prevalence. No case of bulimia nervosa was found in the age groups of 10-14 and 30-59 years.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Cotrufo et al (1998) [75]	Italy, province of Naples, high school students, year NR	13–19 F	919 (interview: 95%)	2 stage: - Self-reported questionnaire - Interview of probable cases	DSM-IV	F: 2.3
Hay (1998) [76]	Australia, southern part, random community-based sample, 1995	> 15 (∅ 46) F & M	3,001 F: 1,785 M: 1,216 (72%)	Structured interview	DSM-IV	0.3
Santonastaso et al (1997) [77]	Italy, Padua, freshman and sophomore college students, year NR	∅ 20 F	395 (80%) (interview: 93%)	2-stage: - Self-reported questionnaire (EAT) - Interview of probable cases	DSM-IV	F: 0.8[16]
Kuboki T. et al (1996) [78]	Japan, hospitals, 1992	All ages (range and mean NR) F & M	5,057 hospitals (37%)	Questionnaire completed by hospitals	Diagnosed cases (criteria NR)	0.001–0.003[17] F: 0.003–0.004 F, age 13–29 y: 0.01
Pemberton et al (1996) [79]	US, Texas, random sample of undergraduate students in 2 universities, 1990	∅ 22 F & M	1152 F: 684 M: 468 (70%)	Self-reported questionnaire (revised BULIT)	DSM-III-R (BULIT-R score > 103)	0.9 (0.4–1.6) F: 1.3 (0.6–2.5) M: 0.2 (0.0–1.2) Whites: 1.5 (0.6–3.1) Non-whites: 0.4 (0.0–1.3)

[16] The prevalence was calculated based on the information provided, i.e., 3 cases in 395 female students who participated in the study.
[17] These prevalence rates were calculated based on the information provided in the publication. Ranges represent projections from the sample of hospitals surveyed to all hospitals in Japan. Prevalence rates for men were not reported.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Basdevant et al (1995) [80]	France, samples of non-patients & outpatients seeking help with weight control, year NR	18–60 F	- 447 community (89%) - 292 private practice - 85 hospital outpatients	Self-reported questionnaire by Spitzer (community & private practice) Diagnosis by physician (hospital)	Recurrent binge eating & compen-satory behavior	F-Community: 0.2 F-Private practice: 4.1 F-Outpatient hospital: 4.7
Götestam et al (1995a) [81]	Norway, representative sample of population, 1991	∅ 37 F	1,849 (75%)	Self-reported questionnaire	DSM-III-R	F: 0.7
Götestam et al (1995b) [82]	Norway, all psychiatric outpatients, Feb. 1990[18]	All ages F & M	10,125 (91%)	Staff-reported questionnaire	Diagnostic criteria NR	F: 7.3 M: 0.7
Heatherton et al (1995) [83]	US, random sample of students (freshmen & seniors), Northeast, 1982 & 1992	1992: ∅ 20 F & M	1982: F–625, M–276 (78%, 69%) 1992: F-564, M-235 (71%, 59%)	Self-reported questionnaire (by mail, EDI)	DSM-III-R	1982: F: 7.2 M: 1.1 1992: F: 5.1 M: 0.4
Kurth et al (1995) [84]	US, Midwest, freshman students, 1991	∅ 18 F	Survey 1,367 (66%) Interview 306 (80%)	Self-reported questionnaire Clinical interview of random sample	DSM-III-R	F: 2.2 F: 2.0

[18] Inpatient data are not reported, since they did not differentiate between anorexia nervosa and bulimia nervosa.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Rathner et al (1995) [85]	Europe, medical students [85]	F & M	1,221	Self-reported questionnaires (EDI)	DSM-III-R (≥ 2/week binging & ≥ 1/week counter-regulative behavior)	[19]
	Austria, Innsbruck 1988 – 1990 [85]	∅ 23 F ∅ 23 M	379 (92%)			F: 0.60 (0.02–3.46) M: 0.00 (0.00–1.65)
	Hungary, Debrecen 1989 [85;86]	∅ 22 F ∅ 21 M	538 (F-290, M-248) (72%)			F: 1.00 (0.20–2.95) M: 0.00 (0.00–1.47)
	German Democratic Republic, Leipzig 1989 [85]	∅ 22 F ∅ 23 M	304 (75%)			F: 0.00 (0.00–2.07) M: 0.00 (0.00–2.87)
Pagsberg & Wang (1994) [87]	Denmark, Island of Bornholm (inpatients, outpatients, registries, readers of a news-paper), 1970–1989	10–24 F & M	Population of 47,000	Diagnosis according to outpatient/inpatient record; physician interview of probable cases (primary care)	ICD-10	1989: 0.09 1977–1986: 0.05
Tordjman et al (1994) [88]	France, Paris, medical students, year NR	∅ 20 F	F: 38 (83%)	Clinical interview	DSM-III-R	F: 7.9
Lee (1993) [89]	China, Hong Kong, students at a bilingual university, 1988–1991	17–25 (∅ 20) F & M	1,020 - F: 646 - M: 374 (98%)	2-stage: - Self-reported EAT - Interview of high-risk cases	DSM-III-R	0.0
Rathner & Messner (1993) [90]	Italy, Southern Tyrol, schoolgirls in a small, rural town (Brixen) year NR	11–20 F	517 (76%) Interview: 105 (94%)	2-stage: - Self-reported EAT - 1-year follow-up interview[20] (hospital case register review)	DSM-III-R	F: 0.0 (0.0–0.7) 15–20 y: 0.0 (0.0–1.6)

[19] Results from different countries were not combined.
[20] The 1-year follow-up included the at-risk group according to the EAT as well as random samples of sub-risk and non-risk groups.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Warheit et al (1993) [91]	US, Florida random sample of adults, 1984–1986	≥ 18 F & M	2,075 - 339 blacks - 1,736 whites (80%)	Clinical interview	DSM-III	0.4 (0.1–0.7) Blacks: 0.6 (0.0–1.3) M: 1.3 (0.0–3.1) F: 0.0 Whites: 0.3 (0.0–0.6) M: 0.0 F: 0.7 (0.1–1.3)
Bruce, Agras (1992) [92]	US, San Francisco Bay, random sample of a community-based population, Sept. 1990–Jan. 1991	18–75 F	455 (62%)	Structured telephone interview (based on Stanford Eating Behaviors Questionnaire)	DSM-III-R non-purging[21] Binges ≥ 2/week	F: 1.8 F: 3.8
Chun et al (1992) [93]	China, Chongqing and Shanghai, medical college freshman, year NR	Age NR F & M	509 F: 401 M: 108 (100%)	2-stage: - Self-reported questionnaire - Interview of possible cases	DSM-III DSM-III-R	1.3 M: 1.8 F: 1.2 1.1 M: 1.1 F: 0.0
Joergensen (1992) [94]	Denmark, Fyn County (island), 1977–1986	10–24 F	186 GPs (64%)	2-steps: questionnaires sent to GPs; interview of probable cases	DSM-III-R	F: 0.02[22] 15–19 y: 0.07 20–24 y: 0.04
Rand et al (1992) [95]	US, Florida, random sample of general population, 1984 – 1985	Age 18–96 F & M	2,115 (approx. 80%)	Structured interview in respondents home	DSM-III	1.1 F, 18–30: 4.1 M, 18–30: 0.0[23]

[21] Individuals who purged or had history of purging behavior were excluded.
[22] The prevalence was estimated by the authors as follows: incidence * average duration (3.5 years based on published data).
[23] Results for other age groups were not reported.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Whitehouse et al (1992) [96]	UK, Cambridge, general practice attendees, 1987	16–35 F	521 (97%) (interview 88%)	2-stage: - Self-reported questionnaire - Clinical interview of probable cases	DSM-III-R	F: 1.5
Hay & Hall (1991) [97]	New Zealand, Wellington, inpatients at 8 acute psychiatric wards, year NR	∅ 36 F & M	101 F: 59 M: 42 (94%)	2-stage: - Self-reported questionnaire - Interview of probable cases	DSM-III-R	7.9 F: 11.9 M: 2.4
Hoek et al (1991) [98]	Netherlands, representative sample of population, 1985–1986	All ages F & M	151,781 (approx. 1% of Dutch population)	Cases identified by 58 GPs	DSM-III and/or DSM-III-R	0.02 2-year prevalence:[24] rural area: 0.02 urbanized area: 0.02 cities: 0.08
Pyle et al (1991) [99]	US, Midwest, freshman at 2 universities, 1986	Age NR F & M	1,836 F: 925 M: 911 (97%)	Self-reported questionnaire	DSM-III ≥ 1/week binge/ purge DSM-III-R	F: 4.3 M: 0.1 F: 1.1 M: 0.0 F: 2.2 M: 0.3
Szabo, Tury (1991) [100]	Hungary, college population, year NR[25]	19–36 ∅ 23 F & M	356 F: 224 M: 132 (40% 1st stage)	2-stage: - Self-reported questionnaire (EAT) - Interview of probable cases	DSM-III (EAT) DSM-III-R (interview)	F: 4.0 M: 0.8 F: 1.3 M: 0.8

[24] The 2-year prevalence was determined as point prevalence plus incidence in 1985 and 1986.
[25] The results from the adolescent sample are not reported.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Bushnell et al (1990) [101]	New Zealand, Christchurch, random sample, year NR	18–64 F & M	1,498 M: 504 F: 994 (70%)	2-stage: - DIS applied by lay interviewer - Clinical interview of possible cases	DSM-III DSM-III-R Russell's criteria	0.2 (0.0–0.8) 0.5 (0.2–1.3) 0.0 (0.0–0.5)
Johnson, Hillard (1990) [102]	US, Cincinnati, random sample of psychiatric emergency service patients, year NR	18–45 F & M	143 F: 67 M: 76 (94%)	2-stage: - Self-reported questionnaire - Interview of probable cases	DSM-III-R	F: 3.0 (0.4–10.8) M: 2.6 (0.3–9.4)[26]
Welch, Hall (1990) [103]	New Zealand, Wellington, students in tertiary education, year NR	∅ 21 F	243 (90%)	Self-reported questionnaire	DSM-III-R	F: 2.5 (1.0–5.6)
Jones (1989) [104]	US, Illinois, freshman university students, year NR	Age NR F	150 (response rate NR)	Self-reported questionnaire (BULIT)	DSM-III	F: 4
King (1989) [105;106]	UK, London, 4 general practices, year NR	16–35 F & M	720 F: 534 M: 186 (96% EAT) (89% interview)	2-stage: - Self-reported questionnaire (EAT) - Clinical interview of high-risk cases	Russell's criteria	F: 1.1 (0.1–2.1) M: 0.5
Kurtzman et al (1989) [107]	US, Los Angeles, students, year NR	∅ 21 F	716 (response rate NR)	Self-reported questionnaires (EDI)	DSM-III	F: 2.1

[26] The prevalence was based on a 3-week time period.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Striegel-Moore et al (1989) [108]	US, Yale, university freshman, year NR	M: ∅ 18 F: ∅ 18 F & M	F: 450 M: 590 (75%)	Self-reported questionnaire	Modified DSM-III-R (≥ 3 binges week)	F: 3.8 M: 0.2
Ben-Tovim et al (1988) [109]	South Australia, community & clinical samples [shopping center (1), family practice (2), high school (3), weight disorder clinic (4), dietetics department (5)], year NR	Age NR F	(1) 389 (66%) (2) 220 (94%) (3) 792 (74%) (4) 78 (NA) (5) 31 (NA) (66%–94%)	Self-reported questionnaire	DSM-III / DSM-III-R	F: 12.7 / 1.7 (1) 10.0 / NA (2) 11.8 / 1.4 (3) 15.2 / 2.0 (4) 100.0 / 66.6 (5) 29.0 / 6.5
Cullenberg, Engström-Lindberg (1988) [110]	Sweden, 2 suburban municipalities, retrospective assessment of case records, 1984–1985	16–35 F & M	Catchment area of 77,729 population	Survey of records provided by healthcare workers (psychiatric teams, GPs, hospitals, eating disorder clinics, school psychologists)	DSM-III	0.041[27] F: 0.031 M: 0.003 Age 16–24 y:[28] F: 0.47 M: 0.02
Drewnowski et al (1988) [111]	US, Michigan, longitudinal survey of college students, year NR	Age NR F	Fall: 931 (42%) Spring: 588 (64%)	Self-reported questionnaire (mail), 2 waves	DSM-III-R (≥ 2/week binge eating)[29]	F, fall: 2.9 (1.9–4.2) F, spring: 3.3 (2.1–5.1)

[27] Results reflect 2-year prevalence rates.
[28] Results for other age groups were not reported.
[29] The frequency of symptoms was assessed over a 1-month period rather than 3 months, as required by DSM-III-R.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Drewnowski et al (1988) [112]	US, national probability sample of college students (undergraduate and graduate), April 1987	∅ 21–30 (under-graduate – graduate) F & M	1,007 F: 507 M: 500 (56%)	Telephone interview	DSM-III-R	F: 1.0 (0.2–1.8) M: 0.2 (0.0–0.6)
Kiriike et al (1988) [113]	Japan, 2 cities, school of nursing (1) and junior college (2), 1986	18–21 ∅ 19 F	451 (1) 220, (2) 231 (response rate NR)	Self-reported questionnaire	≥ 1/week binging & purging or vomiting	F: 2.9 (1) 3.6 (2) 2.1
Lachmenmeyer, Muni-Brander (1988) [114]	US, students at 2 high schools: low/middle (1), middle/upper class (2), year NR	13–19 F & M	(1) 712 (2) 549 (response rate NR)	Self-reported questionnaires (EAT, Binge-Eating Questionnaire)	DSM-III	(1) 7.6 (2) 4.7
Martin, Wollitzer (1988) [115]	US, California, family practice outpatient clinic (patients and non-patients), year NR	∅ 32 F	277 (52%)	Self-reported questionnaire	DSM-III (≥ 1/week purging)	F: 3.7
Mintz, Betz (1988) [116]	US, Ohio, undergraduate attendees of psychology course, 1986	∅ 19 F[30]	643 (response rate NR)	Self-reported questionnaire	DSM-III-R	F: 3.1
Whitehouse, Button (1988) [117]	England, technical college students, year NR	88% were 16–19 F & M	578 F: 446 M: 132 (99%)	2-stage: - Self-reported questionnaire (EAT) - Interview of high-risk cases	DSM-III Russell's criteria	F: 1.6 F: 1.6 M: 0.0

[30] Students who were anorexic or obese were excluded.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Cooper et al (1987) [118]	UK, Cambridge, attendees at two family planning clinics, 1986	≥ 15 F	331 (89%)	Self-reported questionnaire	Probable BN[31]	F: 1.8
Gray et al (1987) [119]	US, undergraduate students attending psychology classes, year NR	Age NR F & M (Black)	507 F: 341 M: 166 (approx. 100%)	Self-reported questionnaire	DSM-III Russell's criteria	F: 3.0 M: 2.0 F: 1.5 M: 0.0
Greenfeld et al (1987) [120]	US, students at a private preparatory boarding school, year NR	13–19 (∅ 16) F & M	761 F: 424 M: 337 (78% M, 76% F)	Self-reported questionnaire	DSM-III (≥ 1/week binging) DSM-III without "C"[32]	F: 4.0 M: 0.8 F: 8.4 M: 1.2
Pope et al (1987) [121]	US, Massachusetts, bingo tournaments, (3 lower and 6 upper income communities) year NR	18–60 F	408 accepted (response rate NR)	Self-reported questionnaire (Eating Disorder Questionnaire)	DSM-III DSM-III-R (without B & E)[33]	F: lower income: 17.2 upper income; 13.4 F: lower income: 10.8 upper income: 8.2
Schotte, Stunkard (1987) [122]	US, Philadelphia, cross-sectional sample of college students, year NR	∅ 22 F & M	1,936 F: 994 M: 942 (97%)	Self-reported questionnaire, interview of a sample of definitive, probable, and non-bulimics	DSM-III or DSM-III-R (adjusted for false positive rate)	DSM-III/DSM-III-R: F: 1.3 M: 0.1 DSM-III-R: F: 0.7 M: 0.1

[31] Probable bulimia nervosa was defined according to the following criteria: bulimic episode, self-induced vomiting, and morbid fear of fatness.
[32] Criterion C: awareness that the eating pattern is abnormal and fear of not being able to stop eating voluntarily
[33] Criterion B: feeling of lack of control of the eating behavior; criterion E: persistent overconcern with body shape and weight"

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Thelen et al (1987) [123]	US, Missouri, college students (3 groups), year NR	Age NR F	(1) 619 (2) 598 (3) 641 (response rate NR)	Self-reported questionnaire (BULIT)	DSM-III (BULIT score > 101)	F (1) 3.8 (2) 2.0 (3) 3.4
Herzog et al (1986) [124]	US, graduate students at a northeastern university, year NR	∅ 26 F	550 (49.8%)	Self-reported questionnaires	Modified DSM-III (≥ 1 binge/ week)	F: 10.2
Meadows et al (1986) [125]	UK, Leicestershire, 2 GP practices, year NR	18–22 F	411 (70% survey, 54% interview)	2-stage: - Self-reported EAT - Interview of probable cases	 EAT ≥ 30 DSM-III	 F: 6.8 F: 0.2
Nasser (1986) [126]	Arab university undergraduates in: Egypt, Cairo, 1982–83 UK, London, 1981–82	∅ 23 (Egypt) ∅ 22 (UK) F	Egypt: 60 UK: 50 (response rate NR)	2-stage: - Self-reported EAT - Interview of high-risk cases	Russell's criteria	F-Cairo: 0.0 F-London: 12.0
Pyle et al (1986) [127]	US, Midwest freshman students at 2 colleges, 1983	Age NR F & M	1,382 F: 722 M: 660 (96%)	Self-reported questionnaire	DSM-III ≥ 1 binge & purge/week	2.2 F: 4.1 M: 0.2 0.7 F: 1.0, M: 0.0
Rand & Kuldau (1986) [128]	US, Florida, community sample of normal weight adults, year NR	19–59 (∅ 35) F & M	232 F: 144 M: 88 (response rate NR)	Structured interview (at home, work, etc.), plus self-reported questionnaire	DSM-III	0.4 F: 0.7 M: 0.0

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Zuckermann et al (1986) [129]	US, New England, college freshman and seniors, 1982	Age NR F & M	907 F: 631 M: 276 (75%)	Self-reported questionnaire (EDI, mail)	DSM-III ≥ 1 binge/ week	F: 8.0 M: 0.7 F: 4.0 M: 0.4
Gray & Ford (1985) [130]	US, students at a private, urban university, year NR[34]	F: ∅ 20 M: ∅ 21 F & M	339 F: 220 M: 119 M (54%)	Self-reported questionnaire	DSM-III	F: 13 M: 4
Healy et al (1985) [131]	Ireland, Dublin, college and university students, year NR	17–25 F & M	1,063 F: 702 M: 361 (> 95%)	Self-reported questionnaire	Modified DSM-III (≥ 1 binge/ week)	F: 2.7 M: 0.0
Nevo (1985) [132]	US, California, college under-graduates, year NR	17–30 (∅ 20) F	689 - 505 Caucasian (90%)	Self-reported questionnaire	DSM-III	F: 5–11 Caucasians: 6–14[35]
Katzman et al (1984) [133]	US, college students, year NR	Age NR F & M	812 F: 485 M: 327 (response rate NR)	1) 2 screening questions 2) Self-reported questionnaire of probable cases (F only)	DSM-III	F: 3.9
Pope et al (1984) [134]	US, Boston, clients at a shopping centre, 1983	≥ 12 years F	300 (99% of those who accepted)[36]	Self-reported questionnaire	DSM-III	F: 4.7

[34] The authors confused incidence with prevalence. Even though the manuscript refers to incidence rates, results are correctly reported as prevalence rates here.

[35] The ranges for point prevalence estimates are based on different criteria for the diagnosis of BN, which were derived from the self-reported questionnaire. Prevalence rates for other ethnicities were not reported separately.

[36] The overall number of people who were approached was not reported.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Zinkand et al, 1984 [135]	US, Iowa, family practice population, year NR	14–42 F & M	176 F: 136 M: 40 (95%)	Modified EAT-26 (additional questions added)	DSM-III	10.9
Cooper, Fairburn (1983);[136] Fairburn, Cooper (1983) [137]	Southern England, attendees of a family planning clinic, Oct. 1982 – Feb. 1982	15–40 (∅ 24) F	369 (96%)	Self-reported questionnaire (EAT)	Probable bulimia nervosa[37]	F: 1.9
Pyle et al (1983) [138] [38]	US, Midwest, freshman students at 2 universities, 1980	Age NR F & M	1,355 F: 575 M: 780 (98%)	Self-reported questionnaire	DSM-III (without "C")[39] ≥ 1/week binging & purging	4.1 F: 7.8 M: 1.4 0.6 F: 1.0 M: 0.3
Collins et al, 1982 [139]	US, Philadelphia, freshman college students, year NR	F & M	244 F: 100 (88%)	Self-reported questionnaire (EDI)	DSM-III	F: 9
Halmi et al (1981) [140]	US, state of NY, summer college session attendees, year NR	14–67 (∅ 26) F & M	355 F: 212 M: 119 [40] (66%)	Self-reported questionnaire	DSM-III	13.0 F: 19.0 M: 5.0

[37] Bulimia nervosa was defined by the following criteria: current binging-eating, current vomiting as means of weight control, morbid fear of fatness.
[38] The authors confused incidence with prevalence; results reported in the table represent prevalence rates, even though the publication refers to incidence rates. Since the history of the frequency of binging and purging was assessed, results might present lifetime history estimates rather than current point estimates.
[39] Criterion C: awareness that the eating pattern is abnormal and fear of not being able to stop eating voluntarily
[40] Gender information was missing for 24 persons.

Table 1 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Point prevalence, % (95% CI, if reported)
Stangler & Printz (1980) [141]	US, Washington, attendees of a university psychiatric outpatient clinic, year NR	17–53 ∅ 25 F & M	500 F: 318 M: 182 (response rate NR)	Case record review	DSM-III	3.8 F: 5.3 M: 1.0

Abbreviations: y = year; Resp. rate = response rate; CI = confidence interval; T = time; F = female; M = male; NA = not applicable; NR = not reported

Questionnaires:

- ANIS: Anorexia Nervosa Inventory for Self-Rating
- BITE: Bulimic Investigatory Test
- BULIT: Bulimia Test
- DIS: Diagnostic Interview Schedule
- DSM: Diagnostic and Statistical Manual of Mental Disorders
- EAT: Eating Attitude Test
- ED: Eating Disorder
- EDI: Eating Disorder Inventory
- SIAB-EX: Structured Inventory for Anorexic and Bulimic Disorders

2.3.1.1 United States

DSM-IV-based prevalence estimates

Numerous epidemiological studies have been published in the U.S. since the recognition of bulimia nervosa as a distinct disorder, especially in the 1980s and 1990s. The most recent DSM-IV-based study, which Kaplow et al (2002) conducted in 1997/1998 in female and male primary care patients at least 18 years of age, found a prevalence of 1.0% among those younger than 65 years of age, and 0.0% among the elderly (aged ≥ 65 years).[57] The authors note that the two age groups may not have been comparable, and observed differences in the prevalence may have been due to the more frequent underreporting of binging and purging by the elderly. In addition, the reason for the office visit and thereby the inclusion in the study may have been different for the two age groups, as younger patients are more likely to visit a physician for acute symptoms, while in older patients office visits are often scheduled follow-up visits for an existing illness. Furthermore, the proportion of women was 68% in the younger age group compared to 60% in the elderly, which could have resulted in a higher overall prevalence estimate in the non-elderly. General limitations of this study were the reliance on patients' self-reported symptoms and the non-representativeness of patient samples. However, the main advantage of this research was the inclusion of a broad age range, in contrast to the focus on young patients in most other epidemiological studies.

Similar findings were reported in a study by Johnson et al (2001) of adult patients, recruited in primary care and gynecology clinics, according to which the average DSM-IV-based prevalence was 0.9%, highest in those 26 to 35 years of age (1.3%) and lowest in those older than 55 years (0.3%).[61] Results are however not directly comparable with the study by Kaplow et al, as Johnson et al included only women. Important additional findings were that only 3% of the cases had been recognized by the clinicians prior to the survey and that ethnicity was not significantly associated with the prevalence of bulimia nervosa. This study offered a major advantage over other epidemiological research in the U.S., since it included a validation of the patients' self-reported symptoms by the physician, who reviewed the survey together with the patient. Findings are likely conservative (i.e., provide an underestimate of the prevalence), since patients may have

been reluctant to disclose their eating disorder in an attempt to avoid treatment. Another strength of this study was the cross-sectional design, which included women of all age groups, different ethnicities, and from various geographical locations across the US.

The DSM-IV-based prevalence estimates derived from adults in primary care are generally comparable to the results of population-based surveys. In a longitudinal cohort study, conducted by Kotler et al (2001) over a 17-year period, the prevalence was estimated at 1.1% in the last survey, when participants were approximately 22 years old (young adults).[62] The highest prevalence among females was observed during late adolescence (3.2%), while among males the highest prevalence occurred in young adults (1.1%). However, the DSM-IV criteria were only used in the last survey, while prior ones applied the DSM-III-R criteria, potentially confounding the results. An additional finding of this study was that early adolescent bulimia nervosa was associated with a 9-fold increased risk of late adolescent bulimia nervosa and a 20-fold increased risk of young adult bulimia nervosa. Furthermore, late adolescent bulimia nervosa increased the risk of young adult bulimia nervosa 35-fold. Despite this substantial risk of adolescent eating disorder symptoms to continue until adulthood, the stability of a bulimia nervosa diagnosis was found to be only moderate. This implies that the majority of adolescents either did not continue to suffer from the eating disorder as young adults due to recovery over time or due to treatment, or they did not demonstrate the full syndrome at the time of the survey because of the fluctuating nature of bulimia nervosa symptoms.

In another longitudinal study by Lewinsohn et al (2000), the point prevalence rates were between 0.3% and 0.5% in female high school attendees and young adults.[67] The much lower rates in this survey compared to Kotler et al could be due to differences in the study populations as well as the diagnostic instruments used by interviewers. Since Lewinsohn et al applied a non-eating disorder-specific questionnaire (the Schedule for Affective Disorders and Schizophrenia for School-Aged Children), it is possible that potential cases of bulimia nervosa were not identified because of lack of specificity of the survey instrument.

Contrary to studies that focused mainly on Caucasians, none of the participants in a survey of African-American college women were found to meet the DSM-IV criteria for bulimia nervosa.[63] To account for potential false-negative cases, the authors adjusted the observed prevalence rate, which resulted in predicted rates between 0% and 1%. The main limitations of this study were the reliance on self-reported symptoms by students and the use of a questionnaire not validated in an African-American population. Since the predicted prevalence estimates were similar to those reported in Caucasians, further research is warranted to assess potential differences in the prevalence of bulimia nervosa between Caucasian and African-American women.

Based on the available evidence, it can be concluded that about 1% of young adult women in the U.S. suffer from bulimia nervosa according to the DSM-IV criteria, while studies in men are too scant to draw final conclusions.

DSM-III-R-based prevalence estimates

More prevalence research has been conducted using DSM-III-R than DSM-IV criteria, primarily in students. Depending on the study methodology and the student population selected, prevalence estimates vary between 1% and 5% for females and are less than 1% for males. Since only one researcher used the 2-stage approach for case identification, the results of the majority of studies are subject to the limitations of population-based surveys and interviews.

In the most recent DSM-III-R-based study, Keel et al (2005) assessed three randomly selected samples of college students in 1982, 1992, and 2002, thereby enabling a time-trend analysis.[39] The authors found that among women the prevalence decreased significantly from 4.2% in 1982 to 1.3% and 1.7% in 1992 and 2002, respectively. Among men, the observed decline in the prevalence was only a nonsignificant trend (1.1% in 1982, 0.4% in 1992, 0.0% in 2002). While the proportion of respondents who reported binge eating significantly decreased over time, the prevalence of purging remained relatively constant. Since the response rates in the three surveys were only modest and the characteristics of cohorts may have differed, the observed decrease in the

prevalence could at least partially be due to non-comparability of populations. A general limitation of this study, which was conducted in undergraduates of a prestigious university, was the lack of generalizability of findings to a general student population.

In two further studies in student populations, which were conducted in 1991 and 1990, the prevalence of bulimia nervosa in women was estimated at 2.0% and 1.3%, respectively.[84,79] The prevalence estimate of 2.0% is likely unrepresentative of the general U.S. student population, since this study predominantly considered white students.[84] In contrast, the study by Pemberton et al (1996) included students of different ethnicity and both genders.[79] The authors found a higher prevalence in white (1.5%) than non-white students (0.4%), which might at least partially explain the different findings of these two studies conducted around the same time.

Pemberton et al also reported a higher prevalence in women (1.3%) than in men (0.2%). In an earlier cross-sectional study of freshman college students, which applied the DSM-III-R criteria and which had an excellent response rate of 97%, the prevalence was 2.2% in females and 0.3% in males.[99] Since the authors used both the DSM-III and the DSM-III-R criteria, the impact of different diagnostic standards could be assessed. The point prevalence of bulimia nervosa was found to be lower with the DSM-III-R than the DSM-III criteria in females (2.2% versus 4.3%), but not in males (0.3% versus 0.1%), a phenomenon that could be due to the omission of the criterion of "feeling depressed and self-deprecatory after binging" in the DSM-III-R, as this symptom has been found less frequently in men with bulimia nervosa than women.

A relatively high DSM-III-R-based prevalence rate of 5.1% in female and 0.4% in male students was reported in a survey conducted in 1992 by Heatherton et al (1995) at a prestigious U.S. university.[83] The authors found that the prevalence had decreased from 7.2% in women and 1.1% in men in a 1982 survey. However, results do not support the conclusion of a general reduction in the prevalence of bulimia nervosa, since student populations differed in terms of ethnic composition and average body weight (the 1992 sample was more ethnically diverse and heavier), and—as suggested by the author—

participants might have been more reluctant to report eating disorder symptoms in 1992 than in 1982 due to an increased stigmatization of eating disorders in the 1990s.

Striegel-Moore et al (1989) also reported a comparatively high prevalence of 3.8% in female university freshmen, while only 0.2% of the male freshmen were found to be bulimic.[108] Since the revised diagnostic criteria had not been published at the time this study was implemented, the frequency criterion of the DSM-III-R had not been included in the survey and the prevalence had to be approximated based on the available data, i.e., a minimum of 3 rather than 2 binge eating episodes per week. Results are therefore conservative and might underestimate the DSM-III-R-based prevalence in this student population. It should be noted that neither the results of this study nor ones reported by Heatherton et al could be generalized to the U.S. student population, as both were conducted in highly competitive universities (Yale and Harvard). Based on these two surveys it could be hypothesized that high-achieving individuals may be particularly at risk of developing bulimia nervosa, potentially due to their perfectionism, a risk factor of the disorder.[5]

Based on two surveys approximately 6 months apart, Drewnowski et al (1988) reported DSM-III-R-based prevalence rates of 2.9% and 3.3% at baseline and follow-up, respectively, in female college students.[111] In another study, the same researcher found a much lower DSM-III-R-based prevalence of 1.0% and 0.2% among female and male students, respectively.[112] This difference in results is likely due the fact that the former study was based on anonymous mail questionnaires, while the latter one used telephone interviews, which are more prone to respondents not disclosing their eating disorder symptoms. Results of both studies are subject to a very low response rate (42%–64%) and therefore cannot be considered representative of the U.S. student population.

Mintz and Betz (1988) performed a study in female undergraduates who were neither anorexic nor obese.[116] Based on self-reported symptoms of participants, the prevalence was estimated at 3.1%, with 85% of the cases being in the normal weight category, 5%

being underweight, and 10% overweight.[41] This result supports the hypothesis that physicians might not diagnose many cases of bulimia nervosa, since body weight of those with bulimia nervosa is not indicative of an eating disorder.

In the first study to apply the DSM-III-R criteria in a student population, only 0.7% of women and 0.1% of men were found to suffer from bulimia nervosa, even though bulimic symptoms were relatively common: 10.1% and 15.0% of the female and male students, respectively, binged at least twice per week.[122] The main strength of this study was the correction of prevalence estimates for false-positive cases, which likely contributed to the comparatively low prevalence rates.

Only two studies applied the DSM-III-R criteria in non-student populations. Bruce and Agras (1992) conducted a telephone survey of females randomly selected from the community and estimated the prevalence of bulimia nervosa based on the DSM-III-R criteria, excluding purging behavior.[92] While 1.8% of the participants were found to suffer from bulimia nervosa, 3.8% met all the criteria apart from twice-weekly binging. Study results should be interpreted with caution, since the response rate was very low (62%) and selection bias cannot be ruled out (individuals without telephones could not be canvassed).

In an earlier study, which applied a 2-stage case identification process and which was conducted in a sample of psychiatric emergency service patients, Johnson and Hillard (1990) found prevalence rates of 3.0% and 2.6% in women and men, respectively.[102] These results cannot be considered representative for a general patient population, as young adults and individuals with a lower socioeconomic status were likely overrepresented in the emergency room setting. Furthermore, people seeking healthcare are potentially at a higher risk of eating disorders than the general community.

[41] There were too few underweight and overweight subjects to reliably estimate the prevalence for these two categories.

DSM-III-based prevalence estimates

While only very limited evidence exists regarding the DSM-III-R-based prevalence of bulimia nervosa in non-students, more research has been generated in general population studies that applied the DSM-III criteria. However, due to differences in the methods of case identification as well as in the characteristics of participants, prevalence estimates vary widely between studies, from 0.4% to over 10%.

Based on interviews of adults in Florida, Warheit et al (1993) reported an average prevalence of 0.4%.[91] Prevalence was higher in blacks than in whites (0.6% and 0.3%, respectively), and highest in the subgroup of black males (1.3%), a result that had not been reported previously. The authors hypothesize that in previous studies, which focused on student or patient samples, black men might have been underrepresented, since their access to college and healthcare is often restricted.

Conversely, Rand and Kuldau (1992) found no significant differences in bulimia nervosa prevalence between black and white adults in Florida assessed by a structured interview approach.[95] The average DSM-III-based prevalence was 1.0%, which was slightly higher than that reported by Warheit et al.[91] Among young women (age 18–30 years) the prevalence was 4.1%, with no significant differences between students (5.5%) and same-aged non-students (3.1%).

In an earlier study by the same authors, which was the first to use a structured interview approach in a general population sample, the average prevalence was only 0.4% (0.7% in women and 0.0% in men).[128] This relatively low rate could be due to bias in the sample selection process, such as the exclusion of non-normal weight adults.

Among the first general population-based studies were those by Pope et al (1987, 1984), who assessed two different samples. In their survey of bingo tournament players, the authors reported a very high prevalence of 17.2% and 13.4% in lower and upper income respondents, respectively.[121] Even though results were limited due to the small number of respondents and a non-representative sample of the population, an important finding was

the inverse relationship between bulimia and income, an effect that could not be entirely attributed to age differences between the income groups. The authors do not provide an explanation for the much higher prevalence estimate compared to other DSM-III-based studies, but it can by hypothesized that bingo players may be at a higher risk for addictive behaviors, including eating disorders, and that the financial compensation of respondents ($1) may have biased results.

In another study by the same author, which was conducted in female shoppers, an average prevalence of 4.7% was reported, with the highest rate among those 13 to 20 years of age (11.4%).[134] Since this study applied the same questionnaire as that in the bingo tournament players and also offered a $1 compensation to participants, it is likely that either the survey instrument or the payment may have lead to the more frequent reporting of eating disorder symptoms than in other population-based studies.

Compared to studies in general population samples, generally higher DSM-III-based prevalence estimates have been reported in the clinical setting. In a survey of family practice attendees, Martin and Wollitzer (1988) found that 8.3% of respondents purged at least once weekly, defined as either vomiting, laxative use or fasting, and 3.7% met the DSM-III criteria for bulimia nervosa.[115] Due to the very low response rate of 52%, the prevalence in this population may have been underestimated, if eating disordered individuals were less likely to participate. On the other hand, findings may overestimate the prevalence in the general population, since outpatient clinic attendees could be at higher risk for eating disorders.

Another study, also conducted in a family practice population, reported that over 10.9% of the study participants appeared to be bulimic.[135] However, the DSM-III-based prevalence was estimated based on a modified version of the EAT questionnaire, which assessed the frequency of a behavior in a qualitative rather than quantitative manner (six response choices from ‘never’ to ‘always’), and results are therefore not comparable with those of Martin and Wollitzer.

In addition to evidence on the DSM-III-based prevalence in the general population, numerous studies have been conducted in students, most of which were based on self-reported questionnaires. Since different survey instruments were applied, results cannot be directly compared. However, more recent studies have used primarily validated instruments, which might have resulted in more reliable estimates of the prevalence of bulimia nervosa.

Based on a small sample of 150 female freshmen students in Illinois, Jones (1989) reported a DSM-III-based prevalence of 4%,[104] which is slightly higher than the estimate of 2.1% by Kurtzman et al (1989), who conducted a survey of female students in Los Angeles. The difference in findings might be due to the inclusion of a wider range of students in the latter study.[107] In addition, Kurtzman et al reported that prevalence rates varied between student groups: 0.0% of dance students, 0.8% of athletes, 1.9% of attendees of a women's health service, 2.5% of sorority members, 2.8% of primary care clinic attendees, and 3.3% of psychology class participants. Even though the small number of students per group and high rates of non-response in some groups limit generalization of these results, findings nevertheless indicate that certain types of students might be at a higher risk of developing bulimia nervosa.

The findings in student samples in Illinois and Los Angeles are corroborated by an earlier study in Missouri, conducted among female college students attending introductory psychology classes, which found prevalence rates of between 2.0% and 3.8% in three surveyed student groups.[123]

Similar results were reported by Katzman et al (1984), who attempted to overcome the limitations of previous studies by operationalizing some of the DSM-III criteria, e.g., "large amount of food" was quantified as more than 1,200 calories, thereby providing a less biased and likely more conservative estimate of the prevalence. Based on this approach, the prevalence was estimated at 3.9% in female college students.[133]

With the aim of evaluating potential risk factors for bulimia nervosa, Lachenmayer and Muni-Brander surveyed two high school populations, which differed in socioeconomic class and the proportion of minority students.[114] Even though most students were below the age of 18 years, the study has been included in this review, since it was the first to assess these risk factors. Prevalence rates were found to be significantly higher in females than males, while—contrary to the authors' expectations—socioeconomic differences were small (prevalence was 7.6% versus 5.2% in the lower and higher socioeconomic classes, respectively) and the frequency of bulimia nervosa was very similar in white, black, and Hispanic students.

Compared with first-year university students, similar rates of eating disorders and preoccupation with food and weight have been reported in adolescents in a preparatory boarding school. Based on the modified DSM-III criteria with at least weekly binging episodes, the prevalence was found to be 4.0% in female and 0.8% in male adolescents attending this prestigious private secondary school.[120]

A much higher prevalence of 10.2% was reported in female graduate students at a highly competitive university, even though the modified and more restrictive DSM-III criteria with a minimum of weekly binging were applied.[124] These results, which indicate that high-achieving graduate students may be at particular risk for eating disorders, are in accordance with the findings of more recent studies in student samples of prestigious universities.

The feasibility of comparing prevalence rates over time has been limited due to differences in study populations or methodologies applied. The first researchers to perform a time trend analysis were Pyle et al (1991, 1986, 1983), who conducted three cross-sectional surveys in similar student populations, while applying each time nearly the same self-reported questionnaire. Based on the results of the two most recent studies, the authors concluded that the prevalence among females might be declining, as the percentage of students with a lifetime history of bulimia nervosa was estimated at 3.2% in 1983, and 2.2% in 1986, while the point prevalence rates were similar.[99]

According to the DSM-III criteria, the point prevalence estimates were 4.1% and 2.2% in 1980 and 1983, respectively.[127;138] If the modified criteria with at least weekly binging and purging behavior were applied, rates were found to be much lower: 0.6% and 0.7%, respectively. It should be noted that the initial survey in 1980 did not include the diagnostic criterion C, i.e., "awareness that the eating pattern is abnormal and fear of not being able to stop eating voluntarily", which might explain the comparatively high prevalence estimate of 4.1%.

While according to the above-mentioned studies the DSM-III-based prevalence can be estimated at about 2% to 4% in a general female student population, much higher rates were reported in the early 1980s. For example, among college freshmen and seniors in New England, the prevalence was estimated at 8.0% in women and 0.7% in men.[129] When the additional requirements of at least weekly binging and a minimum of 1,000 calories per binge were considered, respective prevalence estimates dropped to 4.0% in women and 0.4% in men, rates that are still higher than those reported in later studies also applying the modified DSM-III criteria.

Gray and Ford (1985) reported a prevalence of 13% and 4% in female and male students attending a private university, respectively.[130] The authors speculate that this relatively high rate could have been due to the wording of the non-validated questionnaire. In addition, the low response rate (54%) could have contributed to a positive selection bias, if respondents were more likely to suffer from an eating disorder than non-respondents.

Another study in undergraduate females, which was the first to employ a 2-stage case identification procedure, also reported a fairly high prevalence of 6% to11%.[132] This range was derived from two different sets of criteria for the diagnosis of bulimia nervosa, selected in the absence of defined cut-off points for the questionnaire and the interview. In addition, this study found ethnic differences with about 14% of Caucasian female students being probably bulimic compared to only 2.7% of the Asian students.

The first study, which was published for a college population, also reported a fairly high prevalence of 9% in female freshman students.[139] However, these results were based on a very small sample of 100 women and are therefore likely unrepresentative.

While most studies relied on young student populations, Halmi et al (1981) surveyed attendees of a summer university session, which also attracted non-students (e.g., housewives).[140] The authors found a 13% prevalence of bulimia nervosa according to the DSM-III criteria, with higher rates in women than men (19.0% and 5.0%, respectively). However, this population cannot be considered representative, as certain socioeconomic groups are more likely to attend these programs.

While the above-mentioned prevalence estimates were derived in surveys of students, a case-record approach was applied in the first prevalence study, published in 1980. The authors found a rate of diagnosed bulimia nervosa of 5.3% and 1.0% in female and male attendees of a university outpatient psychiatric clinic, respectively, thereby highlighting the impact of the disorder on university healthcare services.[141] While the prevalence rate can be expected to be higher in the psychiatric setting, the inclusion of only diagnosed cases has likely resulted in an underestimate of the true prevalence in the general student population. Results are therefore not comparable with those obtained in surveys of student populations.

Based on the evidence generated in various studies in the U.S. since the recognition of bulimia nervosa as a distinct disorder, the following conclusions can be drawn:

- The DSM-IV-based prevalence is about 1% in young women; evidence in men is scant.
- The DSM-III-R-based prevalence is estimated at 1% to 5% in women and less than 0.5% in men, with evidence mainly being derived from student populations.
- Estimates of the DSM-III-based prevalence vary significantly from less than 1% to more than 10% in women and from 0% to about 4% in men, with variability of results likely due to differences in population characteristics (e.g., age, students

versus non-students, and ethnicity), methods of case identification, wording and validation of questionnaires, and study setting.

- The prevalence has been found to be higher in females than in males.
- Limited evidence supports a higher prevalence in whites than in blacks; however, since contradictory findings have been reported, additional research is warranted.
- Evidence from well-designed, 2-stage epidemiological studies in representative, general U.S. population samples is currently lacking.

2.3.1.2 Europe

In addition to the U.S., prevalence estimates have been published for many European countries. The available evidence is summarized below by country in alphabetical order.

i) Austria

In Austria, Kinzl et al (1998 and 1999) used telephone interviews to assess the prevalence of DSM-IV-based bulimia nervosa in two population-based random samples of women and men.[71-74] The overall rate was much lower in men than in women (0.5% vs 1.5%, respectively), although men were found to have a higher risk of subthreshold eating disorders (e.g., EDNOS). Significant differences between age groups were evident in both sexes, with the highest prevalence in women younger than 25 years (6.2%), and among men aged 25 to 34 years (1.7%). No significant differences between weight groups were found in either sample, indicating that bulimia nervosa could be present in underweight, normal weight, and obese individuals.

Since neither survey included a clinical evaluation of potential cases, prevalence estimates are subject to the limitations of respondents' self-reporting of symptoms as well as the time restrictions of telephone interviews. Misclassifications of eating disorder cases cannot therefore be excluded. However, results are similar to DSM-IV-based prevalence rates reported by researchers in other industrialized countries, which indirectly supports the findings by Kinzl et al.

The expectation that bulimia nervosa prevalence in Austria should be comparable to that in other Western countries was incorporated in a study by Rathner and Rainer (1997), who compensated for the lack of prevalence and incidence data for Austria by using estimates from other industrialized countries.[142] This study assessed the potential undertreatment of bulimia nervosa in Austria by comparing the number of patients treated in outpatient and inpatient facilities in 1994 with the estimated prevalence and incidence of the disorder. This resulted in an estimated 6,571 prevalent cases, based on the population of 20- to 30-year-old women, and an additional 828 incident cases, based on the group of 10- to 64-year-old women. In contrast, only 346 treated patients were reported by facilities participating in the survey. Since only 23% of the outpatient and inpatient institutions originally contacted agreed to complete the questionnaire, the number of treated patients may have been underestimated. The authors concluded that there were insufficient treatment facilities for bulimia nervosa in Austria in 1994, as the difference between the estimated number of prevalent and treated cases was unlikely to be entirely explained by the delay of bulimic individuals to seek treatment.

ii) Denmark

Pagsberg and Wang (1994) assessed the prevalence of bulimia nervosa in Bornholm County, Denmark, based on a comprehensive review of all outpatient and inpatient records as well as physician interviews of probable cases.[87] It should be noted that this approach provided an estimate for the prevalence in the clinical setting; i.e., diagnosed cases. The ICD-9 prevalence was found to have remained relatively stable during the period from 1970 to 1983, but increased from 1984 to 1989, with a peak rate of 89 cases per 100,000 women 10 to 24 years of age in 1989. This result could have been due to heightened awareness and more frequent reporting of cases by physicians rather than a true increase in the prevalence.

To facilitate comparison with results from a prior study by Jørgensen (1992), which was based on the DSM-III-R criteria, Pagsberg and Wang matched their prevalence estimates to the time period and case detection methods applied in the prior study.[94] For females 10 to 24 years of age and for the period from 1977 to 1986 Pagsberg and Wang found a

higher prevalence (0.032% if matched by case detection method, 0.054% if all case detection methods are considered) than that reported by Jørgensen (0.016%).[94]

However, Jørgensen estimated the prevalence of bulimia nervosa based on the observed incidence and an assumed mean duration of the disorder of 3.5 years (prevalence = incidence x mean duration), while Pagsberg and Wang assessed cases on a yearly basis. This might have contributed to the lower prevalence estimate reported by Jørgensen, since according to the study by Pagsberg and Wang the duration of bulimia nervosa is much longer than 3.5 years. The main limitation of both studies is their restriction to persons seeking help in the healthcare system; therefore, results represent an underestimate of the prevalence in the general population. In addition, recall bias of the physician might have affected results.

iii) England

In England, research has primarily focused on populations that were likely at a higher risk of demonstrating eating disorder symptoms (e.g., patients in the outpatient setting). Contrary to U.S. studies, most of the evidence in England has been generated in studies that applied a 2-stage case identification process.

According to a survey conducted in 1997 in female general practice attendees in Cambridge, approximately 1.5% fulfilled the DSM-III-R criteria for bulimia nervosa.[96] Since this study had a high response rate (97%) and diagnoses were confirmed by clinical interviews, results are likely representative for the population of female general practice attendees aged 16 to 35 years, but are not generalizable to the overall population. An additional finding was that half of the cases had not been diagnosed by the general practitioners prior to the study.

In an earlier survey of 16- to 35-year-old attendees of general practitioners in London, which also applied a 2-stage case identification process, similar prevalence rates of 1.1% in women and 0.5% in men were reported.[105;106] However, this study applied Russell's

criteria for bulimia nervosa and results are therefore not directly comparable with those derived from the DSM-III-R.

Meadows et al (1986) were the first to apply a 2-stage approach in a general practice setting in the U.K., conducting a survey of females aged 18 to 22 years in Leicestershire.[125] While 6.8% of the respondents had an EAT score of at least 30, only one (0.2%) was identified by clinical interview as meeting the DSM-III criteria for bulimia nervosa. It should be noted that these results are likely biased, as the participation rate was 70% and only 54% of the probable cases could be interviewed. Since the studies in London, Cambridge, and Leicestershire applied different diagnostic criteria, and population characteristics varied as well, no time trend analysis could be performed.

The potential impact of using DSM-III or Russell's diagnostic criteria on the prevalence of bulimia nervosa has been evaluated in a 2-stage survey of technical college students.[117] The authors found a prevalence of 1.6% irrespective of the criteria applied. Based on this result, they concluded that the much lower prevalence in students in England than in the U.S. was unlikely to be due to differences in the diagnostic criteria applied: Russell's criteria in the early studies in the U.K. versus the DSM-III criteria in surveys in the U.S.

In women attending a family planning clinic, prevalence rates based on Russell's criteria of 1.9% and 1.8% were reported in two replicate studies, conducted in 1982 and 1986.[118;136] Since attendees who reported use of laxatives for unknown reason, but no vomiting, were not considered as cases, results likely represent an underestimate of the prevalence. Findings are further limited by the unrepresentative study population and the reliance on patients' self-reported eating behaviors.

The authors of the two last-mentioned studies also conducted a survey in women identified via a popular women's magazine in 1980.[137] Of the bulimia nervosa cases according to Russell's criteria, only 30% were found to have ever discussed their eating difficulties with a physician and only 2.5% were receiving medical treatment for their disorder. This finding indicates that prevalence estimates derived from clinical records

are prone to underestimate the occurrence of bulimia nervosa in the general population, as most bulimic individuals either never seek outpatient or inpatient care or they are not diagnosed or treated.

In addition to the magazine survey, the authors surveyed women who self-reported that they might suffer from bulimia nervosa after watching a television documentary on this disorder.[143] Respondents with probable bulimia nervosa were found to demonstrate severe eating disturbances; for example, 33% had daily eating binges, 47% vomited daily, and 42% used laxatives. However, only a third had been referred for psychiatric treatment. Even though these study samples are not representative for the general population and results are subject to self-report biases, findings nevertheless demonstrate the undertreatment of bulimia nervosa in England in the early 1980s.

iv) France

A study in France that assessed the prevalence of bulimia nervosa in three different female populations (non-patients identified from the community and patients seeking help with weight control in either private practices or a hospital outpatient clinic), found significantly higher rates in the weight-control groups than in the community (0.2% versus 4.1% and 4.7%).[80] While for the hospital group the prevalence was derived from clinical diagnoses, probable cases in the other two groups were identified via respondents' self-reported binge eating and use of compensatory behaviors. Since the researchers did not apply the DSM criteria, comparisons with other studies are not feasible. Nevertheless, findings demonstrate that people who seek help to control their weight may be at higher risk for bulimia nervosa.

In a survey of female medical students, the DSM-III-R-based prevalence was estimated at nearly 8% based on clinical interviews of those who volunteered to participate.[88] However, these results cannot be generalized, as the sample was very small and unrepresentative of a general student population.

v) Germany

According to the "Bundeszentrale für gesundheitliche Aufklärung", approximately 600,000 15- to 35-year-old women in Germany suffer from bulimia nervosa.[144] However, no prevalence estimate could be derived from this report, as no further information regarding the data sources and diagnostic criteria was provided.

The most recent evidence stems from a 3-year prospective cohort study conducted among young women in Dresden. Based on psychological interviews, the authors found DSM-IV-based prevalence rates of 0.5% and 0.7% at baseline and follow-up, respectively.[37] Due to the low response rate of only 59%, results likely underestimate the true prevalence of bulimia nervosa in young women in Dresden, as it can be assumed that bulimic individuals might have been reluctant to participate. By linking the results from the interviews with data from health insurance claims, the researches found that only 20% of the women with an eating disorder (either anorexia nervosa or bulimia nervosa), who consulted a primary care physician during the study period, were diagnosed.

In another study in gynecologist practices, in which the DSM-IV-based prevalence was simulated based on patients' self-reported symptoms, 1.9% of the participants were found to meet the criteria for bulimia nervosa.[58] The higher rate in this survey compared to the one in Dresden is likely explained by the expectation that patients who consult a gynecologist (e.g., for menstrual irregularities) are more likely to suffer from an eating disorder. In addition, the reliance on patients' self-reported eating behaviors without clinical validation of the diagnosis of bulimia nervosa could have resulted in an overestimation of the prevalence.

Based on a survey of students in 1993 to 1995, Thiels and Garthe (2000) reported prevalence rates of 0.6% and 5.3% according to DSM-IV and DSM-III criteria, respectively.[69] The authors compared these findings with those from another study in dental practice patients and found no significant differences in the prevalence of probable bulimia nervosa. However, results are likely not representative for general student

populations, as nearly 40% of the respondents had participated in eating disorder seminars. An additional limitation was the lack of a clinical validation of potential cases.

With the aim of assessing differences in the prevalence of bulimia nervosa over time and between West and East Germany, Westenhöfer (2001) conducted two surveys in representative samples of adult men and women in 1990 and 1997.[65] However, only the 1997 survey included both West and East Germany, while the 1990 survey was limited to West Germany. Results of this study are not directly comparable with those reported by other researchers, since a diagnosis of bulimia nervosa was established by at least two binging episodes and one compensating behavior per week, rather than the strict DSM criteria. The authors found that the prevalence of bulimia nervosa decreased in West Germany between 1990 and 1997 from 1.5% to 0.7% in women and from 2.4% to 1.5% in men. In 1997, rates were higher in men than in women in West Germany and in men in West Germany than men in East Germany (0.7%), while they were comparable in women in West and East Germany (0.7%). However, bodybuilding was considered as a method of compensating behavior and observed rates in men therefore likely overestimate the prevalence of bulimia nervosa. This is supported by the fact that in 1997 rates of purging type bulimia nervosa were lower in men than in women and in West and East Germany (0.8% versus 1.0% in West Germany and 0.4% versus 1.3% in East Germany). The main limitations of this study were the lack of applying the DSM diagnostic criteria and the reliance on respondents' self-reported symptoms, which likely led to an overestimation of the true prevalence in these population samples.

vi) Greece

To assess the influence of the cultural environment on the prevalence of bulimia nervosa, Fichter et al (2005) conducted two surveys in 1998, one in Greek adolescents in Greece and one in migrant Greek adolescents attending a Greek school in Germany. The overall DSM-IV-based prevalence was found to be similar in both groups (0.93% in Germany versus 0.95% in Greece), with higher rates among girls than in boys.[36] Since in a similar survey in 1980, Greek adolescents in Greece had demonstrated higher bulimic symptom scores than those living in Germany, while in 1998 bulimic behaviors were decreased in

Greek adolescents living in Greece, Fichter et al concluded that differences between the two locations had diminished over time. Even though the prevalence rates in 1998 were similar to those reported for other Western countries, it should be noted that the majority of participants were adolescents and results can therefore not be generalized to other age groups.

vii) Hungary & Eastern Europe

For Hungary, evidence on the prevalence of bulimia nervosa has been generated in four studies; however, all except one focused exclusively on student populations. The two most recent studies, which applied the DSM-IV criteria, came to slightly different conclusions. While according to Szumska et al (2005) the prevalence among 15- to 24-year-old women was only 0.4%, with no significant differences between students and non-students (0.47% vs 0.34%, respectively), Tölgyes and Nemessury (2004) reported a prevalence of 3.6% and 0.4% in female and male students, respectively.[40;41] Estimates of both studies were derived from respondents' self-reported symptoms, although screening questionnaires differed. The study by Szumska et al was conducted in a nationally representative sample of young women, while the one by Tölgyes and Nemessury was limited to students attending selected secondary schools and colleges in two major cities in Hungary (Budapest and Pécs), which might at least partially explain the differences in findings.

The study by Tölgyes and Nemessury also applied a 2-stage process for case identification (i.e., interviews of at-risk respondents), according to which the revised prevalence estimates were 0.6% in women and 0.0% in men. Even though this result seems to concur with the one reported by Szumska et al, findings were limited by a low participation rate in the interviews, leaving the authors to hypothesize that the true prevalence in this student study population was much higher.

In an earlier study, Rathner et al (1995) assessed the prevalence of bulimia nervosa in medical student populations in two Eastern European countries before the political changes in 1989, the German Democratic Republic (GDR) and Hungary, as well as in

one Western democracy, Austria.[85;145] Cases were identified based on self-reported questionnaires and by applying the DSM-III-R criteria. Prevalence rates were found to be low: 0.6%, 1.0%, and 0.0% among female students in Austria, Hungary and the GDR, respectively, and 0.0% among male students in all three countries. These findings seem to support those of Szmuska et al.[40] However, the study by Rathner et al included only medical students and results are therefore not generalizable. Since prevalence rates were generally low and the samples small, observed numerical differences between countries could have occurred by chance and no comparative conclusions can be drawn.

In another survey of college students, the DSM-III-R-based prevalence was estimated at 1.3% in women and 0.8% in men, respectively.[100] Even though this study applied a 2-stage approach, findings are subject to a very low response rate to the survey as well as a low participation rate in the clinical interview, and are therefore likely subject to bias.

Based on a review of English and non-English publications on the epidemiology of eating disorders in Eastern European countries before and after the political and social changes, Rathner et al (2001) concluded that eating disorders are not exclusively a characteristic of Western societies.[146] They hypothesized that globalization and the impact of mass media may have contributed to the existence of eating disorders in Eastern Europe.

viii) Ireland

Healy et al (1985) conducted a survey of college and university students in Dublin, and found prevalence rates of 2.7% and 0.0% in females and males, respectively, based on the modified DSM-III criteria with at least weekly binging episodes.[131] Since the response rate to the self-reported questionnaire was very high, results are unlikely to suffer from nonresponse bias. However, in the absence of clinical interviews to verify potential cases, results may overestimate the prevalence of bulimia nervosa in this student population.

ix) Italy

In Italy, several studies have been conducted to assess the prevalence of bulimia nervosa, the majority of which included only adolescents and young adults. The most recent evidence stems from a survey of female high school students in Naples, which found a DSM-IV-based prevalence of 0.8%.[35] This rate appears low compared to the results of two other studies, which reported DSM-IV-based prevalence rates of 1.8% in young women in Padova and 2.3% in high school students in Naples.[43;75] While all three studies included only females in an urban or suburban setting and cases were identified by a 2-stage process, the most recent one was based on a much smaller sample (fewer than 300 participants), therefore limiting comparability of results.

A 2-stage case identification process was applied in another study of female college students in the city of Padua.[77] Since the authors did not report the prevalence rate, it was estimated at 0.8% based on the information provided: three cases who fulfilled the DSM-IV criteria among 395 study participants.

Based on these four studies in female students and young adults, it can be concluded that the prevalence of DSM-IV-based bulimia nervosa is about 0.8% to 1.8% in Italy. Even though more recently published studies seem to indicate a decline in the prevalence to less than 1.0%, evidence is limited and conclusions regarding a time trend are therefore not feasible.

In an earlier study, which applied a 2-stage approach and which was conducted in schoolgirls 11 to 20 years of age in a rural town in northern Italy, no case of bulimia nervosa was identified.[90] While these results could support the hypothesis of a lower prevalence of bulimia nervosa in rural areas than in larger cities, the finding could also be explained by the fact that most of the participants had not yet passed the age threshold for the development of bulimia. In addition, clinical interviews were done one year after the initial survey, and therefore probable cases could have already been in remission at the time of the interview.

The prevalence was also approximated in another survey of adolescents, in which a probable diagnosis of bulimia nervosa was determined by a BITE score of at least 20.[45;46] Based on this approach, 0.3% of the boys and 4.0% of the girls were bulimic. However, since this study did not include a clinical validation of cases, findings are subject to an over-reporting of disordered eating behaviors by respondents and are therefore likely biased.

With the aim of assessing the prevalence of psychiatric disorders among the offspring of immigrants, Carta et al (2002) conducted a study in two different population samples, Sardinian immigrants living in Paris and Sardinian residents.[51] The authors found a much higher ICD-10-based prevalence in the immigrant group than in those living in Sardinia (2.0% versus 0.4%).[42] Even though this result could have been due to a higher proportion of 18–24-year-olds in the immigrant sample, findings nevertheless indicate an increased vulnerability of young immigrants to develop an eating disorder.

x) Netherlands

Hoek et al (1991) reported a relatively low DSM-III-R-based prevalence of 0.02% for the general Dutch population during 1985 and 1986.[98] However, this rate was derived from the number of cases identified by GPs, and therefore the same limitations apply as for the Danish study by Pagsberg and Wang. Since many bulimic individuals never seek care or do not get diagnosed, the prevalence in the Dutch community can be assumed to be much higher.

The authors also found a higher 2-year prevalence in large cities of more than 100,000 inhabitants (0.08%) than in rural areas (0.026%) and urbanized areas of less than 100,000 inhabitants (0.026%). They hypothesize that this finding could support the so-called "drift hypothesis"; that is, people might develop bulimia at the age when they leave home and move to a city for work and further education, resulting in higher prevalence estimates in cities than rural areas.

[42] The study included also a population sample of Parisians, but no prevalence rates were provided for this group. Results were therefore not included in the study description.

xi) Norway

Augestad and Flanders (2002) performed a study in female students in Norway and found a DSM-IV-based prevalence of 5.1%, with a higher rate among those exercising at least 5 hours a week than those who engaged less frequently in physical activities (7.3% versus 4.2%).[50] However, the difference between the two groups was not statistically significant, precluding any conclusions regarding physical activity as a potential risk factor for bulimia nervosa. Since this study relied on students' self-reported symptoms, the comparatively high prevalence could be due to a lack of specificity of the survey instrument applied.

In an earlier study, the DSM-III-R-based prevalence was found to be 0.7% in the general female population, with the highest rate among those aged 18 to 29 years.[81] The main advantage of this study was the inclusion of a representative population sample, which likely resulted in a lower prevalence estimate compared to studies in at-risk groups. However, findings were based on self-reported symptoms and therefore should be interpreted with caution.

Another study by the same researcher, which was conducted in outpatient psychiatric patients, reported prevalence rates of 7.3% in women and 0.7% in men.[82] These results indicate that psychiatric patients might be at an increased risk of bulimia nervosa. However, since the researchers did not apply clearly defined diagnostic criteria, findings cannot be compared with evidence from other studies in the outpatient setting.

xii) Spain

The prevalence of bulimia nervosa has been assessed in several studies in Spain; however, all of them focused on high-risk populations, either students or general practice attendees. Based on a 2-stage case identification process and the DSM-IV criteria, the prevalence has been estimated at 0.8% in a sample of female adolescents (aged 12–21 years) in the northern region of Spain.[53;55] These results likely provide an underestimate of the prevalence in young women, since some of the study participants were below the usual age of onset of bulimia nervosa.

Similar results were found in a survey of adolescents in Malaga, according to which the DSM-IV-based prevalence rates were 0.6% and 0.2% in female and male students, respectively.[64] Contrary to the previously mentioned study, results were derived from students' self-reported eating behaviors and are therefore subject to response bias. The authors also conducted a similar survey of students' eating behaviors reported by their parents, which resulted in a prevalence of 0.0%, indicating that parents were not aware of the disordered eating behaviors of their children.

In a survey of students in Galicia, the DSM-IV-based prevalence was estimated at 2.9%, with gender-specific rates of 4.3% and 0.0% among women and men, respectively.[52] Since participants were on average 20 years of age and therefore much older than the ones in the two before-mentioned studies, results are not directly comparable. It should be noted that the applied survey instrument included dieting and consumption of low-caloric foods as compensatory behaviors, which likely resulted in an overestimation of the prevalence in women.

Based on interviews of female attendees of a primary healthcare center, Blesa et al (2003) reported a relatively high DSM-IV-based prevalence of 5.3%.[42] Since women who seek outpatient care may be at a higher risk of eating disorders, results cannot be generalized to the overall population. In addition, it is possible that respondents may have over-reported their eating problems in an attempt to receive treatment for their disorder.

xiii) Sweden

The most recent prevalence estimate for Sweden stems from a survey of a population-based random sample of young women (age 20–32 years), which found a DSM-IV-based prevalence of 1.3%.[59] While this result is comparable to those of population-based surveys in other countries, it is nevertheless limited by the reliance on respondents' self-reported symptoms and, according to the author, a relatively low positive predictive value of the screening questionnaire.

In addition, the prevalence was estimated in a case-record study conducted in 2 municipalities in Sweden, which included a review of all outpatient, inpatient, and school records. For the period from 1984 to 1985, the authors report a relatively low average DSM-III-based prevalence of 0.04%, highest among women 16 to 24 years of age (0.47%).[110] However, these results reflect the prevalence of clinical cases known to the healthcare system, but not the prevalence in the community, and findings are therefore subject to the same limitations as the studies by Hoek et al in the Netherlands and Pagsberg and Wang in Denmark. In addition, results may be biased, as potential cases may have been missed if the eating disorder diagnosis was not noted in the patients' record.

xiv) Turkey

Only one study providing evidence on the prevalence of bulimia nervosa in Turkey has been published to date. Kugu et al (2006) conducted a 2-stage survey in a random sample of students and reported DSM-IV-based prevalence rates of 1.6% in women and 0.0% in men.[34] Since cases were confirmed by a clinical interview and since the participation rate in the study was high, the observed prevalence is likely representative for this student population. However, the university was located in a rural area of the country and generalizability of findings to other student populations is therefore limited. Nevertheless, findings indicate that the prevalence of bulimia nervosa in Turkish students may be similar to that in Western countries.

According to Elal et al (2000), bulimia nervosa has only recently emerged as an eating disorder in Turkey.[147] The authors explain this finding by the Westernization of Turkey, which included an import of Western values relating to the role of food in the society. Furthermore, Elal et al note that bulimia nervosa might even be more of a concern in Turkey than in Western countries, since Turkish women may be in a conflict between traditional Turkish values regarding food and eating and Western ideas of controlled eating.

Based on the currently available evidence regarding the prevalence of bulimia nervosa in Europe, the following conclusions can be drawn:

- Estimates of the DSM-IV-based prevalence in the general population vary between 0.4% and 1.8% in women and between 0.0% and 0.5% in men.
- The prevalence is higher in the clinical setting than in the community; estimates of the DSM-IV-based prevalence in female outpatient practice attendees vary between 1.9% and 5.3%.
- The prevalence is generally higher in students than in the general population; however, estimates of the DSM-IV-based prevalence range from 0.6% to 5.1% and from 0.0% to 0.7% in female and male students, respectively.
- Case record reviews provide a minimum estimate of the prevalence, since only diagnosed cases can be accounted for; prevalence rates of between 0.02% and 0.09% have been reported.
- A large majority of bulimic individuals do not receive a diagnosis of bulimia nervosa from their physician.
- Bulimia nervosa is not restricted to Western nations; it has also been found in former Communist (Eastern European) and Muslim countries (Turkey).
- Since only few well-designed, population-based studies have been conducted, further evidence should be generated. In addition, studies applying a clinical validation of cases (i.e., 2-stage surveys) as well as studies with large sample sizes of men are scant.

2.3.1.3 Australia and New Zealand

i) Australia

In addition to the U.S. and Europe, evidence on the prevalence of bulimia nervosa has been generated in Australia and New Zealand. In a recent Australian study in 500 male general practice attendees, only one case of DSM-IV-defined bulimia nervosa was found.[38] The authors compared their results with those of an earlier study in women, and concluded that men were less likely to be weight-concerned, use self-induce vomiting, and seek treatment than women. However, findings may be biased and might underestimate the prevalence in the community, since some men refused to participate in

the screening and interview phases of the study and since the population sample was small.

In another community-based study, which applied a structured interview approach, the overall DSM-IV-based prevalence in men and women was estimated at 0.3%.[76] This result likely underestimates the prevalence in the general population, as people with an eating disorder are often reluctant to participate in a survey or are unwilling to disclose their disturbed eating habits. Since this study included a broad age range, results are not directly comparable with those derived from student or other high-risk samples.

Ben Tovim et al (1988) were among the first to assess the impact on prevalence estimation of using different DSM-based diagnostic criteria.[109] In a community-based survey of women in South Australia, the authors found a DSM-III-based prevalence of 12.7%, compared with 1.7% according to the DSM-III-R criteria with at least weekly binging. Since results were derived from self-administered questionnaires without a validation of the diagnosis by a clinician, the prevalence in the community might have been overestimated and results are therefore not directly comparable with those derived in studies applying a 2-stage case identification method.

ii) New Zealand

Altogether, three studies provided evidence on the prevalence of DSM-III-R-based bulimia nervosa in New Zealand. In a survey of female students in tertiary education, the prevalence was estimated at 2.2% based on self-reported symptoms.[103] In contrast, the Christchurch survey, which applied a 2-stage case identification process in a broad range of the female and male adult population (age 18–64 years), found a much lower prevalence of 0.5%.[101] Since the two studies differed with regard to the methods of case detection applied as well as population inclusion criteria, results are not directly comparable. It can be assumed that the true population prevalence is higher than reported in the Christchurch study, since interviews have been shown to be associated with an underreporting of disordered eating symptoms.

In analogy to the study in psychiatric hospitals in Norway reported above,[82] bulimia nervosa was found to be a prevalent condition among patients admitted to psychiatric hospital wards in Wellington, New Zealand, with about 8% of the inpatients meeting the DSM-III-R criteria.[97] However, only one patient had been admitted for the management of an eating disorder, reflecting the low referral rate and undertreatment of eating disorders New Zealand in the late 1980s.

In summary, the evidence on the prevalence of bulimia nervosa in Australia and New Zealand seems to corroborate findings from the U.S. and Europe, including the lack of well-designed studies in general population samples. No conclusions can be drawn regarding potential differences in the prevalence between Australia/New Zealand and Europe or the U.S., since the available evidence is too scant.

2.3.1.4 Other countries

While many studies have estimated the prevalence of bulimia nervosa in Western countries, less evidence is available for Latin America, Asia, and Africa. However, non-Western and developing countries have received more research attention in recent years and respective findings are summarized below on a regional basis.

i) Middle East and Africa

Morocco

In Morocco, the prevalence of bulimic symptoms has been assessed in two samples of students, one from a typical Moroccan secondary school and one from a French school.[60] The authors found a higher prevalence of bulimia nervosa (1.9%) in students of the French school than in those attending the Moroccan school (0.8%), but results for the former were limited by a very small sample size and no comparisons between student groups can therefore be drawn. Since the prevalence was estimated based on a cut-off point of 25 on the BITE questionnaire, which is higher than the threshold of 20 applied in some European surveys, findings are likely conservative. The main limitation of this study was the lack of application of the DSM criteria, due to which results are not directly comparable with those of Western countries.

Oman

In a study of a culturally diverse adult sample in Oman, the prevalence of bulimia nervosa was estimated at 1%, based on a cut-off point of 25 or more on the BULIT questionnaire.[49] This relatively low prevalence could be due to the fact that the population was on average much older and tended to be heavier (mean age of 38.7 ± 5.4 years and mean BMI of 27.4 ± 2.7) than the ones included in studies in Europe and the U.S. Compared to adults, teenagers, especially those of Omani origin, were found to have a higher propensity for bulimia, indicating that the prevalence of bulimia in adults might rise in the future.

Egypt

Nasser (1986) was probably the first to assess the impact of exposure to Western culture on bulimia nervosa prevalence. He conducted two 2-stage studies in Arab female student populations: one in 1981 to 1982 in London and one in 1982 to 1983 in Cairo, which was matched to the Arab students in London with regard to social class and marital status. While no case of bulimia nervosa was found in Cairo, 12% of the students in London met Russell's criteria.[126] Even though results are limited to young women, they nevertheless suggest that exposure to the Western culture could be a risk factor for the development of eating disorders. According to the author, eating disorders might become more prevalent in Arabic countries in the future due to socioeconomic changes and Westernization of the culture.

To test this hypothesis, Nasser (1994) conducted a follow-up 2-stage survey among secondary school girls in Cairo and found that 1.2% met Russell's criteria for bulimia nervosa.[148] This is likely an underestimate of the prevalence in the Egyptian population, since students were 15 to 16 years of age and therefore still at risk of developing bulimia nervosa later in life. Since the Arab students surveyed in the earlier studies were older and had passed the mean age of onset of bulimia nervosa (average age of 22 and 23 years in the studies in London and Cairo, respectively), results of the two studies are not directly comparable. Nevertheless, findings from Nasser (1994) demonstrate the

existence of bulimia nervosa in Arabic cultures, possibly due to increasing exposure to Western cultural values via an increasingly globalized mass media.

ii) Latin-America

The limited evidence available suggests that bulimia nervosa has a comparable prevalence in Latin America as in North America and Europe. Based on a survey of a national sample of the adult population, the prevalence of bulimia nervosa in Mexico according to the ICD-10 has been estimated at 0.3%, with a higher rate in women than in men (0.4% and 0.0%, respectively).[44] However, findings likely underestimate the true population prevalence, since the applied survey methodology, interviews in respondents' homes, may have led to response bias.

In high school attendees in Venezuela, the DSM-IV-based prevalence has been estimated at 1.6%.[47] This result was derived from a self-reported symptom checklist, which was developed by the investigators and completed by students, and is therefore not directly comparable with findings of other studies. Contrary to most other studies, the prevalence was the same in girls as in boys.

Abnormal eating behaviors have also been found in a community sample of young women in Porto Alegre, Brazil. Among respondents, 2.9% had a BITE symptom score of at least 20 and 1.4%, 8.5%, and 2.8% of women reported the use of laxatives, diuretics, and vomiting, respectively, to control their weight. [149]

iii) Asia

China

In a survey of more than 1,200 Chinese schoolgirls (age 12–19 years), the prevalence of DSM-IV-based bulimia nervosa was estimated at 0%.[56] However, results are not representative for the high-risk group of young females, since the majority of participants had not reached the average age of onset of bulimia nervosa. The fact that 3.9% of the girls reported binging at least weekly might be an indication that they were at risk for developing bulimia nervosa.

A prevalence of 0% was also reported in a study of university students in Hong Kong.[89] The authors acknowledge that this rate might underestimate the prevalence in general student populations, since respondents might have been embarrassed to disclose their eating disorder in the interview phase of this 2-stage survey.

In contrast to the study in Hong Kong, a 2-stage survey of college freshmen in two large cities in China found prevalence rates of 1.3% and 1.1% according to the DSM-III and DSM-III-R criteria, respectively, with a higher prevalence in females than in males.[93] Even though this result is comparable to findings of similar surveys in Western countries, the main difference was that purging-type bulimia nervosa as well as laxative misuse were rare, while most Chinese students seemed to engage in restrictive dieting and fasting for weight control. The authors hypothesize that social pressure regarding maintenance of body weight might contribute to the prevalence of non-purging bulimia nervosa in China.

India

Only very limited evidence exists regarding the prevalence of bulimia nervosa in India. One study of female students attending a private college reported a rate of 0.4%, which was based on a BITE cut-off of 20 points.[66] No case was identified in the interview phase of at-risk students. According to the authors, the relatively low prevalence of bulimic symptoms may be explained by the fact that personal relationships and being part of a family were more important than Western values for young women in India.

Japan

Based on interviews of primary care patients who were suspected to suffer from an eating disorder, Nakamura et al (2000) reported prevalence rates of 0.001% and 0.003% according the DSM-IV and DSM-III criteria, respectively.[68] Even in the high-risk group of 15- to 29-year-old patients, the prevalence was found to be much lower than those observed in clinical samples in Europe or the U.S. However, results likely provide an underestimate of the population prevalence in Japan, since the survey was restricted to persons seeking primary care in a metropolitan area, was based on clinical interviews

rather than anonymous responses of patients, and relied on the investigator's ability to identify suspected cases.

A very low prevalence was also reported in another study in the clinical setting, in which cases were identified via a survey sent to hospitals.[78] Based on physicians' responses, the prevalence was estimated at 0.01% in females aged 13 to 29 years, while it was approximately 0.002% in the total patient sample. Since these results reflect only diagnosed cases, they underestimate the general population prevalence. In addition, results may have been biased, as the response rate of hospital physicians was only 37%.

In a study of outpatient attendees at the Yamagata University hospital in the north of Japan, the DSM-III-R-based prevalence of bulimia nervosa was found to have increased during the period from 1978 to 1992, not only in terms of the absolute number of diagnosed cases (an increase from six cases during the period from 1978–1982 to 26 cases from 1988–1992), but also as a proportion of new outpatients (from 0.2% to 0.8%).[150] However, this finding could be due to better accessibility of treatments and the wider recognition of eating disorders in Japan rather than an increase in the prevalence and incidence of bulimia nervosa.

Contrary to studies in the hospital setting, a survey of young female workers found that about 1.5% were likely to suffer from bulimia nervosa, since they had an EAT-26 score of at least 20, which is lower than the cut-off point of 30 used in other studies to estimate the DSM-III-based prevalenc.[70] This result is corroborated by a study of female nursing school and junior college students, in which 2.9% of participants reported binge eating and self-induced vomiting or purging at least on a weekly basis.[113] Even though this survey did not assess all diagnostic criteria for bulimia nervosa, results nevertheless demonstrate that bulimic symptoms are prevalent among young Japanese women. Similar findings were reported in a study of high school students (average age 16 years), which estimated the DSM-III-R-based prevalence at 1.9% in females and 0.7% in males based on students' self-reported symptoms.[151]

The results from different studies in Japanese population samples reported above seem to indicate that bulimic behaviors are not uncommon in Japan. The low prevalence in the clinical setting is likely explained by the fact that bulimic individuals are often unwilling to disclose their disordered eating habits in interviews and are frequently not seeking professional help for their disorder. This might even be more of an issue in Japan than in Western countries, since greater social stigma adheres to mental disorders in Japan.[152]

South Korea

Only one study has so far attempted to estimate the prevalence of bulimia nervosa in South Korea, among college and high school females. According to the BULIT questionnaire, 4.6% of the college and 1.5% of the high school students were found to be bulimic.[48] However, this study did not apply the DSM criteria and a comparison with findings from other countries is therefore not feasible.

Tsai (2000) reviewed the evidence on eating disorders among Asian populations published between 1966 and 1999, and found in general a lower prevalence in Asian than in Western countries.[153] The author notes that numerous studies may have underestimated the true prevalence of bulimia nervosa, due to such factors as lack of knowledge of the disorder among medical professionals or sufferers not seeking help from traditional practitioners. In addition, most studies published to date focused on children and adolescents below the age of 18, which might have contributed to the low prevalence estimates, since girls and boys had not yet passed through the age at highest risk for the development of bulimia nervosa.[154] Nevertheless, recent evidence indicates that bulimia nervosa is not uncommon in Asian countries.

Based on currently available evidence from Latin American, African/Middle-Eastern, and Asian countries, the following conclusions can be drawn:

- Bulimia nervosa exists in Middle-Eastern and African countries, and it has been suggested that its prevalence may rise as a result of globalization and Westernization of the culture. However, results from well-designed population-

based studies applying the DSM criteria are currently lacking, precluding rigorous comparisons with findings from U.S. or Europe.

- Very limited evidence indicates that bulimic behaviors are prevalent in Latin American countries, but estimates of the DSM-based prevalence in adults are currently unavailable.
- Studies in Asia have come to divergent conclusions. While the prevalence has been found to be very low in the clinical setting as well as in adolescents, surveys in students and general population samples have found prevalence rates very similar to those of Western countries. Many studies, especially those in the clinical setting and those applying interview techniques, have likely underestimated the prevalence, since bulimic individuals often do not seek treatment or are unwilling to disclose their disordered eating behaviors.
- Well-designed studies in representative population samples are needed to reliably assess cross-cultural and cross-country differences in the prevalence of bulimia nervosa.

2.3.1.5 At-risk populations

Potential at-risk groups for the development of bulimia nervosa have been assessed in numerous studies, with the most frequently evaluated risk factors being age and gender, while less evidence has been generated for such factors as ethnicity, comorbidities, or specific occupations. Since the assessment of the prevalence of bulimia nervosa in specific at-risk groups was not the primary focus of this thesis, only selected recent evidence, not already described in previous chapters, is summarized below.

i) Age

Results of studies presented in Chapters 2.3.1.1 to 2.3.1.4 demonstrate that young individuals appear to be particularly at risk of bulimia nervosa, as higher prevalence rates have been reported in young adults than in older age groups. According to a review by Hoek et al (2003), the highest-risk group is 20- to 24-year-old women.[155] Results from studies in student populations cannot therefore be considered representative for the general population.

ii) Gender

The higher prevalence of bulimia nervosa in women than in men, which has been reported in several studies (Chapters 2.3.1.1–2.3.1.2), could be attributable to biological factors; e.g., a later onset of puberty in boys than girls, different effects of puberty on body shape, and a higher basal metabolic rate in men.[156] Another explanation could be that the prevalence in men has been underestimated, since men might be less likely to report disordered eating habits and seek treatment than women due to the stigma of bulimia nervosa being perceived as a disorder of women and homosexuals.[157] Furthermore, lack of knowledge by physicians that eating disorders also occur in men might have resulted in a diagnostic bias and therefore underreporting of male bulimic cases.

Current evidence indicates that the etiology of eating disorders is likely similar in men and women, since men with bulimia nervosa were found to express clinical similarities to women with eating disorders, while men with eating disorders differed from men without eating disorders with regard to comorbid psychiatric disorders and dissatisfaction with body image.[158;159]

Based on an extensive review of the literature, published between 1966 and 1990, Carlat et al (1992) reported that men accounted for 10% to 15% of all bulimic subjects.[156] Compared to women, men were found to have a later onset of the disorder (age 18–26 years versus 15–18 years in females), with a significant delay between age at onset and age at first treatment. This could be attributable to a reluctance of men to discuss eating disorder symptoms with healthcare professionals or due to physicians being less likely to investigate the existence of an eating disorder in men than in women.

The treatment delay was confirmed in a subsequent case study of 135 male patients with eating disorders, which found that treatment was on average initiated 8.4 years after age at onset.[160] However, results of this study might not be representative for the whole

population, as they were derived from a sample of men seeking primary or secondary care.

An additional finding of the case study was that male patients more frequently had a history of being overweight, and reported on average a higher desired body weight than women, which could indicate that men were less concerned about their weight. The hypothesis that men might in general be less troubled by their eating disorder than women is supported by other studies that reported a higher prevalence of prebulimic or subclinical eating disorders in men compared to women.[72;73]

Controversy exists regarding homosexuality and bisexuality as risk factors for men, with some researchers reporting a higher prevalence of homosexuality and bisexuality in men with bulimia nervosa than in the general population and in females with this eating disorder. [156;158;160-162] However, additional prospective observational studies are needed to assess the contribution of sexual orientation to the development of bulimia nervosa.

It can be concluded that the lower prevalence in men than in women might be partially attributable to diagnostic bias by physicians as well as reluctance of men to seek treatment.[157] Even though evidence regarding specific risk factors for the development of bulimia nervosa in men is limited, it appears that men might be less concerned about their weight, which could be a protective factor against the development of bulimia nervosa.

iii) Ethnicity

For many years bulimia nervosa has been considered a disorder of middle to upper-class Caucasian women, uncommon among ethnic minorities.[163] However, recent studies, including those reported in Chapters 2.3.1.1 to 2.3.1.4, indicate that bulimia nervosa is also prevalent in non-Western cultures as well as among some ethnic minority groups.

Based on a review of the literature published between 1982 and 2003, Makino et al (2004) concluded that eating disorders appear to be less common in non-Western countries than in Western ones, although the prevalence in non-Western countries seems

to be increasing.[2] Similar results were reported in an earlier review by Smith (1995), who found that bulimia nervosa existed in ethnic minority groups, but at a lower prevalence than in Caucasians.[163]

Most authors argue that the exposure to Western ideals and the internalization of Western standards regarding female attractiveness attributes could be predisposing factors for the development of bulimia nervosa in non-Caucasian and non-Western cultures.[1;2] The hypothesis that acculturation to a Western society may provoke a higher vulnerability to eating disorders is supported by studies in immigrants.[36;51] Reasons for an increased risk in immigrants are debatable and may include difficulties experienced in growing up with incompatible cultural values or acceptance of new norms and values, including standards of beauty.

Crago (1996) reviewed the literature on minority groups in the U.S. and reported that, compared to Caucasian girls and female adolescents, eating disorders were more common in Native Americans and equally common among Hispanics.[164] This finding is supported by a recent survey of female adolescents aged 11 to 20 years, according to which bulimic symptoms were as frequent in Hispanics as in non-Hispanics.[165]

Crago (1996) further reported that eating disorders were less common among Black and Asian than Caucasian women. Since the majority of the literature on bulimia nervosa identified in this review referred to children, generalization of findings to an adult population is limited.

To assess potential differences in the prevalence of bulimia nervosa between Blacks and Whites, Gray et al (1987) conducted a survey of Black undergraduate college students and compared the results with those from a study of similar methodology in Caucasian college students.[119;130] The prevalence was found to be significantly lower in the Black than the Caucasian population; only 3% and 2% of the female and male Black students, respectively, fulfilled the DSM-III criteria, compared to 13% and 4% of the Caucasian students. While the prevalence of binging was higher among Black students, purging

(e.g., vomiting or use of laxatives or diuretics) was less frequent than among Caucasian students. Gray et al concluded that the difference in the prevalence of bulimia nervosa between Black and Caucasian students might be attributable to cultural factors, as Black students were significantly less likely to experience food and weight control in their families or to consider themselves overweight.

These findings are supported by a study that assessed the nature of disordered eating behaviors in Black and White college students recruited from a university psychology department.[166] White students were found to express significantly greater disordered eating attitudes and behaviors than Black students, while Black students were more likely to be satisfied with their body shape, even though they were on average heavier than White students. The authors hypothesize that a greater acceptance of a range of body weights exists in the Black culture and that restrictive eating habits occur more frequently in those Black women who reject their Black identity and culture.

Contrary to Gray et al (1987), Striegel-Moore et al (2000) found in their community survey that Black women were not only significantly more likely than White women to engage in recurrent binge eating, but also in fasting, use of laxatives, or use of diuretics, with no difference regarding the frequency of vomiting.[167] The difference in the frequency of purging between the two studies could indicate an increase in bulimic behaviors in Black women in the 1990s. However, results are not directly comparable, since Striegel-Moore et al assessed only binge eating and weight control behaviors, but not all the diagnostic criteria of bulimia nervosa, preventing the determination of the prevalence rate of the disorder.

No study has so far been published on the prevalence of bulimia nervosa among Native Americans. In a small survey of 85 Chippewa women and girls, a high proportion of participants was found to engage in pathogenic purging techniques, such as vomiting (12%), use of laxatives (6%), and use of diuretics (6%), especially those with a higher body mass index.[168] Although results are limited, they nevertheless indicate that bulimic behaviors exist in Native Americans.

It can be concluded that bulimia nervosa affects not only Caucasians, but also ethnic minority groups and non-White populations. Existing studies are subject to methodological limitations, including the use of instruments that were only validated in Caucasians in Western cultures, bias in the detection and reporting of eating disorders especially in minority groups, and the focus on convenience samples.[2;169] Lower prevalence rates among minority groups than in Caucasians might reflect a limited access to healthcare, different treatment-seeking behaviors, or lack of diagnosis of the disorder by the physician, rather than real ethnic differences. Further research is therefore needed to assess risk factors and potential protective factors for the development of bulimia nervosa in ethnic minority groups and to evaluate differences in the prevalence.

iv) Athletes

Athletes have been suspected to be at risk for eating disorders, including bulimia nervosa, due to pressures to conform to weight and body shape ideals. The majority of studies published to date focused on eating disorders in general, while only limited evidence exists on the prevalence of bulimia nervosa in particular.

A recent meta-analysis of studies in female athletes published before 2000, found that elite athletes, especially those competing in sports emphasizing leanness, were at an increased risk of eating disorders compared with non-athletes.[170] In addition, the prevalence was lower in non-elite athletes than non-athletes, although this trend was not significant. The findings of this meta-analysis are corroborated by a literature review, which in addition assessed gender differences. Eating disorders were found to be more frequent among male athletes than male non-athletes, with men competing in sports with weight restrictions being at a higher risk.[171] By analogy to gender differences observed in general population samples, eating disorders were less common among male than female athletes.

For bulimia nervosa in particular, the most recent evidence stems from a 2-stage survey of the entire population of female and male elite athletes in Norway as well as a matched

control group of the general population (average age between 23 and 25 years).[172] The DSM-IV-based prevalence was found to be 6% in female athletes versus 3% in controls and 3% in male athletes versus 0% in controls, with higher rates among athletes competing in leanness-dependent and weight-bearing sports than in others.

These results are supported by two prior studies of Norwegian elite female athletes, one case-control and one non-controlled study, which also applied a 2-step case identification process. In the case-control study the DSM-III-R-based prevalence was estimated at 8.0% in females athletes versus 1.1% in controls.[173] The non-controlled study reported a rate of 7.0% in female athletes, with an increased risk among those competing in sports emphasizing leanness.[174] The authors note that questionnaires alone were of limited value with regard to the identification of eating disorder cases, since athletes tended to underreport pathological weight control methods.

In elite female long distance runners (mean age 29 years) in the UK, the prevalence of present or past bulimia nervosa was found to be low (1.1%) and generally comparable to estimates for the general population.[175] This indicates that only athletes competing in leanness-dependent and weight-dependent sports are likely at an increased risk of bulimia nervosa, but not those in sports requiring endurance.

A survey of 283 elite female adolescents and young women competing in 20 different sports in Spain (average age of 25 years) reported that 20.1% demonstrated bulimic behaviors.[176] Since the questionnaire applied in this study did not contain any measure of frequency or duration of disordered eating habits, results likely represent an overestimate of the prevalence of bulimia nervosa in this at-risk population. An additional finding of this study was that pressures from coaches as well as exposure of the body in public seemed to be risk factors for bulimia in sportswomen.

Contrary to the studies in elite athletes in Norway, a much lower DSM-IV-based prevalence has been found in female and male amateur student athletes in the U.S. (1.1% and 0.0%, respectively).[177] Differences in results may be partially explained by the

reliance on self-reported eating disorder symptoms, which could have led to a conservative prevalence estimate due to underreporting of disturbed eating behaviors by athletes. The investigators note that the collaboration with the National Collegiate Athletic Association might also have biased results, since athletes may have attempted to protect their respective school by not disclosing eating disorders. An additional explanation for the different findings in Norway and the U.S. could be that non-elite athletes might not be at an increased risk of bulimia nervosa.

In another survey of female college athletes in the U.S., the overall prevalence of bulimia nervosa was estimated at 2.3%, with slightly, but not significantly, higher rates in those athletes engaging in aesthetic sports (5.6%) than those in endurance and team or anaerobic sports (1.6% and 2.1%, respectively).[178] Since the prevalence was calculated based on the number of cases previously diagnosed by a physician, it can be assumed that results underestimate the prevalence in this population.

The prevalence of bulimia nervosa has also been assessed in amateur performers in Italy. No significant differences in the DSM-IV-based prevalence were found between non-elite ballet dancers (2.7%), female gymnasium users (0.0%) and female controls (3.2%), or between male non-competitive body builders (0%) and male controls (0%),[179] supporting the hypothesis that only elite athletes may be at an increased risk of bulimia nervosa. However, a low degree of competition might not protect young adults from disordered eating attitudes either, since the non-professional athletes demonstrated a similar prevalence of bulimia nervosa as controls. Since sample sizes in this study were quite small, generalization of results is limited.

In conclusion, current evidence seems to suggest that elite athletes engaging in sports emphasizing leanness or imposing a specific weight limit are more likely to develop bulimia nervosa than non-athletes and athletes competing in other sports. Further research is needed to determine whether non-elite athletes are at an increased or reduced risk of bulimia nervosa compared with non-athletes.

v) Fashion models

Since fashion models are under extreme pressure to be thin, they have been assumed to be at a high risk for the development of eating disorders. However, in a recent case-control study, Santonastaso et al (2002) found no case of current bulimia nervosa (defined as binge eating and compensatory behavior on at least 8 days during the past month) in a sample of female professional fashion models, while in the control group the prevalence was 2.4%.[180] The authors hypothesize that active fashion models might less likely practice dangerous eating behaviors since they need to preserve their attractiveness and professional efficiency.

vi) Military officers

Since the military imposes strict weight and fitness standards and restricts promotional opportunities if standards are not met, officers might be at risk of bulimia nervosa. In a survey of active duty women serving in the Army, Navy, Air Force, and Marines, a DSM-IV-based prevalence of 8.1% was found, with significantly higher rates among Marines (15.9%) compared to the other groups.[181] While results are limited due to a low response rate (about 34%) to the survey, they nevertheless indicate that female officers might be at a higher risk of developing bulimia nervosa.

The authors of the study in female officers also conducted a survey of active duty female Navy nurses, which found a DSM-III-R-based prevalence of 12.5%.[182] In addition, female reserve officers, who are subject to fitness and weight standards, have been reported to be at risk of eating disorders.[183]

The risk of bulimia nervosa appears to affect also active duty men; a survey of officers in hospitals, clinics, and ships at sea estimated a DSM-IV-based prevalence of 6.8%, with the highest rate among those aged 45 to 54 years (11%).[184] An additional finding of this study was that the use of inappropriate weight control measures, like vomiting, fasting, and use of laxatives and diuretics, increased before weigh-ins and fitness testing periods.

Major limitations of all these surveys of active duty and reserve officers are lack of a control group, low response rates to the surveys, and the reliance on self-reported symptoms, which has likely biased findings.

vii) Patients with diabetes mellitus

Diabetic patients could be at risk of bulimia nervosa, since they have to follow dietary restrictions, and use of insulin might lead to weight gain. A recent, extensive literature review of studies in adolescents and adults with type I diabetes mellitus, performed by Nash and Skinner (2005), concluded that existing evidence does not support an increased risk of bulimia nervosa in this population.[175] In contrast, a meta-analysis of case-control studies comparing female patients with type I diabetes mellitus with matched non-diabetic controls, reported a significantly higher prevalence (1.7%) in diabetics than controls (0.7%).[185] The difference in findings could be due to the fact that the meta-analysis included only studies likely to be comparable and being less subject to biases: i.e., those applying the DSM-IV or the DSM-III-R criteria and with diagnoses based on interviews. Due to insufficient samples sizes of the individual studies, the increased prevalence of bulimia nervosa was only detected after combining the eight studies in a meta-analytic approach. This might explain why Nash and Skinner did not find evidence for a higher risk in bulimic patients in their literature review.

The most recent evidence on type I diabetes mellitus stems from a longitudinal survey of patients in Oxford, UK, which found a DSM-IV-based prevalence of 0.0% and 5.6% in adolescents and young adults at baseline (age 11–25 years), respectively, while it was 3.8% and 2.7% at follow-up after 8 to12 years.[186] However, this study did not include a control group, so that a conclusion regarding an increased risk of bulimia nervosa in type 1 diabetics cannot be drawn.

While the above-mentioned studies focused on type 1 diabetes only, a large multi-center study in Germany assessed insulin-dependent and non-insulin-dependent diabetics (IDDM, NIDDM) and reported a higher DSM-IV-based prevalence of bulimia nervosa in IDDM than NIDDM patients (point prevalence 1.5% versus 0.3% and lifetime prevalence

3.2% versus 1.9%).[187] Since patients were recruited from diabetic centers rather than general practitioners, results may not be representative for the overall population of diabetics.

It can be conluded that further research is needed to determine whether patients with type 1 and type 2 diabetes mellitus are at an increased risk of bulimia nervosa. Available evidence is contradictory, which could be due to methodological differences between studies; e.g., self-reported symptoms versus clinical diagnoses and case studies versus case-control studies.

It is of interest that several studies undertaken to date found diabetic patients with eating disorders to often underdose insulin in an attempt to lose weight; it has therefore been suggested to include insulin omission as a specific type of purging behavior in a future revision of the DSM criteria.[12]

viii) Psychiatric comorbidities

Several researchers have assessed the relationship between bulimia nervosa and preexisting or comorbid psychiatric disorders, including alcoholism, obsessive-compulsive disorders, and cocaine dependency. One study reported a significantly higher lifetime prevalence of bulimia nervosa in alcohol-dependent men and women than in individuals with no major psychiatric diagnoses.[188] However, after controlling for psychiatric comorbidities, the prevalence of bulimia nervosa was only modestly higher in alcohol-dependent women and not significantly higher in men than among subjects with no psychiatric disorders. This result suggests that the link between alcoholism and bulimia nervosa is unlikely to be close, as the association occurred in the context of additional preexisting or secondary psychiatric disorders.

In outpatients with obsessive compulsive disorder (OCD), the lifetime prevalence of bulimia nervosa was found to be significantly greater than what would be expected in the general population.[189] However, no final conclusions can be drawn from this study, since

the sample was very small and it could not be determined whether OCD was a risk factor for or a consequence of bulimia nervosa.

The prevalence of bulimia nervosa has also been reported to be higher in cocaine abusers than in the general population, which could either indicate that bulimics misuse cocaine to "self-medicate" bulimic symptoms, or that drug abuse could be a risk factor for the development of bulimic symptoms.[190]

Further evidence from prospective studies is needed to determine which psychiatric conditions are associated with bulimia nervosa, and whether they are risk factors for the development of the disorder or consequences of it.

ix) Other at-risk populations

A number of studies have been performed in other populations considered a priori to be at risk of eating disorders, among them sexually abused women. While childhood sexual abuse has been frequently assumed to be a predisposing factor for the development of an eating disorder, current evidence is contradictory. In clinical samples, a relatively high percentage of women with bulimia nervosa reported childhood sexual abuse.[155] For example, one cross-sectional study of adult women attending a family practice in San Antonio, U.S., found a DSM-IV-based prevalence of bulimia nervosa of 7.7% among those with childhood abuse.[191] However, no conclusions regarding a potentially increased risk can be drawn from this study, since no control group of women without childhood abuse was included.

x) Summary

Based on currently available evidence, it can be concluded that bulimia nervosa appears to be more prevalent in younger than older adults, less prevalent in men than women, more common in Western than non-Western countries and in Caucasian than Black populations. While some evidence supports the hypothesis that exposure to Western societies and standards may contribute to an increasing prevalence of bulimia nervosa in

non-Western populations, additional research on specific risk factors in different cultures and ethnic groups is needed.

Limited evidence seems to suggest that homosexual men are at a higher risk of bulimia nervosa than heterosexual men and that elite athletes competing in certain sports, i.e., those requiring leanness or a specific body weight, may be more vulnerable to bulimic symptoms. In addition, military officers appear to be at risk of bulimia nervosa. The contribution of various comorbidities to the development of bulimia nervosa requires further research, especially longitudinal studies allowing for separate assessment of contributing factors and consequences of bulimia nervosa.

2.3.2 Lifetime prevalence

In addition to the point and period prevalence of bulimia nervosa, the lifetime prevalence (i.e., the proportion of individuals in a defined population who have had a given disease at any time in their life[192]) has been researched in different populations, although to a lesser extent. While some studies reported point as well as lifetime prevalence rates, other focused specifically on the assessment of the lifetime history of the disorder.

Estimates of the lifetime prevalence are dependant on the recall of those who suffered from the disorder. It has been shown that individuals who self-induce vomiting or misuse laxatives have a more reliable recall of bulimia nervosa than those who don't.[193] In addition, frequent binge eating episodes have been associated with a more reliable reporting of a history of eating disorders. It can therefore be expected that recall is better for DSM-III-R and DSM-IV bulimia nervosa, which require frequent binge eating episodes, and for purging type bulimia nervosa.

Results of studies providing evidence on the lifetime prevalence of bulimia nervosa are summarized in Table 2 below in chronological order and are further described in the following chapters on a per-country basis.

Table 2: Lifetime prevalence

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Lifetime prevalence, % (95% CI, if reported)
Wade et al (2006) [194]	Australia, twin registry, 2001–2003	28–39 (∅ 35) F	1,083 (43%)	Phone interview (EDE)	DSM-IV	F: 2.9 (1.9–3.9)
Doll et al (2005) [195]	UK, Oxfordshire, students at 5 universities and colleges, 1996	18–64 (∅ 23) F & M	1,439 (42%) F: 906 M: 533	Postal survey (4 institutions), in-class survey (1 institution)	DSM-IV	3.8 (2.8–4.8) F: 6.1 (4.5–7.6)[43]
Fichter et al (2005) [36]	Greece, adolescents in Greece and migrant adolescents in Germany,[44] 1998	Germany: 13–21 Greece: 12–21 (∅ 16) F & M	Germany: 881 F: 445 M: 436 Greece: 2,920 F: 1,506 M: 1,414 (90%)	2-stage: - Self-reported questionnaire - Interview of random sample of probable cases	DSM-IV	Greece: 2.1 F: 3.5 M: 0.7 Germany: 1.6 F: 3.5 M: 0.0
Hach et al (2005) [37]	Germany, Dresden, prospective sample, 1996/1997	18–24 F	2,064 (59%)	Psychological interview	DSM-IV	F: 1.1
Favaro et al (2003) [43]	Italy, city of Padova, year NR	18–25 F	934 (78%)	Interview (ED section of the structured clinical interview)	DSM-IV	F: 4.6 (3.3–5.9)
Medina-Mora et al (2003) [44]	Mexico, National Survey of Psychiatric Epidemiology (random sample), 2001–2002	18–65 (41%: 18–29 years) F & M	2,432 F: 1,306 M: 1,126 (response rate NR)	Interviews (Diagnostic Interview Schedule, WHO)	ICD-10	1.2 F: 1.8 M: 0.6

[43] Results for men were not reported.
[44] Participants attended private o public schools in Veria and Munich; the schools in Munich were schools of the Greek Republic for Greek students.

Table 2 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Lifetime prevalence, % (95% CI, if reported)
Patton et al (2003) [196]	Australia, state of Victoria, 6-year cohort study, 1992–1998	14–15 at inclusion, ∅ 21 at follow-up F	853 (42%)	- Self-reported questionnaire (1992–1995) - Telephone survey (1998)	DSM-IV	F: 1.2 (0.4–1.9)
Striegel-Moore et al (2003) [197]	US, community sample, participants in 10-year National Heart, Lung, and Blood Institute Growth and Health Study, year NR	19–24 (Whites: ∅ 21; Blacks: ∅ 22) F	2,046 Whites: 985 Blacks: 1,061 (86% of original study cohort)	2-stage: - Telephone screening (EDE, SCID) - Interview of probable cases	DSM-IV	F: 1.3 Whites: 2.3 Blacks: 0.4
Woods (2003) [198]	US, new patients of university-based dental clinic, 2001	18–88 (median 49) F & M	508 F: 255 M: 253	Self-reported mental illnesses (derived from medical records)	Not specified	1.0[45]
Carta et al (2002) [51]	Italy, Sardinia, community samples of Sardinian immigrants in Paris, Sardinian residents, Parisian residents, 1994–96	≥ 18 F & M	153 immigrants (85%) 2,260 Parisians (79%) 1,040 Sardi-nians (79%)	Interview (CIDIS)[46]	ICD-10	Immigrants: 3.9 (1.6–8.7) Parisians: NR Sardinians: 0.5 (0.2–1.2)

[45] Results were not separately reported for men and women.
[46] CIDIS is a simplified version of the Composite International Diagnostic Interview (WHO).

Table 2 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Lifetime prevalence, % (95% CI, if reported)
Dansky et al (2000) [199;200]	US, National Women's Study (household sample, wave 3), 1992	∅ 46 F	3,006 (75% of wave 1)	Structured telephone interviews	DSM-III-R DSM-IV[47]	F: 2.4
Lewinsohn et al (2000) [67]	US, random sample, Oregon Adolescent Depression Project T1: 1987/1988 T2: 1-year follow-up T3: age 24[48]	Age NR for T1 & T2 F	T1: 891 T2: 810 T3: 538 (response rate NR)	T1: In-person interview T2: In-person interview T3: Telephone interview	DSM-IV	F, T1: 0.8 F, T2: 1.5 F, T3: 3.3 (weighted 2.8)[49]
Bulik et al (1998) [201]	US, Virginia registry, longitudinal study of Caucasian twins[50] 1987–1989 (wave 1) 1992–1995 (wave 3)	Wave 1: ∅ 30 Wave 3: ∅ 35 F	1,897 (wave 1: 92%) (wave 3: 88%)	Clinical interview	DSM-III-R broadly defined[51]	F- Wave 1: 4.3 F- Wave 3: 5.6
Sullivan et al (1998) [202]	US, Virginia registry, longitudinal study of Caucasian twins, 1992–1995 (wave 3)	∅ 35 F	1,897 (88% of wave 1)	Clinical telephone interview	DSM-IV DSM-III-R [52]	F: 0.5 F: 0.8[53]

[47] Diagnostic criteria: 1. Episodes of eating large amounts of food in a brief time period. 2. During the worst period, the episodes occurred at least several times each week. 3. Worst period lasted at least 3 months. 4. Engaged in at least two types of binge eating behaviors, which are indicators of loss of control. 5. Compensation for a binge by excessive exercise, vomiting, and laxative or diuretic use.

[48] T3 consists of all participants with a history of major depressive disorder or a nonmood disorder at T2 and a randomly selected subset of those with no psychiatric disorder at T3. Study years for T2 and T3 were not reported.

[49] Weighted for the unequal stratified sampling of participants for the T3 assessment who did not have a history of psychopathology at T2.

[50] Results were only based on waves 1 and 2, when the lifetime history of bulimia nervosa was assessed.

[51] The criterion D from the DSM-III-R, i.e., minimum frequency of binge-eating of twice per week for 3 months, was omitted.

[52] Only vomiting was considered as type of purging, but not other methods like use of laxatives or excessive exercise.

[53] According to the authors, the lifetime prevalence would increase to 0.9% and 1.2% for DSM-IV and DSM-III-R, respectively, if the other purging behaviors were present and would meet the frequency criterion of at least twice weekly for three months.

Table 2 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Lifetime prevalence, % (95% CI, if reported)
Wade et al (1996) [203]	Australia, twin registry, 1992–1993	28–86 F	3,845 (79% of original sample in 1980–81)	Telephone interview 1992/93	DSM-III-R[54]	F: 1.8 (1.4–2.2) < 45 y: 2.3 (1.8–2.8) ≥ 45 y: 1.1 (0.8–1.4)
Garfinkel et al (1995) [204]	Canada, Ontario, participants in Ontario Health Survey — a random sample, 1990	15–65 (∅ 37) F & M	8,116 F: 4,285 M: 3,831 (77%)	Structured interview (based on WHO International Diagnostic Interview)	DSM-III-R	F: 1.1 M: 0.1
Götestam et al (1995a) [81]	Norway, representative sample of population, 1991	∅ 37 F	1,849 (75%)	Self-reported questionnaire	DSM-III-R	F: 1.6
Kendler et al (1991) [205]	US, Virginia registry, longitudinal study of Caucasian twins, year NR	∅ 30 F	2,163 (92% interview phase)	Structured interview (90% face-to-face, 10% by telephone)	DSM-III-R (definitive & probable cases)[55]	F: 2.8 (2.1–3.5) F: Expected lifetime risk by age 50: 4.2
Pyle et al (1991) [99]	US, Midwest, freshman at 2 universities, 1986	Age NR F & M	1,836 F: 925 M: 911 (97%)	Self-reported questionnaire	DSM-III ≥ 1/week binging/ purging	F: 6.5 M: 0.5[56] F: 2.2 M: 0.0

[54] Criterion C (twice weekly binging) was not assessed regarding duration of the symptoms, i.e., at least three months.
[55] For a definitive diagnosis, all diagnostic criteria had to be met with sufficient severity or certainty. A probable diagnosis meant that the diagnostic criteria were met, but symptoms were less severe and/or clearly present.
[56] Lifetime prevalence was assessed based on history of symptoms/diagnosis.

Table 2 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Lifetime prevalence, % (95% CI, if reported)
Bushnell et al (1990) [101]	New Zealand, Christchurch, random sample, year NR	18–64 F & M	1,498 F: 995 M: 504 (70%)	2-step: - DIS by lay interviewer - Clinical interview of possible cases	DIS-based DSM-III Clinician: DSM-III DSM-III-R	1.0 (0.6–1.6) F: 1.9 (1.2–3.0) M: 0.2 (0.0–1.1) 1.7 (1.0–2.9) 1.6 (0.0–2.8)
Kurtzman et al (1989) [107]	US, Los Angeles, students, year NR	∅ 21 F	716 (response rate NR)	Self-administered questionnaires (including EDI)	DSM-III	F: 2.7
Wells et al (1989) [206]	New Zealand, Christchurch, probability sample, 1986	18–64 F & M	1,498 F: 994 M: 504 (70%)	Interview (lay) based on DIS	DSM-III	1.0 F: 1.9 M: 0.2
Pyle et al (1986) [127]	US, Midwest freshman students at 2 colleges, 1983	Age NR F & M	1,389 F: 722 M: 660 (96%)	Self-reported questionnaire	DSM-III ≥ 1/week binging/ purging	4.1l[57] F: 7.5, M: 0.3 1.7 F: 3.2, M: 0.0
Pope et al (1984) [134]	US, Boston, clients at a shopping centre, 1983	≥ 12 years F	300 (99% of those who accepted)[58]	Self-reported questionnaire	DSM-III ≥ 1/week binging/ purging	F: 10.3 lifetime history - 3.0 lifetime history
Pope et al (1984) [207]	US, 2 samples:[59] 1) Prestigious rural college; 2) Urban college (lower SES), year NR	1) ∅ 22 F 2) ∅ 22 F & M	1) 450 (64%) 2) 300 (50%)	Self-reported questionnaire	DSM-III history of bulimia nervosa	1) F: 12.6 2) 12.7 F: 18.6 M: 0.0

[57] Lifetime prevalence was assessed based on past and current symptoms.
[58] The overall number of people approached was not reported.
[59] Results for 3rd sample not reported here, since it referred to high school students.

Abbreviations: y = year; Resp. rate = response rate; CI = confidence interval; T = time; F = female; M = male; NA = not applicable; NR = not reported; SES = socioeconomic status
Questionnaires:

- DIS: Diagnostic Interview Schedule
- ED: Eating Disorder
- EDE: Eating Disorder Examination
- EDI: Eating Disorder Inventory
- SCID: Structured Clinical Interview for DSM-IV

2.3.2.1 North America

As with studies estimating the point prevalence of bulimia nervosa, those assessing the lifetime prevalence differ in terms of populations and diagnostic criteria. The most recent evidence stems from a study by Striegel-Moore et al (2003), who surveyed young women who previously participated in the 10-year National Heart, Lung, and Blood Institute (NHLBI) Growth and Health Study.[197] The authors reported a DSM-IV-based lifetime prevalence of 1.3%, which was higher in White than Black women (2.3% versus 0.4%). Since respondents were 19 to 24 years of age and therefore still at risk of developing an eating disorder later in life, results provide an underestimate of the lifetime prevalence.

A longitudinal study of female, primarily white, participants in the Oregon Adolescent Depression Project reported an increase in the DSM-IV-based lifetime prevalence from childhood (0.8%) to adolescence (1.5%) and young adulthood (2.8%),[67] a finding that would be expected, since the mean age of onset of the disorder is at age 18 to 19 years. The lifetime prevalence in young female adults in this study (2.8%) is comparable to that in white female participants in the NHLBI study (2.3%).

Results are corroborated by a population-based survey of adult women, which found a DSM-III-R/DSM-IV-based lifetime prevalence of 2.3%.[199;200] Since the average age of respondents was 46 years, selective memory and recall bias may have led to an underestimation of past binging and purging behaviors. It should be noted that all three studies are subject to the limitations imposed by telephone interviews; for instance, respondents might not have had sufficient time to think about past eating disorder symptoms.

Altogether, three studies were conducted in Caucasian women participating in the Virginia twin registry. Sullivan et al (1998) used data from the third survey in 1992 to 1995 and estimated DSM-IV- and DSM-III-R-based lifetime prevalence rates of 0.5% and 0.8%, respectively.[202] However, only vomiting was considered as a method of purging, as detailed frequency information on other purging methods was not available, likely leading to an underestimation of the prevalence. If the frequency criterion of at

least twice weekly binging and purging was omitted, the DSM-IV- and DSM-III-R-based lifetime prevalence estimates increased to 1.6% and 2.2%, respectively.

Bulik et al (1998) reported much higher DSM-III-R-based lifetime prevalence rates of 4.3% and 5.6% based on the first and third survey of female twins, conducted in 1987 to 1989 and 1992 to 1995, respectively.[201] However, the frequency criterion of at least twice weekly binging was omitted from this study and therefore the lifetime prevalence estimate likely included cases of lesser severity. Results are not directly comparable with those reported by Sullivan et al, since other purging methods than vomiting were assessed as well.

By comparing the history of bulimia nervosa as reported by the same respondents at two time points approximately 5 years apart, the researchers demonstrated that the reliability of lifetime prevalence estimates was rather low (κ=0.28). Among those interviewed at both waves about a lifetime history of bulimia nervosa with onset before the first survey, 2.1% reported a history of the disorder in the first but not the third survey, 4.0% in the third but not the first survey, and 1.6% in both surveys. This finding is of importance, as it indicates that published studies may have underestimated the lifetime prevalence and therefore the burden in the population.

Data from the first survey in female twins were also analyzed by Kendler et al (1991), who estimated the DSM-III-R-based lifetime prevalence at 2.8%. Discrepancies with the results by Sullivan et al and Bulik et al may be explained by differences in the diagnostic criteria applied, since Kendler et al reported results for definite cases of bulimia nervosa defined as those meeting the diagnostic criteria "with sufficient severity or certainty so that the individual would be considered a case if seen in the clinical setting."

Further to studies in general population samples and in twins, the lifetime prevalence has been assessed in a survey of new female and male patients attending a university-based dental clinic, which found a lifetime prevalence of 1.0%.[198] Since cases were derived from patients' self-reported medical history, as contained in the medical records, results

are likely biased due to underreporting of disordered eating behaviors by patients. In addition, results are not comparable to those of other studies, as this research relied on patient self-report of a history of bulimia nervosa and no specific diagnostic criteria could therefore be applied.

In additional studies conducted in the 1980s, the DSM-III-based lifetime prevalence has been estimated in different student populations. Since students have not passed through the entire age range at risk for the development of bulimia nervosa, lifetime prevalence estimates likely represent an underestimate. Conversely, the application of the DSM-III criteria and the use of self-reported questionnaires without a clinical validation of the diagnosis may have contributed to higher estimates of the lifetime prevalence than in studies applying the DSM-III-R or the DSM-IV criteria in general population samples.

Based on a survey of freshman students in 1986, Pyle et al (1991) reported lifetime prevalence rates of 6.5% and 0.5% in women and men, respectively.[99] If a more stringent definition of bulimia nervosa with at least weekly binging and purging behavior was applied, the estimated lifetime prevalence dropped to 2.2% and 0.0% in women and men, respectively. These findings are comparable to those of an earlier study by the same researchers, which was conducted in freshman students in 1983 and which found a lifetime prevalence of 7.5% in women and 0.3% in men, respectively, with an overall rate of 4.1%.[127] However, only 3.2% and 0.0% of female and male students, respectively, reported at least weekly binging and purging (1.7% of the study population).

In contrast, Kurtzman et al (1989) estimated the DSM-III-based lifetime prevalence at 2.7% in female college students in Los Angeles.[107] However, results from this survey are subject to very low response rates in some subgroups of students (e.g., 54% and 60% in attendees of a primary care clinic and a women's health clinic, respectively, versus 98% in dance students) and are therefore unlikely representative.

In the first study to assess the lifetime prevalence of bulimia nervosa in students, Pope et al (1984) surveyed two samples: one of a prestigious rural college and one of an urban

college representing students of families with a lower socioeconomic status.[207] The authors estimated the DSM-III-based lifetime prevalence at 12.6% and 18.6% in women attending the rural and urban college, respectively. These comparatively high lifetime prevalence rates could be due to the questionnaire applied, especially since point prevalence rates reported by the same researchers and based on the same questionnaire were also found to be much higher than those reported elsewhere.

In another study by Pope et al (1984), which was conducted in 300 women in a shopping mall and which applied a questionnaire similar to the one in the two student samples, the DSM-III-based lifetime prevalence was estimated at 10.3%.[134] If more stringent diagnostic criteria with at least weekly binging and vomiting or laxative abuse were applied, the estimated lifetime prevalence decreased to 3.0%, a finding that is comparable to the results reported by Pyle et al in students. Even though the study by Pope et al suffered from methodological limitations, including a small, potentially unrepresentative sample, it is of epidemiological interest, since it was the first to propose that the prevalence of bulimia nervosa might be increasing. This hypothesis was derived from the observation that younger female shoppers more frequently reported a history of bulimia nervosa than older ones. However, the authors acknowledge that recall bias may have influenced findings.

In addition to studies in the U.S., Garfinkel et al (1995) conducted a survey of a random, non-clinical sample of Ontario residents, and estimated the DSM-III-R-based lifetime prevalence at 1.1% and 0.1% in adult women and men, respectively.[204] It can be assumed that the true lifetime prevalence in Ontario was slightly higher, since respondents may have underreported bulimic symptoms in the interviews and since recall bias, especially in older respondents, may have impacted findings.

2.3.2.2 Europe

Few studies so far have assessed the lifetime prevalence of bulimia nervosa in Europe. In adolescents in Greece and Greek migrant adolescents in Germany, Fichter et al (2005) estimated similar DSM-IV-based lifetime prevalence rates of 2.2% and 1.6%,

respectively, with higher rates among girls than boys.[36] In contrast, Carta et al (2002) found a higher lifetime prevalence in Sardinian immigrants living in Paris (3.9%) than in Sardinians (0.5%) and Parisians (0%), indicating that migrants might be at a higher risk of developing an eating disorder.[51] However, lifetime prevalence rates of these two studies in immigrants cannot be compared, since the study by Carta et al applied the ICD-10 rather than the DSM criteria and was based on an older population than the survey by Fichter et al (age 18–65 years versus an average of 16 years, respectively).

In a sample of Italian women aged 17 to 25 years, Favaro et al (2003) reported a DSM-IV-based lifetime prevalence of 4.6%, with cases being identified by clinical interview.[43] An additional finding of this survey was that about 44% of respondents with a lifetime history of bulimia nervosa were in full remission, resulting in a higher lifetime than point prevalence.

Among male and female students in the UK, Doll et al (2004) found a DSM-IV-based lifetime prevalence of 3.8% overall and 6.8% in women.[195] Apart from a very low response rate (42%), the main limitation of this survey was the reliance on self-reported symptoms without a clinical validation of the diagnosis. Results are therefore only indicative of a probable lifetime history of bulimia nervosa, which might explain the slightly higher lifetime prevalence in female students in the UK than in young women in Italy.

A study of young women in Germany reported a much lower DSM-IV-based lifetime prevalence of 1.1.[37] However, results could be biased, as the response rate to the interviews was low—only 59%. A further limitation was that diagnoses were derived from the Diagnostic Interview for Mental Disorders rather than an eating disorder specific questionnaire, which could have resulted in a higher rate of false negative cases than in other studies.

The only European study assessing a representative population sample of adults, which was conducted in women in Norway, found a DSM-III-R-based lifetime prevalence of

1.6%.[81] The authors reported a 1:2 ratio of point to lifetime prevalence, indicating that about half of the respondents were in remission. Since results were derived from self-reported symptoms and therefore lack a clinical validation of the diagnosis, generalizability of results is limited.

2.3.2.3 Australia and New Zealand

Data from a female twin registry in Australia have yielded similar results to those in the U.S. Based on surveys conducted from 2001 to 2003 and in 1993, Wade et al (2006 and 1996) estimated DSM-IV- and DSM-III-R-based lifetime prevalence rates of 2.9% and 1.8%, respectively (average age of twins: 35 versus 21 years).[194;203] Since the survey population was much smaller from 2001 to 2003 than in 1993, lifetime prevalence estimates might not be comparable and no conclusions regarding a possible trend can be made.

An additional finding of the more recent survey was that only 7% of the women with a lifetime diagnosis of bulimia nervosa diagnosis suffered from the disorder at the time of the interview—about 15 years after the onset of bulimic symptoms—indicating an improvement of bulimic behaviors in most, but not all suffers, over time. The 1993 survey reported a significantly higher lifetime prevalence in women younger than 45 (2.3%) than in those at least 45 years of age (1.1%). However, Wade et al caution not to interpret this result as an indication of a recent increase in the prevalence, as recall bias—especially of psychiatric disorders—is known to be poor.

Further evidence stems from a 6-year cohort study, which assessed females from adolescence until early adulthood and which collected information about the presence of eating disorders on a semi-annual basis.[196] Among those women who participated in the final assessment, the DSM-IV-based lifetime prevalence of bulimia nervosa was 1.2%. This is likely an underestimate, since more than 50% of the initial cohort of adolescents could not be included due to loss of follow-up and since participants were still at risk of developing bulimia nervosa later in life (average age at follow-up was 21 years).

In a survey of a random sample of adults in Christchurch, New Zealand, which applied a 2-step case identification process, the DSM-III- and DSM-III-R-based lifetime prevalence was estimated at 1.7% and 1.6%, respectively.[101] If only the results of the first step (interviews by laypersons) were considered, the DSM-III-based lifetime prevalence would be 1.0%, with gender-specific rates[60] of 1.9% in women and 0.2% in men.[206] This finding indicates a higher false negative rate based on interviews conducted by laypersons compared to those by clinicians, since according to clinical interviews the DSM-III-based lifetime prevalence was 1.6%. As with studies conducted in Europe, estimates of the current prevalence were lower than those of the lifetime prevalence.

2.3.2.4 Other countries

Only one study has so far assessed the lifetime prevalence of bulimia nervosa in a developing country. Based on interviews of a national sample of adults in Mexico, the lifetime prevalence was estimated at 1.2%, with a higher rate in women than men (1.8% and 0.6%, respectively).[44] While these results may indicate a lower lifetime prevalence of bulimia nervosa in Mexico than in the rest of North America and Europe, the application of the ICD-10 rather than the DSM criteria preclude direct comparisons with findings from other countries.

2.3.2.5 Summary

Less evidence has been published on the lifetime prevalence than on the point prevalence of bulimia nervosa. The majority of studies assessing the lifetime prevalence were based on retrospective surveys, which have the inherent limitation of recall bias of respondents. In addition, many researchers focused on samples of young women, who are still at risk of developing an eating disorder later in life, leading to an underestimate of the lifetime prevalence. The lack of evidence from prospective studies of representative population samples could be due to the difficulty of generating reliable data, since longitudinal studies are resource intensive and subject to loss of follow-up.

[60] Gender-specific rates were not reported for prevalence rates determined by clinical interviews.

Based on the existing (albeit limited) evidence, it can be concluded that:

- In Caucasian women, the DSM-IV- and DSM-III-R-based lifetime prevalence is likely at least 2.0%, and may exceed 3.0%.
- Estimates of the DSM-III-based lifetime prevalence are scant and vary greatly between populations studied and methods of case identification applied.
- Compared to the U.S., less evidence is available for Europe. Since study populations differed, especially in terms of age and representativeness of samples, lifetime prevalence rates in the U.S. and Europe cannot be compared.
- The lifetime prevalence in women appears to be comparable in Australia and New Zealand and in the U.S.
- Studies in men and in ethnic groups other than Caucasians are too scant to draw any conclusions.

2.4 Incidence of bulimia nervosa

Incidence is defined as the number of new cases in a given population over a specified period of time,[192] usually expressed as the number of cases per 100,000 population per year. Compared with the amount of epidemiological research generated on the prevalence of bulimia nervosa, evidence on its incidence is generally scant.

Hoek and van Hoeken (2003) identified in their literature review three studies of larger population samples, one in the U.S., one in the Netherlands, and one in the U.K., based on which they concluded that the 1-year incidence was approximately 12 cases per 100,000 population per year.[31] In addition, they estimated incidence rates per 100,000 young women at different levels of care—87 in mental healthcare, 170 in primary care, and 1,500 in the community, demonstrating that only few subjects with bulimia nervosa receive treatment and are therefore known to the healthcare system. Since estimates of the incidence have often been derived from medical records and case registers, existing evidence likely underestimates the incidence in the general population.

To assess time trends in the incidence of bulimia nervosa, Keel and Klump (2003) performed a meta-analysis of seven studies providing incidence data over time and reported a significant increase from 1970 to 1993.[1] The authors note that this trend could have resulted from the formal recognition in 1980 of cases of the disorder that had existed in earlier periods as well, potentially leading to an inflation of reported incident cases in the early 1980s.

Results of studies identified as part of this literature review and providing evidence on the incidence of bulimia nervosa are summarized in Table 3 in chronological order, and are further described in the following chapters on a per-country basis.

Table 3: Incidence of bulimia nervosa

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Incidence per 100,000 per year (95% CI)
Lahortiga-Ramos et al (2005) [208]	Spain, Navarra, 18-month follow-up of a representative population sample, 1997–1998	13–22 (∅ 16) F	2,509 (1st stage: 92%) (2nd stage: 90%)	2 stage: - Self-reported questionnaires (EAT, EDI) - Semi-structured interview[61]	DSM-IV	F: 200 (100–327)
Currin et al (2005) [209]	England & Wales, General Practice Research Database (GPRD), 2000	All ages F & M	Approx. 280 GPs with over 3 million patients (response rate NA)	Medical records	Diagnosis by GP	Age-gender-adjusted: 6.6 (5.3–7.9) 10–19 y: 19.2 (12.6–25.7) 20–39 y: 14.8 (11.1–18.5) ≥ 40 y: 0.6 (0.0–1.1)
Ghaderi & Scott (2001)[59]	Sweden, random population sample, 1999[62]	20–32 F	826 (74%)	Questionnaire (Survey of Eating Disorders)	DSM-IV	F: 480
Turnbull et al (1996) [210]	England & Wales, GPRD, 1993	All ages F & M	550 GPs with about 4 million patients (response rate NA)	Medical records	Diagnosis by GP DSM-IV[63]	Age-gender-adjusted: 12.2 (10.8–13.6) 10–19 y: 20.5 (15.3–25.7) 20–39 y: 29.3 (25.4–33.1) ≥ 40 y: 1.7 (0.9–2.5) 6.7 (4.0–9.3)

[61] Interviews were conducted 18 months after study inclusion. Only those were interviewed, who did not have any eating disorder at baseline and who scored higher than 21 on the EAT. In addition, a random group of those scoring 21 or below on the EAT was interviewed.
[62] The study was a follow-up study of an earlier survey of a random sample of women in 1997.
[63] Validation of diagnoses in GPRD was done in a subsample of 100 GPs. Based on the results, the DSM-IV incidence was estimated by adjusting incidence estimates derived from medical records.

Table 3 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Incidence per 100,000 per year (95% CI)
Soundy et al (1995) [211]	US, Rochester, Minnesota, general practitioners and specialists, 1980–1990	All ages F & M	> 4 million medical records (response rate NA)	Medical records (Rochester Epidemiology Project)	DSM-III-R	Age-gender-adjusted: 13.5 (10.9–16.1) Age-adjusted: F: 26.5 (21.2–31.7) M: 0.8 (0.0–1.7)
Hoek at al (1995) [212]	Netherlands, patients in primary care (58 GPs), 1985–1989	All ages F & M	151,781 (1% sample of Dutch population) (response rate NA)	Medical records	DSM-III-R	11.5 (9.0–13.9) F: 21.9 (17.2–26.7) M: 0.8 (0.3–2.6) Rural areas: 6.6 Urbanized areas: 19.9 Large cities: 37.9
Pagsberg & Wang (1994) [87]	Denmark, Island of Bornholm, participants identified via registries, inpatient & outpatient records, newspapers 1970–1989	10–24 F & M	Population of 47,000 (response rate NA)	Outpatient/ inpatient records, physician interview of probable cases in primary care	ICD-10	1970–1984: 0.7 1985–1989: 3.0 F: 1985–1989: 17.6 1989: 45
Joergensen (1992) [94]	Denmark, Fyn County (island), 1977–1986	10–24 F	NA	National (inpatient) and local (outpatient/ inpatient) registers	ICD-8 Bulimia (no anorexia)	F: 5.5 15–19 y: 3.0 20–24 y: 1.2 ≥ 25 y: 0.1

Table 3 continued

Reference	Population & year of study	Age, year Gender	# of subjects (Resp. rate)	Method of case identification	Diagnostic criteria	Incidence per 100,000 per year (95% CI)
Hoek et al (1991) [98]	Netherlands, representative sample of population, 1985–1986	All ages F & M	151,781 - approx. 1 % of population (response rate NA)	Cases identified by 58 GPs	DSM-III and/or DSM-III-R ≥ 2 binge/ week for 3 months	9.9 8.6
Hall, Hay (1991) [213]	New Zealand, Wellington, patients referred to eating disorder service, 1977–1986	16–29 F	Catchment area of population: > 300,000 (response rate NA)	New referrals Cases identified by interview	DSM-III	F, 1977–1981: 6.0 F, 1982–1986: 44.3
Drewnowski et al (1988) [111]	US, Michigan, longitudinal survey of college students, year NR	Age NR F	Fall: 931 (42%) Spring: 588 (64%)	Self-reported mail questionnaire, 2 waves	DSM-III-R [64]	F: 4.2 During 6 months: 2.1 (1.1–3.6)
Cullenberg, Engström-Lindberg (1988) [110]	Sweden, 2 suburban municipalities, case records 1984–1985	16–35 F & M	Catchment area of population: 77,729 (response rate NA)	Survey of records provided by healthcare workers	DSM-III	F: 3.9 F, 16–24 y: 65

Abbreviations: y = year; Resp. rate = response rate; CI = confidence interval; F = female; M = male; NA = not applicable; NR = not reported; DSM = Diagnostic and Statistical Manual of Mental Disorders; GP = General Practitioner; ICD = International Classification of Diseases

Questionnaires:

- EAT = Eating Attitude Test
- EDI = Eating Disorder Inventory

[64] Frequency of symptoms assessed over a 1-month period rather than 3 months as required by DSM-III-R.

2.4.1 North America

For the U.S., the most recent evidence stems from an analysis of data available through the medical record linkage system in Rochester, Minnesota, which found for the period from 1980 to 1990 an age- and gender-adjusted DSM-III-R-based incidence of 13.5 per 100,000 population per year, while the age-adjusted rates were 26.5 and 0.8 in women and men, respectively.[211] In addition, the study reported an increase in the incidence among women from 7.4 per 100,000 population in 1980 to 49.7 in 1983 and a relatively stable rate thereafter (incidence rates between 21.9 and 40.0). The authors explain the increase in the incidence in 1983 by the initiation of a clinical study that might have led to more cases being identified and reported. Over the period from 1980 to 1990, the highest incidence was observed in women 15 to 19 and 20 to 24 years of age: 125.1 and 82.7 cases per 100,000 per year, respectively. Since only individuals seeking treatment and being diagnosed by physicians were represented in the medical record system, the true incidence in the Rochester area was likely much higher than reported in this study.

In one of the first studies to assess the incidence of bulimia nervosa, Drewnowski et al (1988) surveyed female college students over a 6-month period and estimated a DSM-III-R-based incidence of 2.1 per 100,000.[111] The authors assumed this would equal an incidence of 4.2 per 100,000 per year. The much lower incidence in this survey than in the one in Rochester could be due to a low response rate to the mail questionnaire (42% and 64% in two waves 6 months apart), which might have resulted in an underreporting of new bulimic cases.

2.4.2 Europe

More studies providing evidence on the incidence of bulimia nervosa have been conducted in Europe than in the U.S. In Spain, Lahortiga-Ramos et al (2005) reported a DSM-IV-based incidence of 200 cases per 100,00 population per year, based on an 18-month longitudinal study of women aged 13 to 22 years, who were free of eating disorders at baseline in 1997.[208] The highest incidence was observed among women 17 to 18 years of age (334 cases per 100,000 per year), while no case was detected among

those 18 to 22 years of age. The authors hypothesize that the relatively high incidence of 200 cases per 100,000 could be due to an increased availability of healthcare services, larger social awareness of the disorder, and decreased stigmatization of bulimia nervosa. The main advantage of this study was the assessment of a representative sample of young women in the community, thereby overcoming the limitations of results derived from case registers or medical records. Findings can therefore be assumed to be representative for the population of female adolescents and young women. However, results cannot be generalized to the adult female population, since the sample included respondents below the average age of onset of bulimia nervosa.

The only other study that provided incidence estimates for the general population rather than patients was conducted in Sweden, and reported for the year 1999 an incidence of 480 cases per 100,000 women aged 20 to 32 years.[59] In contrast to the study in Spain, cases were identified based on self-reported symptoms without a validation of diagnoses by a clinician, which may have resulted in false positive cases and therefore a higher incidence rate than in the study by Lahortiga-Ramos. In addition, women in the Swedish survey were older than those in the Spanish study (20–32 versus 13–22 years), which may have resulted in a higher incidence estimate.

Two researchers reported incidence rate of bulimia nervosa in the UK based on data from the General Practice Research Database (GPRD), which is generally representative for the UK with regards to age and gender. Currin et al (2005) estimated for the year 2000 an age- and gender-adjusted incidence of 6.6 per 100,000, with the highest rate among women aged 10 to 19 years (35.8 per 100,00).[209] For the year 1993, Turnbull et al (1998) reported an age- and gender-adjusted incidence of 12.2 cases per 100,000, with the highest rate in women 20 to 39 years of age (57 per 100,000).[210] Age-adjusted incidences were 23.3 and 0.5 per 100,000 women and men in 1993, respectively, implying a female-to-male ratio of 47:1. In 2000, the age-adjusted incidence in women, but not in men, was lower than in 1993 (12.4 in women and 0.7 in men; i.e., a relative risk of 18:1).

By combining their results with those reported by Turnbull et al, Currin et al found that the incidence appeared to have increased in women 10 to 39 years of age, with a peak in 1996 (approximately 60 cases per 100,000), followed by a decline thereafter, which was almost entirely explained by a decrease in the incidence among women aged 20 to 39 years. The authors hypothesize that the increase in the incidence between 1988 and 1996 was in part driven by the increased recognition of the disorder, while the reduction in more recent years could be due to different help-seeking behaviors of patients (e.g., use of Internet-based tools) and changes in public attention to bulimia nervosa (after the death of Princess Diana).

Since diagnoses in computer records are likely to include false positive and false negative cases, Turnbull et al performed a validation study in a small subset of GPs and adjusted estimates derived from medical records in GPRD accordingly. DSM-IV-based incidence rates were lower than those derived from GP records (age- and gender-adjusted incidence of 6.7 per 100,000 per year and age-adjusted rates of 12.8 in women and 0.3 in men), indicating that GPs had likely applied less stringent diagnostic criteria than those of the DSM-IV. While the gatekeeper system in the UK should ensure that all diagnosed patients are recorded in the GPRD database, results of the studies by Currin et al and Turnbull et al cannot be considered representative for the overall population due to the exclusion of cases not seeking help or not being diagnosed by GPs.

Incidence rates in the primary care setting in the UK are similar to those reported by Hoek et al (1995) for the Netherlands. Based on a review of Dutch general practitioner medical records covering about 1% of the population, Hoek et al estimated for the period from 1985 to 1989 a DSM-III-R-based incidence of 11.5 per 100,000 population per year, which was highest in women 20 to 24 years of age (82.1 per 100,000 per year).[212] In an earlier study, the same researchers reported for the period from 1985 to 1986 a slightly lower annual incidence of 9.9 per 100,000,[98] indicating an increase by about 15% each year during the time period from 1985 to 1989 (7.2 per 100,000 person-years in 1985 versus 15.2 in 1989).[212] However, this finding could have resulted from increased

awareness and respective reporting of cases by GPs rather than a true increase in the incidence.

In addition, Hoek et al (1995) reported significantly different age-adjusted incidences in rural areas, urbanized areas, and large cities: 6.6, 19.9, and 37.9 cases per 100,000, respectively. Based on this finding, the authors reject the "drift hypothesis", which assumes that the higher prevalence with increasing urbanization is due to patients with bulimia nervosa being older and more likely to move to larger cities for work and further education. On the contrary, they hypothesize that a causal relationship might exist between living in large cities and the development of bulimia nervosa (e.g., due to social pressures to be thin or due to social isolation).

For Denmark, evidence has been generated by two studies. While Pagsberg and Wang (1994) derived incidence estimates from a survey of cases 10 to 24 years of age, who lived on the Island of Bornholm and were either identified via medical records, registers, or in response to a newspaper article,[87] Joergensen (1992) analyzed medical records of women aged 10 to 24 years living on the island of Fyn County.[94] For the periods 1970 to 1984 and 1985 to 1989, Pagsberg and Wang reported ICD-10-based annual incidence rates of 0.7 and 3.0 per 100,000, respectively. In addition, they found age and gender differences, with the highest incidence being observed among women in the year 1989 (45 per 100,000). While—similar to studies in other countries—cases were identified mainly by medical records, thereby likely underestimating the true incidence in the community, the main advantage of this research was the interview of probable cases by physicians, which likely eliminated false-positive cases.

Joergensen (1992) reported for the time period from 1977 to1986 an ICD-8-based incidence of 5.5 per 100,000 women per year. Pagsberg and Wang matched their findings to those of Joergensen based on time periods, case detection methods, and populations, and found that incidence rates were comparable (4.0 in Pagsberg & Wang versus 5.5 in Jorgensen). The relatively low incidence in both studies compared to those reported for

the UK and the Netherlands is likely explained by the focus on adolescents and young adults, some of whom were below the average age of onset of bulimia nervosa.

Similar results were reported in a Swedish study, which was based on a case record review in two cities.[110] For the period from 1984 to 1985, the average annual incidence was estimated at 3.9 per 100,000 women 16 to 35 years of age, with the highest rate among those 16 to 24 years of age (65 per 100,000). It should be noted the two Danish as well as this Swedish study likely underestimated the incidence in the respective populations, not only due to exclusion of cases not known to the healthcare system, but also due to the fact that bulimia had only been recognized as a disorder in 1980 and it can be assumed that some physicians might not have been aware of its existence or the diagnostic criteria.

2.4.3 Australia and New Zealand

Only one incidence study has so far been conducted outside North American and Europe. Based on referrals to an eating disorder service center in New Zealand, Hall and Hay (1991) estimated for the period 1977 to 1981 an average annual incidence of 6.0 per 100,000 women 16 to 29 years of age. In addition, the researchers found a marked increase in referral rates for the years 1982 to 1986 (44.3 per 100,00), which could have resulted from heightened awareness of this disorder rather than a true increase in the incidence. The main limitation of this survey was the focus on patients referred to tertiary healthcare, therefore providing a very conservative estimate of the incidence, since many cases might not get diagnosed or referred for treatment.[213]

2.4.4 Summary

Estimates of the incidence of bulimia nervosa vary widely between patient and community samples, between different time periods, as well as between age groups and genders. Evidence supporting the hypothesis that the incidence of bulimia nervosa has increased over time is currently lacking, since studies suggesting a secular trend suffer from methodological limitations and the fact that bulimia nervosa was only recognized as

a disorder in 1980. An observed increase in the reporting of treated cases could be due to heightened awareness of the disorder, changes in diagnostic and referral practices, or changes in the health service organization (i.e., easier access to mental healthcare).

Based on the existing, even though limited evidence, it can be concluded that:

- The annual incidence of diagnosed bulimia nervosa is at least 7 cases per 100,000 population, likely 13 per 100,000 or more. It can be assumed that the incidence of undiagnosed bulimia nervosa in the community is much higher.
- The incidence is higher in women than in men.
- The highest incidence occurs in young women in their early 20s; in the community setting it could be as high as 200 to 480 cases per 100,000.
- Additional community-based studies are required to estimate the incidence in the general population, including those who do not seek treatment.
- No evidence has been generated so far for non-Western cultures and different ethnic groups.

3 Burden of illness analysis

3.1 The MEDSTAT database

3.1.1 Database overview

The analysis of the burden of illness of bulimia nervosa in the U.S. in the year 2002 was based on the MarketScan® Commercial Claims and Encounters Database, which was developed by the Medstat Group, Inc., a private research-consulting firm working directly with large employers to develop healthcare claims databases. The Commercial Claims and Encounters Database is constructed from paid medical and prescription drug claims of approximately 45 large employers, health plans, and government and public organizations, and contains anonymous, patient-specific medical information regarding healthcare utilization and expenditures as well as enrollment information. In 2002, data were contributed by approximately 100 insurers, including commercial insurance companies, Blue Cross and Blue Shield plans, and third party administrators.

MarketScan databases have been used by numerous researchers to understand disease progression, health outcomes, treatment patterns, and their costs, and have served as the basis for more than 140 manuscripts published in peer-reviewed journals to date. The Commercial Claims and Encounters Database is generally representative of the non-elderly U.S. population, especially people with employer-sponsored private health insurance. Compared to the U.S. population in 2002, elderly persons as well as those living in the Northeastern region were underrepresented in the Commercial Claims and Encounters Database, while persons in the North Central and Southern regions were overrepresented (Table 4). A comparison of the characteristics of individuals included in the Commercial Claims and Encounters Database with the non-elderly U.S. population with employer-sponsored private healthcare coverage for the year 2004[65] demonstrates that the MarketScan population was representative in terms of age and gender, although not regional distribution (Table 5). Results derived from the Commercial Claims and

[65] A comparison of the MarketScan population with the population with employer-sponsored healthcare coverage was not available for 2002.

Encounters Database can therefore be generalized to the non-elderly population with private employer-sponsored health insurance, if no significant differences exist at the regional level. This implies for the current research that results from the cost of illness analysis can be projected to the non-elderly, privately insured U.S. population, if the prevalence of bulimia nervosa as well as its treatment costs are not subject to significant regional variation.

Table 4: Demographic characteristics of the MarketScan population and the U.S. population (2002)

	MarketScan*	National with private coverage†	National†
Gender, %			
Female	52.50	50.51	51.23
Male	47.50	49.49	48.77
Age group, %			
0–34 years	44.80	45.58	48.97
35–54 years	37.20	34.22	29.83
55–64 years	18.00	10.56	9.22
65+ years	0.00	9.65	11.98
Region, %			
Northeast	12.90	20.25	18.93
North Central	28.00	25.14	22.76
South	38.50	33.17	35.50
West	20.50	21.44	22.81
Other/unknown	0.10	0.00	0.00

* Commercial Claims & Encounters Database

† U.S. Census Bureau

Table 5: Demographic characteristics of the MarketScan population and the non-elderly U.S. population with employer-sponsored private health insurance (2004)

	MarketScan*	National (MEPS†)
Gender, %		
Female	51.80	50.30
Male	48.20	49.70
Age group, %		
0–17 years	26.20	25.80
18–34 years	24.00	24.50
35–44 years	17.10	19.40
45–54 years	18.30	17.90
55–64 years	14.50	12.50
65+ years	0.00	0.00
Region, %		
Northeast	7.10	20.20
North Central	27.60	24.80
South	46.10	33.40
West	18.80	21.60
Other/unknown	0.40	0.00

* Commercial Claims & Encounters Database

† The MEPS (Medical Expenditure Panel Survey) is representative of persons with employer-sponsored healthcare coverage.

Patients in the Commercial Claims and Encounters Database represent active employees, early (non-Medicare) retirees, individuals with continuing coverage under COBRA (Comprehensive Omnibus Budget Reconciliation Act),[66] and their dependants insured by employer-sponsored plans. Medicare-eligible retirees with employer-provided Medicare supplemental plans are captured in different databases, which were not used for analysis, as bulimia nervosa rarely affects older individuals. Medicaid enrollees could not be included, since respective data were not made available for analysis.

The database conforms to the requirements of the Health Insurance Portability and Accountability Act (HIPAA), which was enacted in the U.S. in 1996. In addition to protecting health insurance coverage for workers and their families when they change or lose jobs, HIPAA requires the establishment of national standards for electronic healthcare transactions, which also address the security and privacy of health data. In the

[66] The program gives employees who leave a company the option of continuing their health coverage with that company for a specified period of time, by paying a premium.

Medstat databases, the risk of implicit patient identification through information contained in the claims has been addressed by limiting the amount of information provided on employees and their dependants.

The Commercial Claims and Encounters Database is organized in different data subsets or tables, which are described in more detail below:

- Medical/surgical claims for inpatient services
- Medical/surgical claims for outpatient services
- Outpatient pharmaceutical claims
- Enrollment data

The inpatient service table contains all services provided by individual facilities (e.g., hospitals and laboratories) and professionals (e.g., physicians and surgeons) associated with a hospitalization. For each admission, healthcare services and respective claims can be linked by a unique case and services identification number (CASEID). In addition to information about the services provided, each claim may contain up to five diagnoses. Inpatient claims records also include information that can only be provided after all claims associated with an admission have been identified: i.e., the principal diagnosis for the admission and the major diagnostic category.

All services rendered by doctor offices, hospital outpatient facilities, emergency rooms or other outpatient facilities as well as associated claims are included in the outpatient service table. Analogous to inpatient claims, each outpatient claim may contain up to five diagnoses.

The outpatient pharmaceutical claims table includes mail order as well as card program prescription drug claims. Not represented in Medstat are prescription drug plans with a capitation arrangement, in which a predetermined amount is prepaid for specific services. Unlike the outpatient and inpatient claims, pharmaceutical claims are not linked to any diagnosis.

All healthcare service utilization can be linked to patient-specific enrollment information, which is stored in the enrollment table. Records in this table provide demographic and healthcare plan information for each patient on a monthly basis, thereby allowing the tracking of changes in the enrollment status of patients.

3.1.2 Enrollment identifier

For purposes of analysis, data contained in different datasets can be linked for each patient through his or her unique enrollment identifier (ENROLID), which is assigned by Medstat based on various types of information, including the data contributor, the encrypted employee identifier, the relationship of the enrollee to the contract holder or employee, the gender of the enrollee, and the enrollee's date of birth. As the level of detail provided by data contributors varies, Medstat assigns ENROLIDs by using different methods, taking into account the availability of personal-level enrollment data as well as the patient's date of birth.

If insufficient information is available to assign a unique ENROLID, this field is set to missing. This occurs in fewer than 1% of the records when one or more of the variables required to identify an individual are not provided by the data contributor.

Since the ENROLID is assigned based on the data contributor and the encrypted employee identifier, it may change throughout the year if the employee or contract holder changes employers and both employers are contained in the Medstat database.

3.1.3 Fee-for-service and capitated plans

The Commercial Claims and Encounters Database is based on information provided by various health insurance plans, which differ not only in terms of the amount negotiated and paid for health services, but also with regard to the type of payment of providers and facilities. Two general types exist: fee-for-service plans and capitated plans.

Fee-for-service plans are characterized by payments to the provider or facility for each service provided, based on the fee schedule specific to the health plan. This implies that financial data in fee-for-service claims represent the actual reimbursement of the provider by the payer or insurance company, the patient and potential third parties.

In contrast, for partially or fully capitated healthcare plans, Medstat contains so-called encounter claims, which often provide only limited financial information. Many managed care plans pay services based on a fixed pre-paid sum per member (capitation), thereby eliminating the need to collect financial information at the point of service delivery. As this leads to a disconnection of delivery of services and payments, any financial information contained in encounter claims has to be interpreted with caution.

While some encounter records mention a placeholder payment of zero or one dollar, others provide fee-for-service equivalents, which are intended to approximate payments for medical services and procedures under fee-for-service conditions. However, in 2002 the implementation of fee-for-service equivalents was in its early stages, potentially leading to an underestimation of costs of services. Therefore, only patients' payments contained in encounter records (i.e., copayments and deductibles, as well as other savings) were likely recorded with reasonable accuracy.

3.1.4 Healthcare plans

In the Commercial Claims and Encounters Database, healthcare plans are categorized into seven plan types, which differ in terms of incentives, coverage, and the method of reimbursement of providers and facilities. Table 6 shows the basic differences between plan types.

Table 6: Types of health plans[214]

Plan Type	Patient incentive to use certain providers?	PCP assigned?	Referral from PCP to specialist required?	Out of network services covered?	Partially or fully capitated?*
Basic/Major Medical[1]	No	No	n/a	n/a	No
Comprehensive[2]	No	No	n/a	n/a	No
EPO[3]	Yes	Yes	Yes	No	No
HMO[4]	Yes	Yes	Yes	No	Yes
Non-capitated POS[5]	Yes	Yes	Yes	Yes	No
PPO[6]	Yes	No	n/a	Yes	No
Capitated / partially capitated POS[7]	Yes	Yes	Yes	Yes	Yes

Abbreviations: PCP = Primary Care Physician; EPO = Exclusive Provider Organization; HMO = Health Maintenance Organization; POS = Point Of Service; PPO = Preferred Provider Organization

* Capitation refers to the following scenarios:

- A predetermined amount is prepaid to a provider for a specific group of services, which is defined in the contract, usually in an HMO arrangement. The provider is paid based upon the number of members who have selected him/her as their PCP.
- A fixed, predetermined amount is paid to a provider for each member who has elected to seek care from that provider. The total payment to the provider is based on the number of people who enroll without regard to the actual number or nature of services provided to members. This is the typical payment method for primary care in HMOs.

1: Coverage is provided in two phases: A basic policy covers the first set of charges, usually a hospital admission, with no out-of-pocket expenses. For charges beyond those covered by the basic policy, a major medical policy assumes coverage, generally with high patient payments for deductibles and co-insurance.

2: Patient payments for deductibles and co-insurance usually apply.

3: In an EPO, the patient must choose a PCP from a list of providers for all non-emergency care, who then manages all of his/her healthcare.

4: In an HMO, the patient must choose a PCP from a list of providers for all non-emergency care. In contrast to the EPO, services are paid for on a capitated basis.

5: Non-capitated POS plans offer financial incentives for patients to use a particular list of providers, such as lower copayments or deductibles. Although patients may seek treatment outside the network, this is usually associated with financial penalties in terms of higher copayments and deductibles.

6: PPO plans offer financial incentives for patients to use a particular list of providers. Unlike the POS, no selection of a PCP or referrals to specialists are required. Patients may seek treatment outside the network, but usually at a higher cost to the patient.

7: In capitated or partially-capitated POS plans, all or some of the services are paid on a capitated basis.

3.1.5 Financial and clinical variables

With the exception of encounter claims, financial information is based on final payments by the health insurance company or payer. Charges submitted by providers, information on negotiated and allowable amounts, as well as pricing reductions are not available, as these are business-confidential. Cost data therefore do not reflect true opportunity costs of healthcare services used, but rather best estimates of the true healthcare costs.

The following financial variables are recorded in all claims:

- The gross payment to a provider (e.g., physician, hospital, or pharmacy), which for fee-for-service claims is based on the eligible amount according to pricing guidelines and fee schedules, after application of relevant discounts.
- The net payment received by the provider, which equals the amount paid by the health insurance company after deduction of payments by patients and third parties.
- The copayment, which is the payment made by the patient to satisfy copayment or co-insurance provisions according to the insurance plan. The copayment is usually a fixed amount to be paid for a specific service or procedure at the time of service delivery. Co-insurance refers to the percentage of a covered medical expense to be paid after the deductible is met. Both patient payments are aggregated in the variable Copayment.
- The deductible, which is the payment made by the patient to satisfy the provisions of the insurance plan regarding deductibles, i.e., the portion of healthcare expenses that the subscriber has to pay before any health insurance coverage applies.
- The COB, which represents payments by Coordination of Benefits (COB) plans[67], Medicare, and other third party payers, as well as penalties.

[67] Coordination of Benefits (COB) is how healthcare carriers coordinate benefits when a patient is covered by more than one group healthcare plan. Under COB, carriers work together to ensure that the patient receives the maximum benefits available under the healthcare plans, i.e., the level of payments by one plan will cover up to 100% of the eligible expenses, when added to the benefits payable under another group plan. COB can therefore reduce or eliminate out-of-pocket expenses. COB also ensures that the combined payments of all coverages will not exceed the approved cost of care.

The total payment is applicable for inpatient claims only and represents the sum of all gross payments to providers who submitted claims for services rendered during a specific admission.

The following financial variables are recorded for pharmaceutical claims only:

- The ingredient cost of a pharmaceutical product, which, when added to the dispensing fee and the sales tax, usually equals the cost of a prescription. For most claims, the ingredient cost equals the discounted average wholesale price.
- The dispensing fee, which is the administrative fee charged by the pharmacy for dispensing the prescription.
- The sales tax, which, if applicable, is usually calculated based on the sum of the ingredient cost and the dispensing fee.
- The average wholesale price for a drug, which signifies the price charged by the wholesaler for the specific drug and is usually different from the pharmacy cost.

In addition to financial data, inpatient and outpatient claims contain clinical information in terms of diagnosis and procedure codes. Diagnosis codes are based on the 9th version of the International Classification of Disease, Clinical Modifications (ICD-9-CM)[215] classification system. For admissions, a principal diagnosis is also assigned, which is generally equivalent to the discharge diagnosis. It is important to note that pharmaceutical claims are not linked to any diagnosis.

For procedure codes, which may be recorded on outpatient and inpatient records, different classification systems are used by data contributors. The most prevalent system is the Current Procedural Terminology, 4th edition (CPT-4), which is frequently found on physician claims and outpatient facility claims. In addition, HCFA[68] Common Procedural Coding System (HCPCS) codes are used, especially for injectable drugs. For hospital claims based on ICD-9-CM procedure codes, a principal procedure is identified and recorded.

[68] HIPPA (Health Insurance Portability and Accountability Act) Compliance Federation of America

The quality of diagnosis and procedure codes varies between data contributors. Even though Medstat applies checks of reasonableness and validity, and, if needed, edits information provided, clinical information might be inaccurate or missing, as no validation against primary data sources (e.g., hospital records) can be performed.

3.2 Patient population

From the Commercial Claims and Encounters Database for the year 2002 all patients with a unique ENROLID with at least one outpatient or inpatient claim for bulimia nervosa (ICD-9 307.51) were extracted. Patients were eligible for inclusion if bulimia nervosa was listed at least once as either the primary diagnosis or as one of the secondary diagnoses (up to four) on one of the inpatient or outpatient claims. For these patients, all inpatient, outpatient, and pharmaceutical claims records as well as the socio-demographic information in the enrollment table were abstracted.

To be included in the analysis, patients had to be at least 12 years of age. This threshold was chosen because disease onset typically occurs during adolescence. A sensitivity analysis was performed by restricting the patient population to adults only; i.e., excluding those patients less than 18 years of age.

3.3 Data analysis

Patients with fee-for-service claims and encounter claims were analyzed separately, as financial information contained in encounter claims underestimates the costs of healthcare services, requiring approximation by fee-for-service equivalents.

Outcome measures of analysis included use of inpatient, outpatient, and pharmaceutical healthcare services as well as respective costs to insurers and patients. In addition, linear regression analysis was applied to assess whether total healthcare costs were influenced by patient demographic characteristics, including age, gender, relationship to employee,

geographic location (region), and type of insurance coverage, as well as by severity of illness. The number of different ICD-9 codes an individual was diagnosed with during the year was chosen as a proxy for severity of illness, assuming that individuals with more medical diagnoses were more severely ill. Due to the retrospective nature of this claims database analysis, only significance and strength of association between patient-specific factors and costs could be assessed, but no causality.

3.3.1 Fee-for-service claims

3.3.1.1 Data cleaning

Even though claims processors of Medstat attempt to correct potential errors in payments and codes before the database is made available to users for analysis, some inaccuracies in the information provided by contributors might go undetected and unadjusted. Therefore, database cleaning was necessary for this study.

Database cleaning focused on financial variables, as only those could at least partially be checked, whereas the accuracy of nonfinancial variables (e.g., diagnoses and patients' characteristics) could not be verified. As part of the database cleaning, all fee-for-service claims for patients with bulimia nervosa were reviewed in terms of the payments by health plans, patients, and third parties.

The following data checks were applied:

- For each correct claim, the sum of the COB amount, the patient's copayment, the patient's deductible, and net payment by the insurance company should equal the gross payment. An outpatient, inpatient, or pharmaceutical claim was considered inaccurate if this equation was not satisfied.
- In addition, for inpatient services the total payment for a hospitalization should equal the sum of individual payments associated with each admission. If this was not the case, the payments for the respective hospitalization were also considered inaccurate.

As the gross payment is based on the medical plan's fee schedule and as the net payment reflects the reimbursement by the payer, these are likely more accurately reported by data contributors than the information about the patient's copayment or deductible and the COB amount. Therefore, if inaccuracies were identified, it was in most cases assumed that the gross payment and the net payment accurately reflected the payment to the provider and the cost of the healthcare service to the payer, respectively. The inaccuracy was corrected by an adjustment amount, which was added to the respective claim in a newly created financial variable (see "Cleaning of financial records").

The original dataset extracted from Medstat included 20,107 individual fee-for-service claims records. Among these, numerous inaccurate claims were identified following the above-mentioned approach, which had to be resolved using different methods of data cleaning. In addition, the original dataset contained some adjustment records, which were entered by the claims processors as part of their data cleaning, but were not removed from the final database. In the following sections, the data cleaning performed as part of this analysis is described separately for adjustment records and inaccurate financial records.

i) Cleaning of nonfinancial adjustment records

Adjustment records for nonfinancial variables are characterized by a zero dollar amount for all financial variables as well as a zero value for all correctly reported nonfinancial variables, while those nonfinancial variables with originally erroneous information contain the new, revised data entry. Frequent examples include the codes for the standard place of provider, the standard type of provider, and the procedure code. During Medstat's database cleaning process, the original claims record and the adjustment record are normally deleted from the final database and only the corrected record, which contains all financial and nonfinancial information, is retained. However, some adjustment records for nonfinancial variables had not been removed from the 2002 dataset.

Since it was not feasible to uniquely identify for each adjustment record the respective original claims record—for example, due to no matching claim for the same date of service—adjustment records containing zero dollar payments were deleted from the database. The inclusion of these zero dollar claims records would have resulted in an overestimation of the number of healthcare services used, as potentially both the original and the adjustment record would have been included in the analysis. Altogether, 389 records were deleted, leaving 19,718 records for analysis.

ii) Cleaning of financial adjustment records

Two methods of adjustment are used by Medstat claims processors to correct errors in financial variables: the adjustment method and the void-and-replace method.

As part of the void-and-replace method, a new claim is generated that duplicates the original claim except that financial variables are entered as negatives, so that the erroneous claim is fully voided. The claim is then reentered as a new record (replacement record) containing the correct financial information. Claims processors usually delete the void and the original record during the database cleaning process and only the replacement record is retained in the final database. However, as strict matching criteria for void and original claims apply, some records may remain unresolved in the final database provided to users.

Altogether 12 unresolved adjustments were identified in the extracted dataset; i.e., the original record, the void record, and the replacement record existed. The 24 original and respective void records were removed from the dataset and only the 12 replacement records were retained, reducing the database for analysis to 19,694 fee-for-service claims.

In the adjustment method, a new claim is entered by the Medstat claims processors, which duplicates the correct nonfinancial variables of the erroneous claim and contains for incorrect financial variables a positive or negative dollar amount equaling the adjustments to be made. As all correctly reported financial variables of the erroneous claim are set to zero dollars in the adjustment claim, the sum of the financial values in the

erroneous claim and the adjustment claim equals the correct amount. Claims processors usually match the original and the adjustment record and create one new record, which is retained in the final database. However, as strict matching criteria apply, some adjustment and original records may remain in the database provided to users.

Altogether, three pairs of original and adjustment records were found in the dataset, which were resolved by correcting the financial variables in the original claims according to the information in the adjustment records and then removing the supplemental adjustment records. The dataset for analysis was thereby reduced to 19,691 records.

Thirty-eight records containing negative adjustment amounts could not be matched with any of the other claims for the respective patient based on either the date of service or the type of service provided. After careful evaluation of other claims for these patients, the adjustment records were deleted, leaving 19,653 records for analysis.

iii) Cleaning of financial records

The claims that remained after cleaning of adjustment records were checked for inaccuracies as described above. If a difference was identified between the gross payment and the sum of copayment, deductible, COB, and net payment, it was first attempted to resolve this by comparing the inaccurate claims with other similar claims for the same patient. Following this approach, 11 records in which the sum of COB and net payment was higher than the gross payment were corrected by adjusting the inaccurate claims (i.e., the COB and the net payment) according to other claims for the same patient and same type of service.

In some instances, services provided on the same day were contained in two or more financial records, but the net payment, the deductible or the COB were reported for all services combined in one of the respective claims. This led to inaccurate financial information in the individual claims, which was corrected by combining all claims for the same date of service and the same patient into one final record. In addition, the quantity of services was adjusted accordingly in the final claim. Following this approach, claims

for 11 dates of service were combined, leading to a reduction in the number of records analyzed by 82. Of note, the combined records were only used in the cost analysis, while the analysis of healthcare utilization took into account information on specific types of services contained in the individual records.

Finally, four claims with a positive net payment and a zero gross payment were corrected by setting the gross payment equal to the sum of net payment, copayment, and deductible. It was assumed that the net payment was accurately reported by the insurance company, so that a payment to the service provider had occurred.

3.3.1.2 Inclusion of supplemental financial variables

i) Pharmaceutical claims

Data cleaning by correction of the original claim was not always feasible; i.e., none of the methods described above could resolve the inaccuracies identified in some claims. Therefore, additional financial variables were introduced to adjust for differences between the gross payment and the sum of payments by the insurance company, the patient, and third parties. Where possible, it was assumed that the gross and/or net payments were correctly reported, since Medstat data contributors are more likely to record these accurately. As a variety of assumptions and adjustment methods had to be used, different supplemental variables were included to allow the identification of and differentiation between various types of adjustments. However, in the final cost analysis these had to be combined to simplify presentation of results.

For pharmaceutical claims, all financial variables were reviewed to detect and correct erroneous claims. In addition to calculating the sum of net payment, copayment, deductible, and COB as described above, the sum of ingredient cost, dispensing fee, and sales tax was also determined. In a correctly reported claim, both of these sums should equal the gross payment to the pharmacy.

If the net payment to the pharmacy was positive and both sums were equivalent, it was assumed that the gross payment was accurate, even if the two sums were different from

the gross payment. According to Medstat the gross payments are correctly reported in the majority of cases, and an adjustment of the gross payment was therefore not considered necessary. This is also supported by the fact that the drug-specific financial variables could have been erroneous, especially as some records contained a zero dollar sales tax or a zero dollar dispensing fee. To adjust for the difference observed in 118 records between the gross payment and the payments by the insurance company, the patient, and third parties, a new variable "additional drug payment (ADDPAYDRUG1)" was introduced. Assuming the net payment was correctly recorded, either the patient or the third party had likely borne this additional cost.

In addition, there were 12 drug claims for which the sum of the drug-specific financial variables and the sum of the patient's and payer's payments were also equivalent, but the net payment was zero. By analogy to the adjustment method described above, it was assumed that the gross payment to the pharmacy was correctly reported and two new variables "additional drug payment (ADDPAYDRUG2)" and "overpayment for drugs (OVERPAYDRUG1)" were introduced. If one assumes that the net payment was correct (i.e., the insurance company did not pay for the healthcare service), then either the patient or a third party had likely paid the additional cost. This was the case in eight claims records. The overpayment identified in four other claims can potentially be attributed to the patient, as in these records the net payment and the COB were zero.

Altogether, 25 drug claims were identified with both a gross and a net payment of less than $0.10 and a patient copayment of zero dollars. However, a payment to the pharmacy had likely occurred, as indicated by a positive ingredient cost and dispensing fee. For data cleaning purposes, it was assumed that the gross payment was equivalent to the ingredient cost plus the dispensing fee and the sales tax, if applicable. As it could not be determined whether the patient's or the insurance plan's payments were incorrectly reported in these claims, the difference between the adjusted gross payment and the net payment, if any, was captured as an additional drug payment (ADDPAYDRUG3).

In an additional seven drug claims records, the copayment by the patient was positive, while both the net and gross payments were less than $0.10. A drug had likely been dispensed by the pharmacy as indicated by a positive ingredient cost and dispensing fee. In accordance with the before-mentioned data correction method, the gross payment was assumed to be equivalent to the ingredient cost plus dispensing fee plus sales tax, if applicable, while the difference between the adjusted gross payment and the net payment plus copayment was captured as either an additional drug payment (ADDPAYDRUG4) or an overpayment (OVERPAYDRUG2). By analogy to the above, it could not be determined who had likely borne these costs and overpayments. Of note, in the few instances in which both the net and the gross payments were less than $0.10, the net payment could have been incorrect, since the gross payment was also likely inaccurately recorded.

If the gross payment was equivalent to the sum of ingredient cost, dispensing fee, and sales tax, but a difference was found between the gross payment and the sum of the patient's payments, the COB and the positive net payment, it was assumed that the gross payment to the pharmacy was correctly reported and the difference was captured as an additional drug payment (ADDPAYDRUG5) or an overpayment (OVERPAYDRUG3). If one assumes that the net payment was accurate, the additional drug payments in four records were likely made by either the patient or a third party, while the overpayments in an additional 143 records were likely attributable to the patient.

In an additional three claims records, the gross payment was also equivalent to the sum of ingredient cost, dispensing fee, and sales tax, but the net payment was zero. By analogy to the adjustment method described in the previous paragraph, it was assumed that the gross payment was correctly reported, and the differences between the gross payment and the sum of the patient's payments and the COB were captured in two cases as an additional drug payment (ADDPAYDRUG6) and in one case as an overpayment (OVERPAYDRUG4). If one assumes that the net payment was accurate, the additional payment as well as the overpayment were likely attributable to the patient.

Finally, two drug claims with a drug code number of zero and a zero dollar ingredient cost were deleted from the dataset, since zero is not a valid drug code. The gross and net payments in the respective claims were reported as less than $1.

After the above-described data cleaning process of pharmaceutical claims, 34 records with a zero dollar gross payment and net payment as well as a zero dollar ingredient cost remained. These were also removed from the database; an approximation of the ingredient cost and thereby the gross payment based the recorded average wholesale price of these drugs was not possible, as the relationship between the average wholesale price and the ingredient cost is not clearly identified.

ii) Outpatient claims

Among outpatient claims, 155 records were identified in which the sum of the patient's and the payer's payments did not equal the gross payment, while the copayment by the patient was zero. If one assumes that the gross and net payments were correctly reported, the difference had likely been paid by the patient and was therefore captured as an additional patient payment (PATPAY). For two outpatient claims, the difference between the gross payment and the patients' and payer's payments was negative. This overpayment (OVERPAYOUT) was in one case by the payer, since only the net payment was positive, and in the other case by the patient, assuming the net payment was accurate.

In an additional 138 outpatient claims, a difference was found between the gross payment and the payments by the insurance company, the patient, and third parties, but the copayment by the patient was positive. By analogy to the method described in the previous paragraph, it was assumed that the reported gross payment was correct and the differences observed were captured as additional outpatient payments (ADDPAY1) in 37 cases and outpatient overpayments (OVERPAYOUT) in 101 cases. If one assumes that the net payment was accurate, these costs were likely attributable to either the patient or a third party.

Finally, nine outpatient claims with a zero dollar net payment but a positive gross payment were identified. The difference between the gross payment and the payments by the patient and potentially third parties was captured as an additional outpatient payment (ADDPAY2), which had likely been incurred by the patient, if one assumes that the net payment was accurate (i.e., the insurance did not pay for the service).

iii) Inpatient claims

For inpatient claims associated with an admission, data cleaning was performed as described above for outpatient claims. Two inaccurate claims with a difference between the positive gross payment and the positive net payment and zero payments by the patient were identified. This difference was captured as an additional inpatient payment (PATPAYIN), which can be attributed to the patient, assuming the net payment was correctly reported.

A further 13 inpatient claims with a positive gross payment different from the sum of the patients' and insurers' payments were adjusted by capturing the difference either as an additional inpatient payment (ADDPAYIN1) or an inpatient overpayment (OVERPAYIN). Assuming the zero dollar net payment in three cases and the positive net payment in another case were accurate, either the patient or a third party had likely paid the additional costs. The inpatient overpayments in nine cases were likely attributable to the patient, assuming that the positive net payment was correctly reported.

In addition to the check of individual inpatient claims records, all individual payments associated with an admission were compared with the total payment reported for the respective case. This was important, as not all healthcare service utilization associated with an admission might have been billed separately. Fifty-two differences were identified and captured as additional inpatient payments (ADDPAYIN2). However, it was not possible to link these additional payments to specific healthcare services, nor could it be determined whether these payments were more likely attributable to the patient or the insurer.

After completion of the database cleaning, the final dataset of fee-for-service claims contained 19,537 records. It should be noted that in the majority of outpatient and drug claims the adjustment amounts (i.e., the additional payments and the overpayments) were very small. However, the additional financial variables had to be included to be able to perform aggregated financial analyses.

3.3.1.3 Healthcare utilization and costs

Patients' baseline characteristics, including the number and types of unique primary and secondary diagnoses, as well as healthcare resource utilization were analyzed in descriptive analyses. For each type of healthcare service, usage was assessed in terms of the number and percentage of patients having received the respective type of service, the mean number of services per patient, and the total number of services received by all patients included in the analysis. The number of services per patient was derived by multiplying the respective number of claims by the quantity of services reported in each claim. Since all claims with a zero quantity were linked to a specific service and payment, it was assumed that this was a coding error and a quantity of one was applied. For claims that were combined during the database cleaning process, the quantity of services reported in the original claims was used.

The cost of illness of bulimia nervosa was analyzed from the perspective of all payers and therefore the main outcome was the total cost, but individual payments by insurers, third parties, and patients were also reported. As the enrollment period—i.e., the duration of healthcare coverage—differed between patients, costs were converted to per-patient per-day estimates. Descriptive analyses were performed for all financial variables, including those added during the data cleaning process. Mean costs, together with measures of variability (5^{th} and 95^{th} percentile[69], minimum, maximum) were calculated both for all patients as well as for the subset of patients having received the respective healthcare service. Since costs were not normally distributed, the median was determined as well.

[69] Since the data were not normally distributed, the standard deviation was not an appropriate measure of variability and the 5^{th} and 95^{th} percentile were therefore calculated instead.

The main analysis reflected the total medical economic burden of patients with bulimia nervosa, as it included costs of comorbidities and complications. In a sensitivity analysis, the burden directly attributable to bulimia nervosa was estimated by including only those claims with the respective primary diagnosis. Since pharmaceutical claims are not linked to any diagnosis, drug costs could not be included in this analysis. In another sensitivity analysis, costs were determined for adult patients only, excluding those younger than 18 years.

To analyze the impact of patient characteristics on the mean total daily cost descriptively as well as statistically, univariate and regression analyses were performed. Since patient characteristics may change during the calendar year, assumptions had to be made for the seven patients who changed their type of health insurance throughout the year. For these patients, the plan type that covered the majority of days in 2002 was applied. Similarly, the region where patients lived for the majority of days in 2002 was used for the four patients who moved between regions.

Standard univariate and multivariate linear regression analyses were performed to assess the influence of patient-specific variables (predictors) on the mean per-person daily cost (3.3). The following independent variables were considered: age, number of unique primary and secondary diagnoses, gender, relationship to employee (self, spouse, child), type of insurance plan (comprehensive, POS, PPO, EPO, and PPO), and geographical location (Northeast, North Central, South, West, Unknown). In the absence of information on the severity of the patient's condition, the number of diagnoses was included as a proxy for overall health status.

In all regression analyses, a p-value less than or equal to 0.05 was considered to indicate statistical significance. All statistical analyses were performed using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

3.3.2 Encounter claims

3.3.2.1 Data cleaning

Since the encounter claims dataset also contained unresolved adjustment records, some data cleaning was required. Altogether, four claims with a negative gross payment were identified that could not be matched with any other claim for the same patient and the same date of service. These four adjustment claims were deleted from the encounter dataset. A further 12 outpatient claims that referred to adjustment and original records were deleted, and only the records containing the final corrected claims were retained.

Claims with either a zero quantity of services or zero days of supply had to be deleted from the dataset, as fee-for-service equivalents (as described in section 3.3.2.2) could not be determined. This was the case in four outpatient procedure claims and 23 drug claims. Seventeen of these drug claims were likely inaccurate, as they referred to a nonexistent drug code of zero. Others were erroneous, original drug claims, which had been corrected during the Medstat data cleaning process, as indicated by another claim with positive days of supply for the same drug and day of service.

3.3.2.2 Approximation of healthcare costs

As financial information in encounter claims is unlikely to reflect healthcare costs, it was attempted, where possible, to approximate costs of healthcare services based on those observed in the fee-for-service claims dataset. The imputation of healthcare costs based on fee-for-service averages has been used previously by other researchers, who included encounter claims in their analyses.[216] Since not all procedure and drug codes in the encounter claims dataset were also contained in the fee-for-service claims dataset, different methods of cost estimation had to be applied.

i) Approximation of costs of outpatient procedures

To estimate the healthcare costs of outpatient procedures in encounter claims, the respective mean fee-for service equivalents were determined. Since some fee-for-service claims referred to more than one procedure (quantity more than one), the mean gross payment, net payment, deductible, copayment, and COB were calculated per unit of a

specific procedure. Only those fee-for-service claims associated with a positive gross payment and with a quantity of services of at least one, were included in this calculation. Of the 2,416 encounter claims for outpatient procedures, 2,343 could be matched with a fee-for-service equivalent.

If no fee-for-service equivalent could be identified for the specific procedure, cost approximation based on the procedure group was attempted. As procedure groups are more broadly defined, mean fee-for-service equivalents are likely less accurate estimates of the costs in encounter claims. By analogy to the calculation of the mean cost per unit of a procedure, the mean cost per unit of a procedure group was determined. Altogether, 43 of the remaining 73 encounter claims for outpatient procedures could be matched with a fee-for-service equivalent procedure group cost.

If a fee-for-service equivalent for neither the procedure nor the procedure group could be identified, costs in encounter claims were approximated based on the mean unit cost per service type as derived from fee-for-service claims. This was feasible for 12 encounter claims. As service types reflect an even more aggregated level than procedure groups, respective fee-for-service equivalents provide only rough estimates of the costs in encounter claims.

For the remaining 18 encounter claims, no fee-for-service equivalents could be assigned. Instead it was assumed in 14 cases that the reported positive gross and net payments were reflective of the healthcare costs. Four encounter claims that contained a zero dollar gross payment had to be excluded from the analysis, as costs could not be estimated by any of the methods described above. One of these claims related to “therapy for vision” and three to “radiotherapy”.

ii) Approximation of costs of the remaining outpatient services

After the above-mentioned approximation of costs of procedures in the encounter dataset, there remained 120 outpatient records that were not linked to any specific procedure or procedure group code. It was therefore attempted to estimate costs based on fee-for-

service equivalents for the respective standard type of service. Following this approach, 88 outpatient claims could be associated with a fee-for-service equivalent.

For the remaining 32 encounter claims, assumptions had to be made, as approximation of costs by fee-for-service equivalents was not feasible. If the encounter claim referred to a quantity of at least one and contained a positive gross payment, it was assumed that this gross payment was reflective of the costs of services rendered. This approximation affected 21 of the remaining encounter claims. For three outpatient claims with a zero dollar gross payment, costs were estimated based on those recorded for another patient in the encounter claims dataset who recieved services at the same standard place and by the same standard provider type.

Finally, seven outpatient claims with a zero dollar gross payment had to be deleted, as it could not be established whether these claims reflected adjustment records or true healthcare service utilization. In addition, one outpatient claim that did not contain any information about the type of service rendered was excluded.

Fee-for-service equivalent costs were then estimated for each outpatient encounter claim by multiplying the quantity of services reported in the claim with the respective unit cost estimate.

iii) Approximation of costs of pharmaceuticals

By analogy to the encounter claims for outpatient procedures, costs of drugs were approximated by fee-for-service equivalents. Where possible, the mean unit cost per day of supply of the same drug was applied as a fee-for-service equivalent. Means were calculated based on all fee-for-service drug claims with a positive gross payment and at least one day of supply. Of the 4,537 encounter drug claims, 3,388 could be matched with drug-specific fee-for-service equivalents.

If no fee-for-service equivalent could be identified for the same drug, costs were approximated by the mean fee-for-service cost per day of supply of the respective

therapeutic drug class. As the latter encompasses a variety of different drugs, these fee-for-service equivalents are less accurate estimates for drug costs in encounter claims. Mean daily costs per therapeutic group were calculated as for drug-specific mean daily costs. Altogether, 1,086 encounter drug claims could be matched with fee-for-service equivalents based on the therapeutic drug class.

For the remaining 63 encounter drug claims with no fee-for-service equivalents for either the specific drug or therapeutic drug class, it was assumed that the payments reported in these encounter claims were reflective of the costs. For all but one, the net payment, copayment, deductible, and COB added up to the gross payment, and no further adjustment was required. However, one drug claim was associated with a zero dollar gross payment and, as a conservative estimate, it was assumed that the true gross payment was equivalent to the copayment.

Fee-for-service equivalent drug costs were estimated for each encounter claim by multiplying the recorded days of supply with the respective unit cost estimate.

iv) Approximation of costs of inpatient services

Due to the limited number of inpatient claims, it was not possible to estimate fee-for-service equivalents for each type of hospital service. Approximation of inpatient costs in encounter claims was therefore performed based on the Diagnosis Related Group (DRG) of the respective hospitalization. Mean total payments per case were calculated for each DRG contained in the fee-for-service dataset and then used to estimate costs of the 24 hospitalizations in the encounter claims dataset.

For those DRGs in the encounter dataset for which no fee-for-service equivalent could be identified, approximation by a similar DRG with a fee-for-service equivalent was attempted as follows:

- The fee-for-service equivalent for DRG 297, which applies to non-complicated cases, was substituted for DRG 296, which refers to nutritional and miscellaneous metabolic disorders with complications in persons at least 17 years of age.

- The fee-for-service equivalent for DRG 432, which refers to other mental disorder diagnoses, was substituted for DRG 431, which refers to childhood mental disorders.
- The fee-for-service equivalent for DRG 449, which applies to complications in patients at least 18 years of age, was substituted for DRG 451, which refers to poisoning and toxic effects of drugs in patients up to 17 years of age.

While the approximations for DRG 296 and DRG 451 affected one case each, that for DRG 431 was applied for three different hospitalizations of the same patient.

For two DRGs in the encounter claims dataset, no fee-for-service equivalent could be established. It was assumed that the total payment recorded in these encounter claims was reflective of the healthcare costs. This was the case for DRG 371 (Caesarean section) and DRG 383 (other antepartum diagnosis with medical complication).

The gross payments in inpatient encounter claims had to be adjusted for the purpose of data analysis, as the sum of the recorded individual gross payments for each case did not equal the total estimated payment for the respective admission. This was done by adding the difference to the gross payment of one of the inpatient claims associated with the case. Since the burden of illness was analyzed on a per-patient basis, this correction did not affect results, but was nevertheless necessary to enable calculation of average inpatient costs per patient.

After database cleaning and estimation of costs, as described above, the final encounter claims database consisted of 7,065 records.

3.3.2.3 Healthcare utilization and costs

The same analyses of patients' baseline demographics, healthcare utilization and respective costs were performed as for fee-for-service claims. The primary analysis of the cost of illness used the approximated costs, which were derived by fee-for-service equivalents for most encounter claims. In a secondary analysis, costs were calculated

according to the financial data contained in the original encounter claims. While the primary analysis is subject to the limitations imposed by an approximation of costs, the secondary analysis can be interpreted as a minimum estimate of the cost of illness.

The same sensitivity and univariate analyses were performed as for fee-for-service claims. Standard linear regression analyses, with the same independent variables as for the fee-for-service dataset, were applied to assess potential predictors of daily per-patient costs. Since the secondary analysis did not reflect the real costs of healthcare services, univariate and regression analyses were conducted only for the approximated mean daily per-patient cost, but not the unadjusted cost.

3.4 Results

3.4.1 Total patient population

Altogether, 980 patients with at least one outpatient or inpatient claim containing a primary or secondary diagnosis of bulimia nervosa were identified, two of whom had to be excluded because they were less than 12 years old. There were 22 claims for these two patients, including two outpatient claims and 20 drug claims, which were removed before database cleaning.

The final dataset for analysis consisted of 978 patients, 75 of whom were hospitalized at least once in 2002, while the remainder received only outpatient care. For these 978 patients, all outpatient and inpatient claims (9,173 and 503, respectively) were abstracted from the Medstat database, irrespective of whether the individual claim contained the diagnosis bulimia nervosa. In addition to the 9,676 outpatient and inpatient claims, 17,625 drug claims, which are not linked to any diagnosis, were identified, increasing the total dataset for analysis to 27,301 claims.

To be able to analyze the total cost of illness, including potential comorbidities and complications of bulimia nervosa, all claims for these 978 patients were considered. In a sensitivity analysis, claims were limited to those with a primary diagnosis of bulimia

nervosa, thereby reducing the sample to 933 patients with 9,007 outpatient and inpatient records.

3.4.2 Fee-for-service claims

After the cleaning of fee-for-service claims, the dataset contained 19,538 records for 675 patients with bulimia nervosa. These comprised 6,142 outpatient claims incurred by 649 patients, 438 inpatient claims for 55 patients, and 12,958 drug claims for 619 patients.

Since the healthcare enrollment period is critical for the determination of average daily treatment costs per patient, two patients with missing information regarding their start and/or end date of enrollment had to be excluded. The dataset was thereby reduced to 673 patients with bulimia nervosa and 19,535 fee-for-service claims.

3.4.2.1 Patient characteristics

Thirty-five patients were male (5.2%). The distribution of patients by age and other patient baseline characteristics is displayed in Table 7. About two thirds were younger than 30 years of age, and more than half (57.8%) were the children of the primary beneficiaries: i.e., the employees. The predominant health plan was the preferred provider organization (PPO) (51.6%). More employees and their dependents (41%) were located in the North Central region of the U.S. than in any other region.

Table 7: Patient baseline characteristics (fee-for-service dataset)

Patient characteristic	Frequency	Percent
Age group (years):		
• 12–19	228	33.88
• 20–29	227	33.73
• 30–39	89	13.22
• ≥ 40	129	19.17
Relationship to primary beneficiary:		
• Employee	205	30.46
• Spouse	79	11.74
• Child	389	57.80
Type of healthcare plan:		
• Comprehensive Care	178	26.45
• EPO	43	6.39
• POS	105	15.60
• PPO	347	51.56
Region:		
• North East	94	13.97
• North Central	279	41.46
• South	204	30.31
• West	95	14.12
• Unknown	1	0.15

Abbreviations: EPO = Exclusive Provider Organization; POS = Point Of Service; PPO = Preferred Provider Organization

In addition to treatment for bulimia nervosa, patients had also received healthcare services for a variety of other conditions. Based on only primary diagnoses of claims, 87% of the patients were treated for one condition, while the remainder received treatment for one or two additional conditions (Table 8). However, if all primary and secondary diagnoses were considered, approximately 19% of patients had received treatment in relation to two or more conditions.

Table 8: Number of diagnoses per patient* (based on primary and secondary diagnoses in the fee-for-service dataset)

Number of diagnoses per patient	Primary diagnosis		Primary & secondary diagnoses	
	Number of patients	Percent of patients	Number of patients	Percent of patients
1	587	87.22	542	80.53
2	75	11.14	80	11.89
3	11	1.63	23	3.42
4			13	1.93
5			9	1.34
6			2	0.30
7			3	0.45
8			1	0.15
Total	**673**	**100.00**	**673**	**100.00**

* Each diagnosis was counted only once per patient. Outpatient and inpatient claims may contain up to 4 secondary diagnoses in addition to the primary diagnosis.

Table 9 shows the frequency of primary and secondary diagnoses by ICD-9 class and ICD-9 code, as recorded in the claims data, with each diagnosis being counted only once per patient. The most prevalent comorbidities or complications of patients with bulimia nervosa based on all diagnoses as well as primary diagnoses only were: symptoms concerning nutrition, metabolism, and development (69 and 65 patients, respectively), episodic mood disorders (40 and 23 patients, respectively), not-elsewhere classified depressive disorders (18 and 5 patients, respectively), nondependent abuse of drugs (13 and 0 patients, respectively), and anxiety, dissociative, and somatoform disorders (12 and 2 patients, respectively). While 641 of the 673 included patients had been treated primarily for bulimia nervosa at least once, the remaining ones had, in addition to a secondary diagnosis of bulimia nervosa, at least once the primary diagnosis of polyphagia, a disorder very similar in symptoms to bulimia nervosa.

Table 9: Frequency of diagnoses per patient* (based on all diagnoses [All DX] and primary diagnoses only [1° DX] in the fee-for-service dataset)

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	ALL DX (%)	1° DX (n)	1° DX (%)
1. Infectious and parasitic diseases			**1**			
75		Infectious mononucleosis	1	0.15		
3. Endocrine, nutritional, and metabolic diseases, and immunity disorders			**13**		**3**	
244		Acquired hypothyroidism	1	0.15		
	244.9	Unspecified hypothyroidism	1	0.15		
250		Diabetes mellitus	1	0.15	1	0.15
	250.13	Diabetes with ketoacidosis (250.1)	1	0.15	1	0.15
263		Other and unspecified protein-calorie malnutrition	1	0.15		
	263.0	Malnutrition of moderate degree	1	0.15		
275		Disorders of mineral metabolism	1	0.15		
	275.2	Disorders of magnesium metabolism	1	0.15		
276		Disorders of fluid, electrolyte, and acid-base balance	9	1.34	2	0.30
	276.0	Hyperosmolatility and/or hypernatremia	1	0.15		
	276.2	Acidosis	1	0.15		
	276.5	Volume depletion	2	0.30		
	276.8	Hypokalemia	5	0.74	2	0.30
5. Mental disorders			**783**		**680**	
291		Alcohol-induced mental disorders	1	0.15		
	291.81	Alcohol withdrawal	1	0.15		
292		Drug-induced mental disorders	1	0.15		
	292.0	Pathological drug intoxication	1	0.15		

Table 9 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	ALL DX (%)	1° DX (n)	1° DX (%)
296		Episodic mood disorders	40	5.94	23	3.42
	296.20	Major depressive disorder, single episode – unspecified	8	1.19	4	0.60
	296.22	Major depressive disorder, single episode – moderate	1	0.15		
	296.23	Major dep. dis., single epi.– severe, w/o mention of psychotic beh.	3	0.45	2	0.30
	296.25	Maj. Dep. Dis., single episode – in partial or unspecified remission	1	0.15	1	0.15
	296.30	Major depressive disorder, recurrent episode – unspecified	7	1.04	3	0.45
	296.32	Major depressive disorder, recurrent episode – moderate	5	0.74	1	0.15
	296.33	Maj. Dep. Dis., recurrent epi.– severe, w/o mention of psy. beh.	3	0.45	3	0.45
	296.34	Maj. Dep. Dis., recurrent epi.– severe, with psychotic beh.	1	0.15	1	0.15
	296.50	Bipolar I disorder, most recent/current episode depressed – unspec.	2	0.30	2	0.30
	296.52	Bip. I dis., most recent/current episode depressed – moderate	1	0.15	1	0.15
	296.53	Bip. I dis., most rec./cur. epi. dep.– severe, w/o mention of psy. beh.	2	0.30	2	0.30
	296.60	Bipolar I disorder, most recent/current episode mixed – unspecified	3	0.45	3	0.45
	296.80	Bipolar I disorder – unspecified	1	0.15		
	296.89	Bipolar I disorder – other	2	0.30	2	0.30
300		Anxiety, dissociative and somatoform disorders	12	1.78	2	0.30
	300.00	Anxiety state, unspecified	5	0.74	1	0.15
	300.02	General anxiety disorder	2	0.30		
	300.3	Obsessive-compulsive disorders	2	0.30		
	300.4	Dysthymic disorder	2	0.30	1	0.15
	300.9	Unspecified nonpsychotic mental disorder	1	0.15		
301		Personality disorders	6	0.89		
	301.83	Borderline personality	2	0.30		
	301.9	Unspecified personality disorder	4	0.59		

Table 9 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	ALL DX (%)	1° DX (n)	1° DX (%)
303		Alcohol dependence syndrome	5	0.74	2	0.30
	303.90	Alcohol dependence – unspecified	3	0.45	1	0.15
	303.91	Other and unspecified alcohol dependence – continuous	2	0.30	1	0.15
305		Nondependent abuse of drugs	13	1.93		
	305.00	Alcohol abuse – unspecified	3	0.45		
	305.1	Tobacco use disorder	3	0.45		
	305.20	Cannabis abuse – unspecified	3	0.45		
	305.70	Amphetamine or related acting sympathomimetic abuse – unspec.	1	0.15		
	305.90	Other, mixed, or unspecified drug abuse – unspecified	3	0.45		
307		Special symptoms or syndromes, not elsewhere classified	681	101.19	646	96.00
	307.1	Anorexia nervosa	4	0.59		
	307.50	Eating disorder, unspecified	1	0.15	1	0.15
	307.51	Bulimia	673	100.00	641	95.25
	307.53	Rumination disorder	1	0.15	1	0.15
	307.54	Psychogenic vomiting	1	0.15	1	0.15
	307.7	Encopresis (fecal soiling)	1	0.15		
309		Adjustment reaction	4	0.59	2	0.30
	309.0	Adjustment disorder with depressed mood	1	0.15		
	309.81	Posttraumatic stress disorder	3	0.45	2	0.30
311	311	Depressive disorder, not elsewhere classified	18	2.67	5	0.74
312		Disturbance of conduct, not elsewhere classified	1	0.15		
	312.32	Kleptomania	1	0.15		
313		Disturbance of emotions specific to childhood and adolescence	1	0.15		
	313.9	Unspecified emotional disturbance of childhood or adolescence	1	0.15		

Table 9 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	ALL DX (%)	1° DX (n)	1° DX (%)
7. Diseases of the circulatory system			**2**			
427		Cardiac dysrhythmias	1	0.15		
	427.9	Cardiac dysrhythmia, unspecified	1	0.15		
458		Hypotension	1	0.15		
	458.0	Orthostatic hypotension	1	0.15		
8. Diseases of the respiratory system			**4**		**2**	
465		Acute upper respiratory infections of multiple or unspecified sites	1	0.15		
	465.9	Unspecified site	1	0.15		
490	490	Bronchitis, not specified as acute or chronic	1	0.15		
507		Pneumonitis due to solids and liquids	1	0.15	1	0.15
	507.0	Due to inhalation of food or vomitus	1	0.15	1	0.15
518		Other diseases of lung	1	0.15	1	0.15
	518.1	Interstitial emphysema	1	0.15	1	0.15
9. Diseases of the digestive system			**8**		**3**	
521		Diseases of hard tissues of teeth	1	0.15		
	521.3	Erosion	1	0.15		
530		Diseases of esophagus	3	0.45	1	0.15
	530.10	Esophagitis, not elsewhere specified	1	0.15		
	530.11	Reflux esophagitis	1	0.15	1	0.15
	530.81	Esophageal reflux	1	0.15		
535		Gastritis and duodenitis	3	0.45	2	0.30
	535.50	Unspecified gastritis & gastroduodenitis, w/o mention obstruction	3	0.45	2	0.30

Table 9 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	ALL DX (%)	1° DX (n)	1° DX (%)
536		Disorders of function of stomach	1	0.15		
	536.8	Dyspepsia and other specified disorders of function of stomach	1	0.15		
10. Diseases of the genitourinary system			**3**		**2**	
581		Nephrotic syndrome	1	0.15	1	0.15
	581.9	Nephrotic syndrome with unspec. pathological lesion in kidney	1	0.15	1	0.14
595		Cystitis	1	0.15		
	595.0	Acute cystitis	1	0.15		
620		Noninflammatory disorder ovary, fallopian tube & broad ligament	1	0.15	1	0.15
	620.2	Other and unspecified ovarian cyst	1	0.15	1	0.15
13. Diseases of the musculoskeletal system and connective tissue			**4**		**1**	
723		Other disorders of cervical region	1	0.15		
	723.1	Cervicalgia	1	0.15		
724		Other and unspecified disorders of back	1	0.15		
	724.5	Backache, unspecified	1	0.15		
729		Other disorders of soft tissues	1	0.15		
	729.1	Myalgia and myositis, unspecified	1	0.15		
733		Other disorders of bone and cartilage	1	0.15	1	0.15
	733.6	Tietze's disease	1	0.15	1	0.15
16. Symptoms, signs, and ill-defined conditions			**82**		**73**	
780		General symptoms	4	0.59	3	0.45
	780.2	Syncope and collapse	2	0.30	2	0.30
	780.4	Dizziness and giddiness	1	0.15	1	0.15
	780.57	Unspecified sleep apnea	1	0.15		

Table 9 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	ALL DX (%)	1° DX (n)	1° DX (%)
783		Symptoms concerning nutrition, metabolism, and development	69	10.25	65	9.66
	783.21	Loss of weight	1	0.15		
	783.41	Failure to thrive	1	0.15	1	0.15
	783.6	Polyphagia	67	9.96	64	9.51
784		Symptoms involving head and neck	2	0.30	1	0.15
	784.0	Headache	2	0.30	1	0.15
786		Symptoms involving respiratory system and other chest symptoms	2	0.30	1	0.15
	786.05	Shortness of breath	1	0.15	1	0.15
	786.51	Precordial pain	1	0.15		
787		Symptoms involving digestive system	1	0.15	1	0.15
	787.03	Vomiting alone	1	0.15	1	0.15
789		Other symptoms involving abdomen and pelvis	4	0.59	2	0.30
	789.00	Abdominal pain – unspecified site	2	0.30	1	0.15
	789.03	Abdominal pain – right lower quadrant	1	0.15		
	789.06	Abdominal pain – epigastric	1	0.15	1	0.15
17. Injury and poisoning			**4**		**3**	
881		Open wound of elbow, forearm, and wrist	1	0.15		
	881.02	Without mention of complication – wrist	1	0.15		
935		Foreign body in mouth, esophagus, and stomach	1	0.15	1	0.15
	935.2	Stomach	1	0.15	1	0.15
965		Poisoning by analgesics, antipyretics, and antirheumatics	1	0.15	1	0.15
	965.1	Salicylates	1	0.15	1	0.15
969		Poisoning by psychotropic agents	1	0.15	1	0.15
	969.0	Antidepressants	1	0.15	1	0.15

Table 9 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	ALL DX (%)	1° DX (n)	1° DX (%)
V. Suppl. class. of factors influencing health status/contact with health services			**5**		**1**	
	V22.2	Normal pregnancy, pregnant state, incidental	1	0.15		
	V58.69	Long-term (current) use of other medications	1	0.15	1	0.15
	V61.10	Counseling for marital and partner problems, unspecified	1	0.15		
	V65.3	Dietary surveillance and counseling	1	0.15		
	V72.6	Laboratory examination	1	0.15		

* Each diagnosis was counted only once per patient. Outpatient and inpatient claims may contain up to 4 secondary diagnoses in addition to the primary diagnosis.

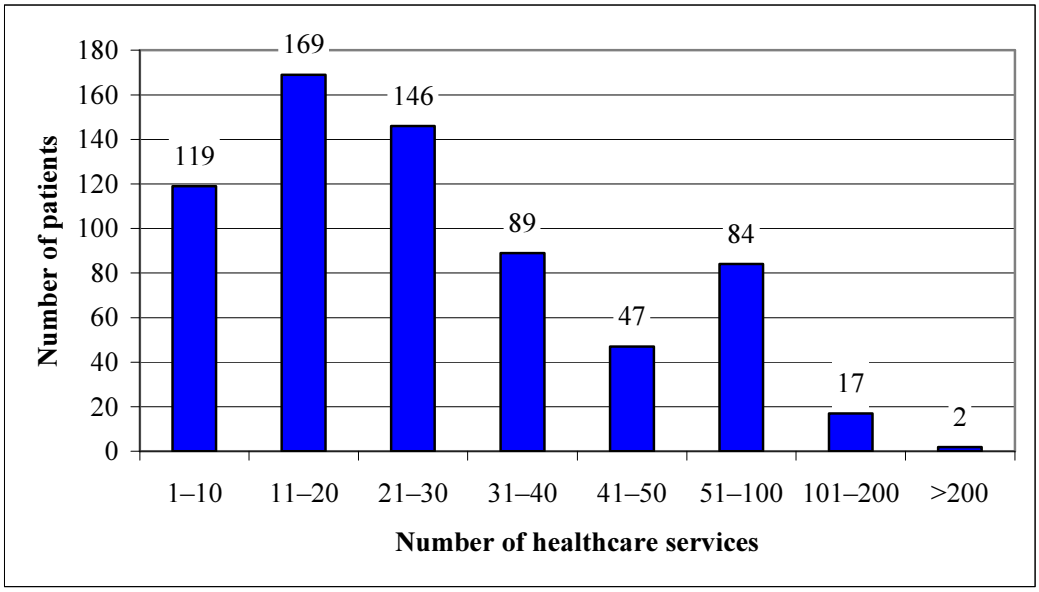
Abbreviation: DX = diagnosis

3.4.2.2 Healthcare utilization

The utilization of healthcare services by patients with bulimia nervosa was explored in terms of the number and types of resources used. Costs incurred due to treatment are described in section 3.4.2.3.

Throughout the year 2002, patients used on average 30.98 outpatient, inpatient, and pharmaceutical services, with a minimum of 1 and a maximum of 448. While the majority of patients received 40 or fewer services, approximately 12.5% had between 51 and 100 (Figure 1). Two patients used more than 200 services: one received the same drug 131 times in an outpatient hospital setting, while the other received 421 applications of the same drug while hospitalized.

Figure 1: Number of healthcare services* used per patient (fee-for-service dataset)



* Healthcare services include outpatient and inpatient services as well as prescriptions.

As services refer to inpatient and outpatient services as well as prescriptions, high-volume users are not necessarily patients receiving resource-intensive treatments and incurring high healthcare costs. A description of the types of healthcare services used is therefore warranted.

However, for many claims included in the analysis, information regarding the procedure code, the place of service, the provider type, or the service type was either not applicable (e.g., in case of pharmaceutical claims), or missing. Therefore, results reported in the following tables reflect only a subset of all healthcare services, which might not be representative if missing information was nonrandomly distributed.

Results are presented in terms of the number and percentage of patients having received the specific service, the average number of services used per patient, the total, combined number of services used by all patients, and the respective percentage distribution. Apart from DRG codes, all other calculations of the number of services take the quantity of services recorded in each claim into account. For example, if one claim referred to five services in the same place, the respective place of service was counted five times.

Among the claims containing information about the place of service—i.e., claims with non-missing information—the most frequent site was the physician office (80.8% of patients and 60.9% of all services), followed by outpatient hospital (16.2% of patients and 8.5% of services) and inpatient hospital (9.1% of patients and 18.8% of services; Table 10). The average number of claims for services in physician offices and outpatient hospital facilities were 8.8 and 6.2 per patient per year, respectively, while the average for inpatient hospital treatments was 24.4 due to the more intensive therapy in the inpatient setting, leading to numerous claims per patient.

Table 10: Frequency of places of service (fee-for-service dataset)

Code	Place of service	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
11	Office	544	80.83	8.83	4,804	60.90
12	Patient home	1	0.15	1.00	1	0.01
21	Inpatient hospital	61	9.06	24.36	1,486	18.84
22	Outpatient hospital	109	16.20	6.15	670	8.49
23	ER – hospital	12	1.78	2.25	27	0.34
31	Skilled nursing facility	1	0.15	3.00	3	0.04
34	Hospice	2	0.30	2.00	4	0.05
51	Inpatient psychiatric facility	6	0.89	11.33	68	0.86
52	Psychiatric facility, partial hospitalization	26	3.86	7.88	205	2.60
53	Community mental healthcare center	1	0.15	12.00	12	0.15
55	Residential substance abuse facility	1	0.15	21.00	21	0.27
56	Psychiatric residential treatment center	2	0.30	10.50	21	0.27
61	Comprehensive inpatient rehabilitation facility	4	0.59	6.75	27	0.34
62	Comprehensive outpatient rehabilitation facility	1	0.15	1.00	1	0.01
81	Independent laboratory	14	2.08	4.64	65	0.82
95	Outpatient (NEC)	47	6.98	9.70	456	5.78
99	Other unlisted facility	4	0.59	4.25	17	0.22
Total					**7,888**	**100.00**

Abbreviations: NEC = Not Elsewhere Classified; no. = number

* Each patient can have been treated at different places of service or at none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 678 and 100%, respectively.

† The mean/patient reflects the average number of times a patient visited the respective place of service.

‡ The total number of services reflects the overall number of times the respective place of service was used by all patients included in the analysis.

§ The total percent shows the overall distribution of the utilization of places of service by all patients.

The predominant types of providers involved in the care of patients were the supportive therapist (25.9% of patients and 28.5% of services) and the psychologist (20.4% of

patients and 18.8% of services; Table 11). Patients received on average 10.9 and 9.2 services from the supportive therapist and the psychologist, respectively, during the year.

Table 12 demonstrates that the most frequent group of procedures was other psychiatric services (78.9 of patients and 79.8% of services). In concordance with this result, the most prevalent type of service was individual psychiatric therapy (60.5% of patient and 50.3% of service; Table 13), with an average number of 9.6 therapies per patient per year.

Table 11: Frequency of provider types (fee-for-service dataset)

Code	Provider type	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
1	Acute care hospital	81	12.04	9.01	730	10.95
5	Ambulatory surgery center	1	0.15	2.00	2	0.03
20	Mental health/chemical dependency NEC	22	3.27	26.95	593	8.89
21	Mental health facility	25	3.71	15.04	376	5.64
22	Chemical dep. treat. center	1	0.15	9.00	9	0.13
23	Mental health/chemical dependency day care	1	0.15	2.00	2	0.03
35	Residential treatment center	3	0.45	10.00	30	0.45
40	Other facility (NEC)	8	1.19	2.50	20	0.30
42	Special care facility (NEC)	1	0.15	4.00	4	0.06
170	Pathology	4	0.59	2.25	9	0.13
180	Radiology	4	0.59	1.00	4	0.06
200	Medical doctor, MD (NEC)	92	13.67	6.76	622	9.33
202	Osteopathic medicine	3	0.45	2.00	6	0.09
204	Internal medicine (NEC)	25	3.71	2.08	52	0.78
206	Multi-specialty physician group	7	1.04	3.43	24	0.36
220	Emergency Medicine	2	0.30	1.50	3	0.04
230	Allergy & immunology	1	0.15	1.00	1	0.01
240	Family practice	42	6.24	2.45	103	1.54
250	CV disorder/cardiology	3	0.45	2.00	6	0.09
260	Neurology	2	0.30	3.50	7	0.10
275	Gastroenterology	1	0.15	1.00	1	0.01
320	Obstetrics & gynecology	2	0.30	1.00	2	0.03
365	Psychiatry	115	17.09	5.97	686	10.29
400	Pediatrician (NEC)	19	2.82	1.53	29	0.43
530	Orthopedic surgery	1	0.15	3.00	3	0.04
810	Dietician	2	0.30	1.00	2	0.03
815	Medical technician	1	0.15	1.00	1	0.01
822	Nursing services	5	0.74	4.80	24	0.36
825	Nurse practitioner	1	0.15	2.00	2	0.03
853	Therapists (supportive)	174	25.85	10.93	1,901	28.51
860	Psychologist	137	20.36	9.17	1,256	18.83
900	Health educator/agency	2	0.30	10.00	20	0.30
905	Transportation	1	0.15	2.00	2	0.03
920	Home health organization/agency	1	0.15	1.00	1	0.01
930	Laboratory	23	3.42	5.91	136	2.04
Total					**6,669**	**100.00**

Abbreviations: NEC = Not Elsewhere Classified; no. = number; dep. = dependency; CV = cardiovascular
* Each patient can have been treated by different provider types or by none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 678 and 100%, respectively.
† The mean/patient reflects the average number of times a patient visited the respective provider type.
‡ The total number of services reflects the overall number of times the respective provider type was visited by all patients included in the analysis.
§ The total percent shows the overall distribution of the utilization of provider types by all patients.

Table 12: Frequency of procedure groups (fee-for-service dataset)

Code	Procedure group	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
31	Venipucture (blood draw)	30	4.46	1.27	38	0.64
101	Office visits, new patient	18	2.67	1.00	18	0.30
104	Office visits, established patient	86	12.78	1.65	142	2.39
111	ER visit, new patient	9	1.34	1.33	12	0.20
120	Consultation	6	0.89	1.00	6	0.10
129	Other medical services	10	1.49	5.50	55	0.93
131	Injections, therapeutic, IV	1	0.15	2.00	2	0.03
133	Preventive medical services	1	0.15	3.00	3	0.05
136	Psychotherapy, family	41	6.09	3.54	145	2.44
137	Psychotherapy, group	35	5.20	9.89	346	5.83
138	Psychiatric advice, non-patient	1	0.15	1.00	1	0.02
139	Other psychiatric services	531	78.90	8.91	4,731	79.71
155	EKG	14	2.08	1.21	17	0.29
157	EKG monitoring	1	0.15	1.00	1	0.02
177	Other neurology services	23	3.42	1.22	28	0.47
197	Specimen handling	6	0.89	1.67	10	0.17
198	Medical supplies	2	0.30	1.00	2	0.03
199	All other medical procedures	9	1.34	3.11	28	0.47
202	X-ray, chest	3	0.45	1.00	3	0.05
205	X-ray, gastrointestinal tract	1	0.15	1.00	1	0.02
229	Diagnosis radiology, miscellaneous/other	2	0.30	1.00	2	0.03
301	Blood chemistry test/automat	5	0.74	1.00	5	0.08
302	Blood chemistry, drug monitor	3	0.45	1.00	3	0.05
303	Lab test, organ/disease panel	41	6.09	1.51	62	1.04
306	Routine urinalysis	10	1.49	1.20	12	0.20
307	Other urinalysis	1	0.15	1.00	1	0.02

Table 12 continued

Code	Procedure group	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
311	Thyroid function test (RIA)	20	2.97	1.40	28	0.47
312	Thyroid function test (non-RIA)	3	0.45	1.33	4	0.07
313	Other radio-immunoassays	9	1.34	3.22	29	0.49
319	Other chemical/toxicology tests	22	3.27	6.55	144	2.43
331	Blood count, automated	30	4.46	1.17	35	0.59
332	Blood count, manual	1	0.15	1.00	1	0.02
334	Blood tests, sedimentation rate	4	0.59	1.00	4	0.07
336	Blood count: Hgb/Hct	2	0.30	1.50	3	0.05
349	Immunology tests	2	0.30	1.00	2	0.03
363	Bacterial culture, urine	2	0.30	1.50	3	0.05
372	Surgical pathology	1	0.15	2.00	2	0.03
379	Other anatomic pathology services	1	0.15	1.00	1	0.02
399	All other pathology/ laboratory procedures	2	0.30	2.50	5	0.08
Total					**5,935**	**100.00**

Abbreviations: no. = number; ER = emergency room; IV = intravenous; EKG = electrocardiogram; RIA = radio-immunoassays

* Each patient can have received different procedure groups or none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 678 and 100%, respectively.

† The mean/patient reflects the average number of times a patient received the respective procedure group.

‡ The total number of services reflects the overall number of times the respective procedure group was used by all patients included in the analysis.

§ The total percent shows the overall distribution of the utilization of procedure groups by all patients.

Table 13: Frequency of service types (fee-for-service dataset)

Code	Service type	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
1	Surgery (NEC)	21	3.12	1.24	26	0.34
50	Physician attendance	127	18.87	2.46	313	4.03
60	Room and board (NEC)	48	7.13	17.19	825	10.63
61	Intensive care unit	1	0.15	5.00	5	0.06
68	All inclusive – room, board, ancillary	3	0.45	16.67	50	0.64
69	Other room charges	10	1.49	1.40	14	0.18
75	Ancillary and facility services (NEC)	5	0.74	5.80	29	0.37
76	Clinic (NEC)	1	0.15	2.00	2	0.03
77	Emergency services	13	1.93	1.77	23	0.30
78	Transportation	1	0.15	2.00	2	0.03
80	Supplies (NEC)	6	0.89	1.33	8	0.10
81	Inpatient pharmacy/IV therapy	17	2.53	4.29	73	0.94
83	Blood	1	0.15	2.00	2	0.03
85	Diagnostic services (NEC)	4	0.59	1.25	5	0.06
86	Diagnostic lab	87	12.93	7.07	615	7.92
87	Diagnostic radiology	8	1.19	1.00	8	0.10
88	Computerized axial tomography scan	1	0.15	1.00	1	0.01
91	Electrocardiogram	13	1.93	1.08	14	0.18
93	Diagnostic cardiology	1	0.15	2.00	2	0.03
100	Psychiatric/substance abuse (NEC)	6	0.89	5.50	34	0.44
101	Psychiatric (NEC)	166	24.67	3.90	648	8.35
102	Substance abuse (NEC)	1	0.15	1.00	1	0.01
104	Psychiatric day/night care	30	4.46	7.10	213	2.74
105	Psychiatric exam/testing	215	31.95	1.25	269	3.47
106	Individual psychiatric therapy	407	60.48	9.59	3,902	50.28
107	Group psychiatric therapy	76	11.29	8.00	608	7.83
110	Therapies/treatments (NEC)	5	0.74	1.20	6	0.08
114	Occupational therapy	3	0.45	2.00	6	0.08
115	Physical therapy	1	0.15	2.00	2	0.03
131	Health education	7	1.04	3.43	24	0.31
155	Drugs (NEC)	3	0.45	9.33	28	0.36
156	Generic drugs	1	0.15	1.00	1	0.01
158	Injectable medications	1	0.15	2.00	2	0.03
Total					**7,761**	**100.00**

Abbreviations: NEC = Not Elsewhere Classified; no. = number
* Each patient can have received different service types or none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 678 and 100%, respectively.
† The mean/patient reflects the average number of times a patient received the respective service type.
‡ The total number of services reflects the overall number of times the respective service type was used by all patients included in the analysis.
§ The total percent shows the overall distribution of the utilization of service types by all patients.

In addition to information about types of services and procedures rendered, the inpatient claims records contain a DRG code for each hospitalization. Among the admissions of patients with bulimia nervosa, the predominant DRG codes were for other mental disorders (3.7% of patients and 44.9% of hospitalizations) and psychoses (2.5% of patients and 26.1% of hospitalizations; Table 14).

As a large number of different branded and generic drugs were prescribed to patients with bulimia nervosa, respective resource utilization is described in Table 15 in terms of groups of therapeutic agents. The most frequently prescribed drugs were those for the central nervous system (79.6% of patients and 49.7% of prescriptions), followed by hormones and synthetic substitutes (46.2% of patients and 14.3% of prescriptions). Patients received these medications for an average of 210 days and 153 days, respectively, during the year. An additional finding was that approximately 60% of patients had at least once filled a prescription for anti-infectives, which could be an indicator of generally impaired health status of these patients.

Table 14: Frequency of DRGs among all admissions[*] (fee-for-service dataset)

Code	DRG	No. of patients[†]	% of patients[†]	Total no.[‡]	Total percent[§]
80	Respiratory infections & inflammations without complications, age > 17 years	1	0.15	1	1.45
94	Pneumothorax with complications	1	0.15	1	1.45
141	Syncope & collapse with complications	1	0.15	1	1.45
182	Esophagitis, gastroenteritis & misc. digestive disorders with complications, age > 17 years	2	0.30	2	2.90
297	Nutritional & misc. metabolic disorders without complications, age > 17 years	2	0.30	2	2.90
331	Other kidney & urinary tract diagnoses with complications, age > 17 years	1	0.15	1	1.45
424	O.R. procedure with principal diagnoses of mental illness	2	0.30	2	2.90
426	Depressive neuroses	2	0.30	2	2.90
427	Neuroses except depressive	2	0.30	2	2.90
428	Disorders of personality & impulse control	2	0.30	2	2.90
430	Psychoses	17	2.53	18	26.09
432	Other mental disorders	25	3.71	31	44.93
449	Poisoning & toxic effects of drugs with complications, age > 17 years	1	0.15	1	1.45
483	Tracheostomy except for face, mouth & neck diagnoses	1	0.15	1	1.45
521	Alcohol/drug abuse or dependence with complications	1	0.15	1	1.45
523	Alcohol/drug abuse of dependence without rehabilitation therapy without complications	1	0.15	1	1.45
Total				**69**	**100.00**

[*] Each DRG refers to one unique admission.
[†] Each patient can have been hospitalized multiple times or not at all; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 678 and 100%, respectively.
[‡] The total number of DRGs reflects the overall number of times the respective DRG was recorded as the primary reason for a hospitalization.
[§] The total percent shows the overall distribution of DRGs among all hospitalizations.

Table 15: Frequency of therapeutic groups (fee-for-service dataset)

Code	Therapeutic Group	No. of patients*	Percent of patients*	Days/ patient†	Total no.‡	Total percent§
01	Antihistamines and combinations	157	23.33	56.62	513	3.53
02	Anti-infective agents	406	60.33	26.31	1,355	9.34
03	Antineoplastic agents	6	0.89	123.00	29	0.20
04	Autonomic drugs	169	25.11	53.25	616	4.24
06	Blood forming/coagulating agents	7	1.04	90.71	31	0.21
07	Cardiovascular agents	57	8.47	255.75	387	2.67
08	Central nervous system	536	79.64	210.46	7,211	49.68
10	Dental agents	7	1.04	20.71	11	0.08
11	Diagnostic agents	7	1.04	312.86	56	0.39
13	Electrolytic, caloric, water	46	6.84	104.02	199	1.37
15	Antituss/expector/mucolytic	70	10.40	10.77	116	0.80
16	Eye, ear, nose, throat	106	15.75	27.63	228	1.57
17	Gastrointestinal drugs	137	20.36	90.34	569	3.92
20	Hormones & synthetic substitutes	311	46.21	153.40	2,070	14.26
21	Immunosuppressants	4	0.59	270.00	14	0.10
23	Oxytoxics	2	0.30	0.50	2	0.01
26	Skin & mucous membrane	245	36.40	32.60	820	5.65
27	Smooth muscle relaxants	8	1.19	98.50	32	0.22
28	Vitamins & combinations	21	3.12	64.33	48	0.33
29	Unclassified agents	54	8.02	59.50	161	1.11
30	Devices & non-drug items	6	0.89	54.17	13	0.09
31	Pharmaceutical aids/adjuvants	5	0.74	18.20	11	0.08
99	Other/unavailable	11	1.63	17.27	22	0.15
Total					**14,514**	**100.00**

* Each patient can have received different therapeutic groups of drugs or none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 678 and 100%, respectively.

† The days/patient reflect the average number of days a patient received the respective therapeutic group prescribed.

‡ The total number reflects the overall number of days the respective therapeutic group of drugs was prescribed for all patients included in the analysis.

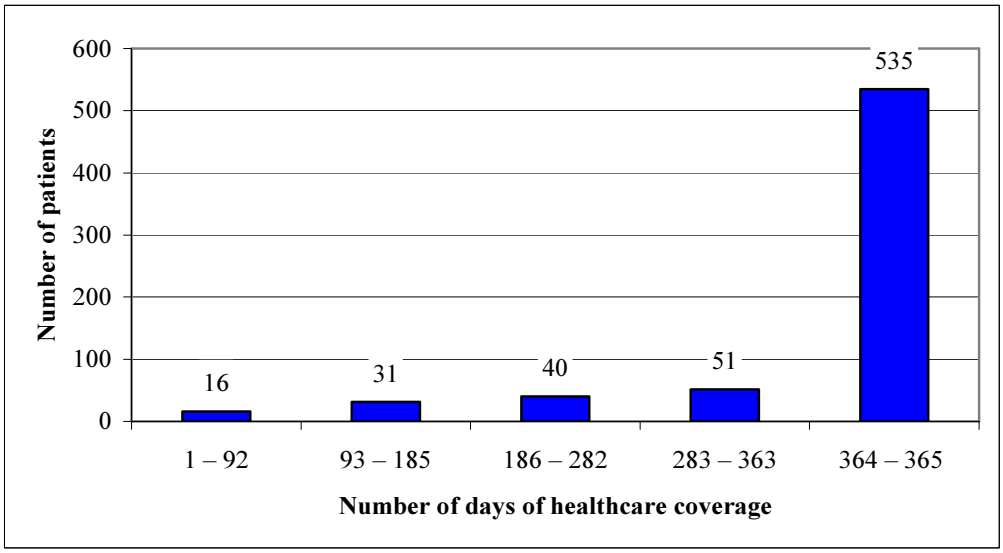
§ The total percent shows the overall distribution of the utilization of therapeutic groups, based on the number of days prescribed.

Payments for these outpatient services, inpatient services, and pharmaceuticals may vary between patients, as they are dependent on the payment schedule specific to the healthcare plan and negotiated with providers.

3.4.2.3 Total cost of illness

The majority of patients (80%) were enrolled in a healthcare plan throughout 2002, while only 7% had less than half a year of enrollment into any of the health plans contained in the Medstat database (Figure 2). Since the time period of enrollment and therefore healthcare coverage varied between patients, the cost of bulimia nervosa was analyzed on a per patient per day basis.

Figure 2: Distribution of patients by number of days of healthcare coverage (fee-for-service dataset)



The mean daily costs of patients at least 12 years of age with fee-for-service claims for bulimia nervosa in 2002 is shown in Table 16. Results reflect averages across all claims, irrespective of whether or not the specific cost (e.g., copayment) was incurred for this claim. In addition to the results for the original financial variables contained in the Medstat database, those for supplementary financial variables, introduced during the data cleaning process, are displayed. Cost data were not normally distributed, and average costs were higher than median costs. To preserve comparability with cost of illness studies in the literature,[13] mean costs are reported here as the main outcome of interest.

The average daily gross payment to providers, e.g., physicians, hospitals, and pharmacies, was $9.36 per patient, while the net payment by insurers was on average $7.85 per

patient. However, the mean gross payment according to the original claims underestimates the mean total healthcare costs, since not all individual hospital services were billed separately (see 3.3.1.2). By adding the mean daily additional gross payment associated with a hospitalization, which was determined based on the reported total payment per case (ADDPATIN2[70]), the mean total daily gross payment per patient increased to $9.80. Since this mean total daily gross payment covers all outpatient, inpatient, and pharmaceutical services, it was used as an estimate of the costs of illness and served as the basis for further subgroup and regression analyses.

According to the information contained in the original claims, the mean daily costs to patients were $1.17 and $0.15 for copayments and deductibles, respectively, while the average payment by third parties was $0.09 per patient. Payments by insurers and/or contributions by patients were likely higher than those reported in the original claims because of the non-reporting of some of the payments, as identified during the data cleaning process (3.3.1.2). Across all patients, the average total additional daily cost per patient was $0.53, while the average total daily overpayment was close to zero. If one assumes that all net payments were correctly reported in the original claims (including zero dollar payments), all additional payments had to be borne by the patients, thereby increasing their financial burden from a daily average of $1.32 per patient for copayments and deductibles to $1.85 in total.

[70] ADDPATIN2 is equal to the difference between the total payment for a hospitalization and the sum of gross payments reported in the individual claims associated with the respective case.

Table 16: Average daily cost per patient - all diagnoses and patients (fee-for-service dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	**673**	**9.36**	**4.90**	**0.56**	**36.58**	**0.00**	**215.91**
Net payment	673	7.85	3.68	0.33	32.44	0.00	215.71
COB	673	0.09	0.00	0.00	0.00	0.00	47.44
Copayment	673	1.17	0.69	0.05	3.41	0.00	29.00
Deductible	673	0.15	0.00	0.00	0.90	0.00	4.44
Dispensing fee	673	0.12	0.08	0.00	0.38	0.00	1.04
Ingredient cost	673	4.07	2.26	0.00	12.83	0.00	85.29
Sales tax	673	0.00	0.00	0.00	0.00	0.00	0.35
Total gross payment*	**673**	**9.80**	**4.94**	**0.57**	**38.39**	**0.11**	**215.91**
PATPAY	673	0.05	0.00	0.00	0.00	0.00	20.92
ADDPAY1	673	0.01	0.00	0.00	0.00	0.00	3.52
ADDPAY2	673	0.00	0.00	0.00	0.00	0.00	0.50
ADDPAYDRUG1	673	0.01	0.00	0.00	0.00	0.00	3.45
ADDPAYDRUG2	673	0.00	0.00	0.00	0.00	0.00	0.08
ADDPAYDRUG3	673	0.01	0.00	0.00	0.00	0.00	0.88
ADDPAYDRUG4	673	0.00	0.00	0.00	0.00	0.00	0.42
ADDPAYDRUG5	673	0.00	0.00	0.00	0.00	0.00	0.11
ADDPAYDRUG6	673	0.00	0.00	0.00	0.00	0.00	0.33
ADDPAYIN1	673	0.00	0.00	0.00	0.00	0.00	0.78
ADDPAYIN2	673	0.45	0.00	0.00	0.82	0.00	49.26
PATPAYIN	673	0.01	0.00	0.00	0.00	0.00	5.71
OVERPAYOUT	673	-0.00	0.00	0.00	0.00	-0.21	0.00
OVERPAYDRUG1	673	-0.00	0.00	0.00	0.00	-0.00	0.00
OVERPAYDRUG2	673	-0.00	0.00	0.00	0.00	-0.01	0.00
OVERPAYDRUG3	673	-0.00	0.00	0.00	0.00	-0.87	0.00
OVERPAYDRUG4	673	-0.00	0.00	0.00	0.00	-0.00	0.00
OVERPAYIN	673	-0.00	0.00	0.00	0.00	-2.22	0.00

* Gross payment plus additional inpatient payments (ADDPAYIN2).

Table 17 shows that the average total daily gross payment per patient was higher for drug claims ($4.14 per day) than for outpatient and inpatient claims ($3.20 and $2.46 per patient, respectively). Since results were based on all 673 patients, including those who did not receive the respective service, the lower mean daily cost per patient for inpatient services reflects the infrequent admission of patients rather than low inpatient costs.

Table 17: Average daily cost per patient - all diagnoses and patients (fee-for-service dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Outpatient	673	3.20	1.20	0.10	11.72	0.00	87.09
Inpatient	673	2.46	0.00	0.00	14.27	0.00	213.14
Drugs	673	4.14	2.35	0.00	13.25	0.00	73.31

In an additional analysis, mean daily costs per patient were calculated based on the subset of patients incurring the respective cost. The results, which are displayed in Table 18, demonstrate that a positive gross payment was recorded for all but one patient, that most patients had to pay copayments throughout the year, and that inaccurate claims records requiring corrections affected numerous patients.

Table 18: Average daily cost per patient based on patients incurring the respective cost – all claims and all patients (fee-for-service dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	**672**	**9.37**	**4.91**	**0.57**	**36.58**	**0.11**	**215.91**
Net payment	667	7.92	3.70	0.42	32.34	0.01	215.71
COB	17	3.69	0.35	0.07	47.44	0.08	47.44
Copayment	659	1.19	0.71	0.08	3.49	0.01	29.00
Deductible	194	0.52	0.31	0.05	1.63	0.02	4.44
Dispensing fee	612	0.13	0.09	0.01	0.40	0.00	1.04
Ingredient cost	619	4.43	2.54	0.19	13.99	0.00	85.29
Sales tax	27	0.05	0.02	0.00	0.18	0.00	0.35
PATPAY	37	0.91	0.14	0.00	4.49	0.00	20.92
ADDPAY1	14	0.40	0.02	0.00	3.52	0.00	3.52
ADDPAY2	6	0.22	0.16	0.05	0.50	0.05	0.50
ADDPAYDRUG1	10	0.82	0.40	0.04	3.45	0.04	3.45
ADDPAYDRUG2	3	0.05	0.06	0.01	0.08	0.01	0.08
ADDPAYDRUG3	25	0.21	0.10	0.01	0.83	0.01	0.88
ADDPAYDRUG4	5	0.22	0.18	0.09	0.42	0.09	0.42
ADDPAYDRUG5	4	0.05	0.04	0.01	0.11	0.01	0.11
ADDPAYDRUG6	2	0.18	0.18	0.03	0.33	0.03	0.33
ADDPAYIN1	2	0.72	0.72	0.66	0.78	0.66	0.78
ADDPAYIN2	42	7.15	1.77	0.30	31.75	0.12	49.26
PATPAYIN	2	3.53	3.53	1.36	5.71	1.36	5.71
OVERPAYOUT	22	-0.03	-0.01	-0.08	-0.00	-0.21	-0.00
OVERPAYDRUG1	2	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00
OVERPAYDRUG2	1	-0.02	-0.01	-0.01	-0.01	-0.01	-0.01
OVERPAYDRUG3	32	-0.05	-0.00	-0.17	-0.00	-0.87	-0.00
OVERPAYDRUG4	1	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00
OVERPAYIN	3	-0.75	-0.02	-2.22	-0.00	-2.23	-0.00

Per patient having received the respective type of service, the mean total daily costs were $30.13 for inpatient services compared to $3.33 and $4.50 for outpatient services and prescriptions, respectively (Table 19). This result reflects the high costs for hospitalizations, and in addition demonstrates that drug therapy was more expensive than outpatient treatment based on those patients receiving the respective type of service.

Table 19: Average daily cost per patient based on patients incurring the respective cost – all claims and all patients (fee-for-service dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Outpatient	647	3.33	1.27	0.14	11.81	0.03	87.09
Inpatient	55	30.13	20.29	4.07	104.53	1.34	213.14
Drugs	619	4.50	2.63	0.19	14.11	0.01	73.31

3.4.2.4 Sensitivity analyses and univariate analyses

i) Cost of illness based on claims with a primary diagnosis of bulimia nervosa

In a sensitivity analysis, the costs directly attributable to bulimia nervosa were determined by including only those claims with the respective primary diagnosis. This reduced the dataset to 6,185 fee-for-service outpatient and inpatient claims, which were incurred by 639 patients. As prescriptions are not linked to any diagnosis, drug costs could not be determined.

The results (Table 20) show that the average total daily cost per patient was about 50% lower compared to the main analysis due to the exclusion of claims without a primary diagnosis of bulimia nervosa and those of prescription claims. While the average total daily gross payment per patient was $5.11, the reported payments by insurers, patients, and third parties were on average $4.01, $0.64, and $0.09, respectively.

Table 20: Average daily cost per patient based on outpatient and inpatient claims with a primary diagnosis of bulimia nervosa - all patients (fee-for-service dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	**639**	**4.80**	**1.24**	**0.14**	**17.62**	**0.03**	**213.14**
Net payment	639	4.01	0.88	0.00	16.75	0.00	213.14
COB	639	0.09	0.00	0.00	0.00	0.00	47.44
Copayment	639	0.50	0.14	0.00	2.23	0.00	10.46
Deductible	639	0.14	0.00	0.00	0.83	0.00	4.44
Total gross payment*	**639**	**5.11**	**1.25**	**0.14**	**26.40**	**0.03**	**213.14**
PATPAY	639	0.05	0.00	0.00	0.00	0.00	20.80
ADDPAY1	639	0.01	0.00	0.00	0.00	0.00	3.52
ADDPAY2	639	0.00	0.00	0.00	0.00	0.00	0.50
ADDPAYIN1	639	0.00	0.00	0.00	0.00	0.00	0.78
ADDPAYIN2	639	0.31	0.00	0.00	0.00	0.00	49.26
OVERPAYOUT	639	-0.00	0.00	0.00	0.00	-0.21	0.00
OVERPAYIN	639	-0.00	0.00	0.00	0.00	-2.22	0.00

* Gross payment plus additional inpatient payments (ADDPAYIN2).

ii) Cost of illness based on all patients at least 18 years of age

Mean total daily costs were also determined for the subgroup of patients at least 18 years of age, limiting the analysis to 522 patients. Results were very similar to those for all patients (Table 21; Table 16); for example, the mean total daily gross payment per patient was $10.24 among those at least 18 years of age compared to $9.80 for all 673 patients. Mean payments by insurers were also similar: $8.30 per patient at least 18 years of age versus $7.85 for all 673 patients.

Table 21: Average daily cost per patient at least 18 years of age, all diagnoses and patients (fee-for-service dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	**522**	**9.87**	**5.37**	**0.77**	**36.58**	**0.14**	**215.91**
Net payment	522	8.30	3.97	0.50	33.13	0.00	215.71
COB	522	0.11	0.00	0.00	0.00	0.00	47.44
Copayment	522	1.21	0.70	0.08	3.41	0.00	29.00
Deductible	522	0.16	0.00	0.00	0.90	0.00	4.44
Dispensing fee	522	0.13	0.09	0.00	0.40	0.00	1.04
Ingredient cost	522	4.29	2.47	0.00	12.83	0.00	50.40
Sales tax	522	0.00	0.00	0.00	0.00	0.00	0.35
Total gross payment*	**522**	**10.24**	**5.37**	**0.77**	**38.39**	**0.14**	**215.91**
PATPAY	522	0.06	0.00	0.00	0.00	0.00	20.92
ADDPAY1	522	0.00	0.00	0.00	0.00	0.00	0.92
ADDPAY2	522	0.00	0.00	0.00	0.00	0.00	0.50
ADDPAYDRUG1	522	0.02	0.00	0.00	0.00	0.00	3.45
ADDPAYDRUG2	522	0.00	0.00	0.00	0.00	0.00	0.08
ADDPAYDRUG3	522	0.01	0.00	0.00	0.00	0.00	0.88
ADDPAYDRUG4	522	0.00	0.00	0.00	0.00	0.00	0.42
ADDPAYDRUG5	522	0.00	0.00	0.00	0.00	0.00	0.06
ADDPAYDRUG6	522	0.00	0.00	0.00	0.00	0.00	0.33
ADDPAYIN1	522	0.00	0.00	0.00	0.00	0.00	0.00
ADDPAYIN2	522	0.36	0.00	0.00	0.70	0.00	49.26
PATPAYIN	522	0.01	0.00	0.00	0.00	0.00	5.71
OVERPAYOUT	522	-0.00	0.00	0.00	0.00	-0.21	0.00
OVERPAYDRUG1	522	-0.00	0.00	0.00	0.00	-0.00	0.00
OVERPAYDRUG2	522	-0.00	0.00	0.00	0.00	-0.01	0.00
OVERPAYDRUG3	522	-0.00	0.00	-0.00	0.00	-0.87	0.00
OVERPAYDRUG4	522	0.00	0.00	0.00	0.00	0.00	0.00
OVERPAYIN	522	-0.00	0.00	0.00	0.00	-2.22	0.00

* Gross payment plus additional inpatient payments (ADDPAYIN2)

iii) Univariate analyses of patient characteristic

In addition, univariate analyses were performed to assess descriptively whether patients' baseline characteristics could have an impact on the average total daily cost, as determined in the primary analysis based on all patients and all claims. Results demonstrate that the mean total daily cost per patient tended to be higher for females than males (Table 22), lower for children than employees and their spouses (Table 23), slightly lower for POS plans than other healthcare plans (Table 24), and higher in the

Northeast and West regions than in the North Central and South regions of the U.S. (Table 25). The observed differences between genders and types of health insurance were as expected a priori. Since women are generally more likely to seek healthcare than men,[217] the higher average mean daily cost in females was not surprising. The cost differences between comprehensive, PPO, and POS plans seem to reflect plan-specific incentives and restrictions, with comprehensive healthcare plans being the least and POS plans the most restrictive. The number of patients with an EPO plan was too limited to draw any conclusions. Since the variable 'relationship to employee' is likely correlated with the age of patients, no conclusions can be drawn from the univariate analysis alone. Some of the regional differences may be explained by an unequal distribution of healthcare plans, as in the North Central region the majority of patients (50.00%) had comprehensive healthcare, compared to only few patients (6.32%) in the West. In addition, the higher cost in the Northeast and West compared to the rest of the U.S. could be the result of the concentration of specialized treatment centers and eating disorder support groups in the Western part of the U.S. (particularly California), as well as in metropolitan cities in the Northeast, e.g., Boston and New York.

Table 22: Total daily cost by gender - all patients (fee-for-service dataset; in US$, 2002)

Gender	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Male	35	6.53	3.84	0.36	23.67	0.28	38.39
Female	638	9.98	5.03	0.57	38.60	0.11	215.91

* Mean refers to the total gross payment per day per patient.

Table 23: Total daily cost by relationship to employee - all patients (fee-for-service dataset; in US$, 2002)

Relationship to employee	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Employee	205	10.77	5.90	0.96	35.60	0.16	215.91
Spouse	79	11.22	5.01	0.95	48.07	0.14	99.02
Child/other	389	9.00	4.42	0.46	37.18	0.11	105.80

* Mean refers to the total gross payment per day per patient.

Table 24: Total daily cost by type of healthcare plan - all patients (fee-for-service dataset; in US$, 2002)

Plan type	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Comprehensive	178	10.42	5.25	0.89	40.30	0.25	215.91
EPO	43	9.67	4.54	0.51	27.86	0.23	105.80
POS	105	8.47	4.49	0.59	31.28	0.30	115.02
PPO	347	9.90	5.21	0.45	38.39	0.11	152.38

* Mean refers to the total gross payment per day per patient.

Table 25: Total daily cost by region - all patients (fee-for-service dataset; in US$, 2002)

Region	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Northeast	94	12.53	4.55	0.52	63.27	0.14	152.38
North Central	279	8.98	5.20	0.67	33.02	0.11	215.91
South	204	9.13	4.50	0.43	42.97	0.14	97.76
West	95	11.03	6.91	0.65	40.32	0.17	99.02
Unknown	1	0.95	0.95	0.95	0.95	0.95	0.95

* Mean refers to the total gross payment per day per patient.

Average daily costs per patient seemed to increase with the number of comorbidities (Table 26). This trend was evident for patients with up to five unique primary and secondary diagnoses, while there were too few patients with six or more diagnoses to allow drawing any conclusions.

Table 26: Total daily cost by number of diagnoses - all patients (fee-for-service dataset; in US$, 2002)

Number of diagnoses	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
1	542	7.19	4.54	0.52	21.11	0.11	97.76
2	80	11.88	6.07	0.58	48.55	0.43	63.66
3	23	20.87	13.15	1.67	64.69	1.45	64.92
4	13	33.19	18.89	6.36	115.02	6.36	115.02
5	9	60.19	27.99	3.62	215.91	3.62	215.91
6	2	28.80	28.80	25.31	32.30	25.31	32.30
7	3	62.44	84.21	4.09	99.02	4.09	99.02
8	1	49.98	49.98	49.98	49.98	49.98	49.98

* Mean refers to the total gross payment per day per patient.

Potential predictor variables of the mean total daily cost per patient were further assessed in linear regression analyses.

3.4.2.5 Regression analysis

Since the mean total daily cost per patient was very similar for those at least 12 years of age and those 18 years or older, regression analyses were performed only for the whole dataset, thereby allowing for greater statistical power and precision.

To assess which patient-specific characteristics influence costs, in terms of the total per-patient daily gross payment, and to develop a model for predicting costs based on patient factors, multivariate linear regression analysis was applied. Potentially relevant explanatory variables, for which information was available from the MedStat database, included: age, gender, plan type, relationship to employee, region, and number of unique diagnoses in 2002 as a surrogate for disease severity.

A priori, before conducting any analyses, it was assessed whether the assumptions underlying linear regression models were satisfied by the data. Since the distribution of daily costs was found to be severely skewed (skewness of 5.60, kurtosis of 45.40), the normality assumption was violated by the original data. The graphical comparison of the histogram of observed daily costs with a theoretical normal distribution (Figure 3) supports the skewed nature of the data and the deviation from the normality curve. In addition, the normal probability or quantile-quantile (Q-Q) plot, which depicts the daily costs, ordered by magnitude, against the associated quantiles of the normal distribution and which also contains the graph for a normal curve, demonstrates the deviation of the observed data from the normal distribution (Figure 4). The curved nature of the Q-Q plot, resembling an exponential function, suggests that a logarithmic transformation of the daily cost function might be suitable to normalize the data.

Figure 3: Normality test – histogram of daily cost and theoretical normal distribution (fee-for-service dataset)

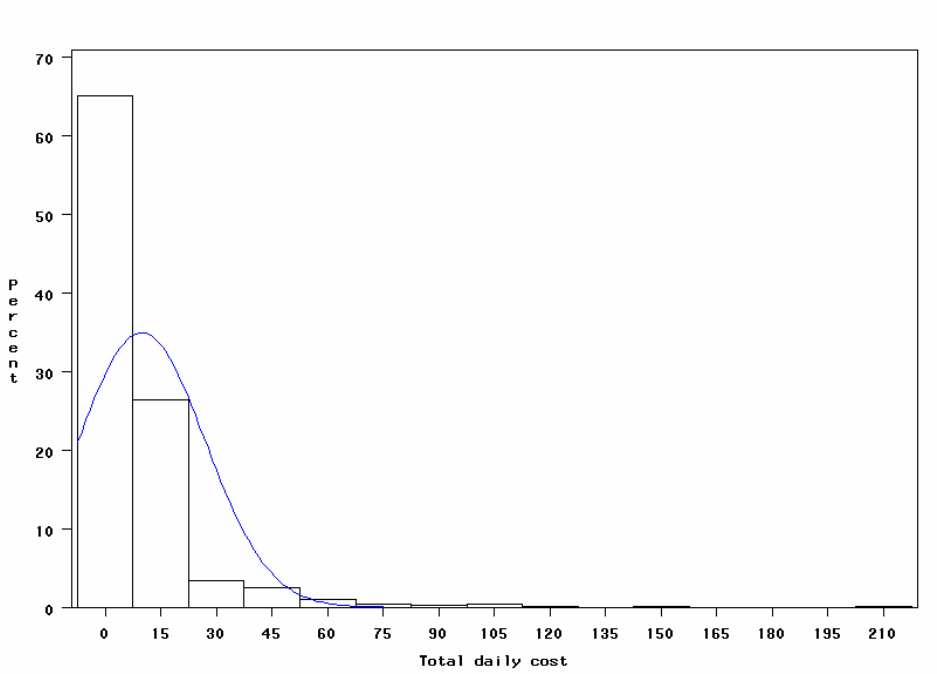
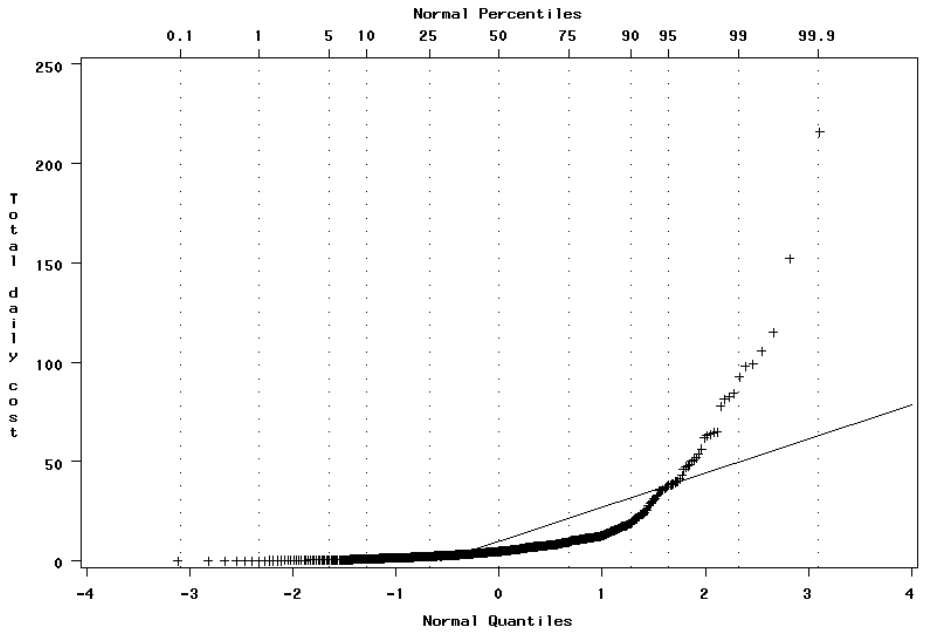


Figure 4: Normality test – normal probability plot of daily cost and theoretical normal distribution (fee-for-service dataset)



The response variable was transformed by applying the natural logarithm of daily costs and the distribution of the log-transformed costs was then checked for normality. With a skewness of –0.15 and a kurtosis of 0.65, the distribution of transformed costs was approximately normal. This was confirmed by the graphical examination, which showed that the histogram of transformed costs had a bell-shaped form similar to a normal distribution (Figure 5). In addition, the Q-Q plot of transformed costs appeared to follow the straight line of the theoretical normal distribution (Figure 6). The natural logarithm of daily costs was therefore used as the dependent variable for further validations of assumptions of linear regression analyses. It should be noted that the distribution of transformed costs was not completely normal and was likely influenced by some extreme values (i.e., outliers), which are visible at the lower tail end of the Q-Q plot in Figure 6. The robustness of the regression model with regard to these outliers was examined as part of the a-posteriori validation described below.

Figure 5: Normality test – histogram of natural logarithm of daily cost versus theoretical normal distribution (fee-for-service dataset)

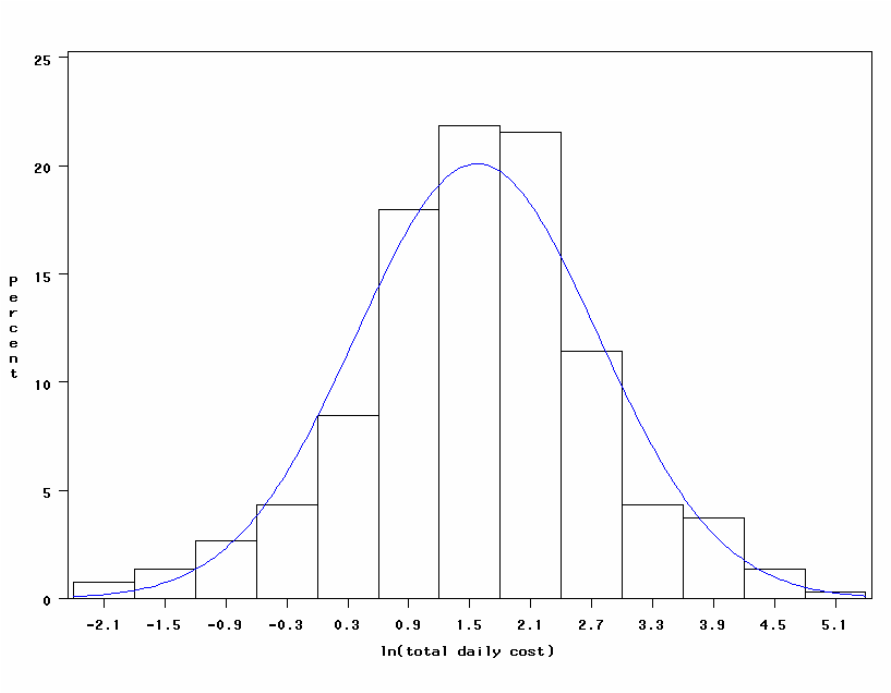
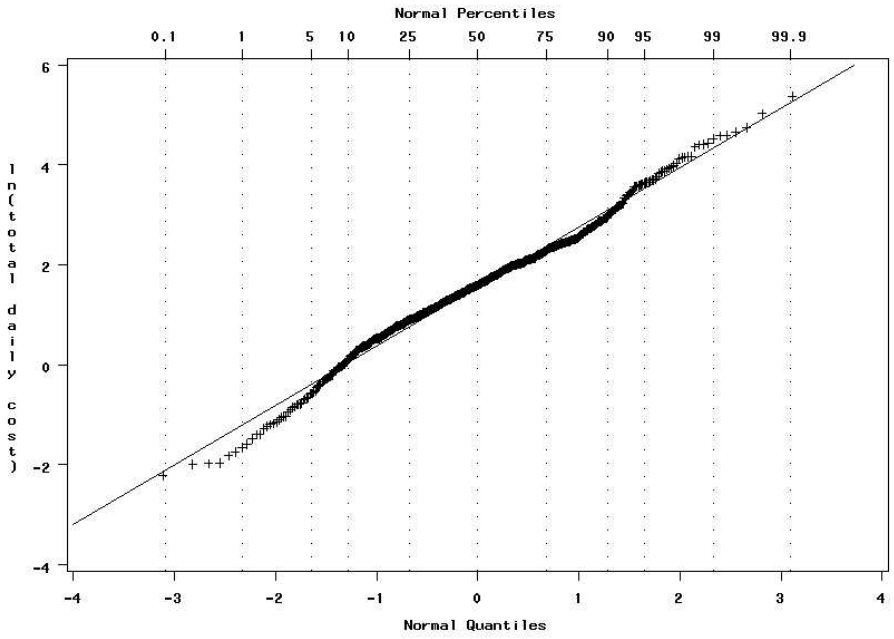


Figure 6: Normality test – normal probability plot of natural logarithm of daily cost and theoretical normal distribution (fee-for-service dataset)



Other important prerequisites of linear regression analyses are a linear association of the dependent and independent variables and an equal variance across the range of possible data values. To assess whether these assumptions were satisfied, bivariate (two-dimensional) scatter plots of the logarithm of daily costs and the different predictor variables were examined as well as the distribution of data points in relation to the respective simple regression lines. Figure 7 and Figure 8 show some linear relationship between the independent variable and the number of diagnoses and age, respectively, as well as relatively symmetrical distribution of the scatter points above and below the regression line, suggesting that the use of a linear regression model would be appropriate for these two predictors. While there appeared to be a strong positive relation between the transformed daily cost and the number of diagnoses, the association with age was less pronounced. By visual examination of the graphs it appears that the variance might be diminishing with increasing number of diagnoses and increasing age; the robustness of the regression model with regard to heteroscedasticity was assessed further as part of the a-posteriori validation of the model described below.

Scatter plots for gender, relationship to employee, regions and plan types (Figure 9, Figure 10, Figure 11, Figure 12) did not show any obvious relationship with the transformed daily costs, as these variables appeared to have very similar means across the range of respective categories. Scatter points were approximately equally distributed around the means, indicating that the assumption of equal variance was likely satisfied by the data.

Figure 7: Bivariate scatter plot of natural logarithm of cost and number of diagnoses (fee-for-service dataset)

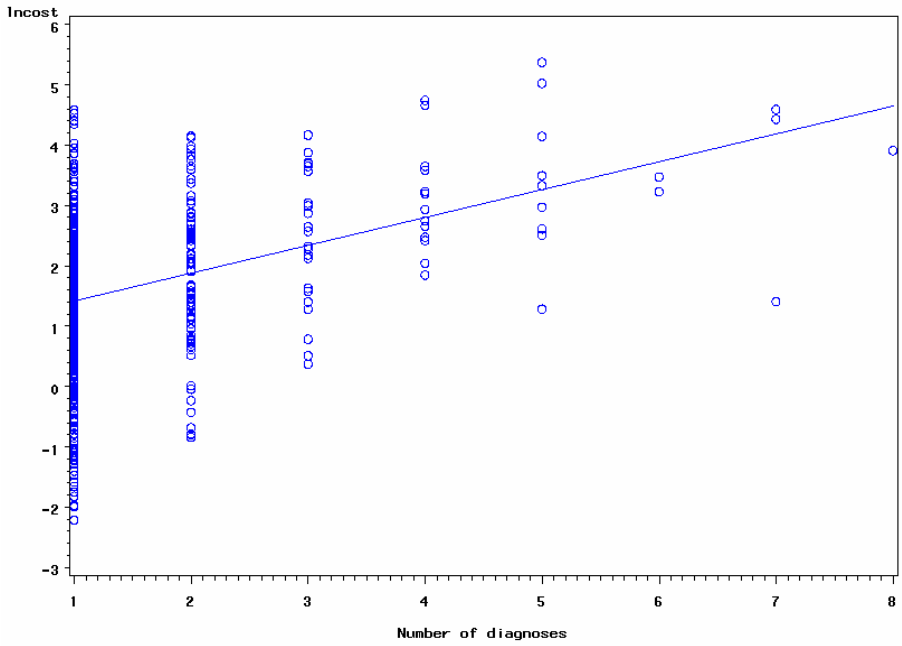


Figure 8: Bivariate scatter plot of natural logarithm of cost and age (fee-for-service dataset)

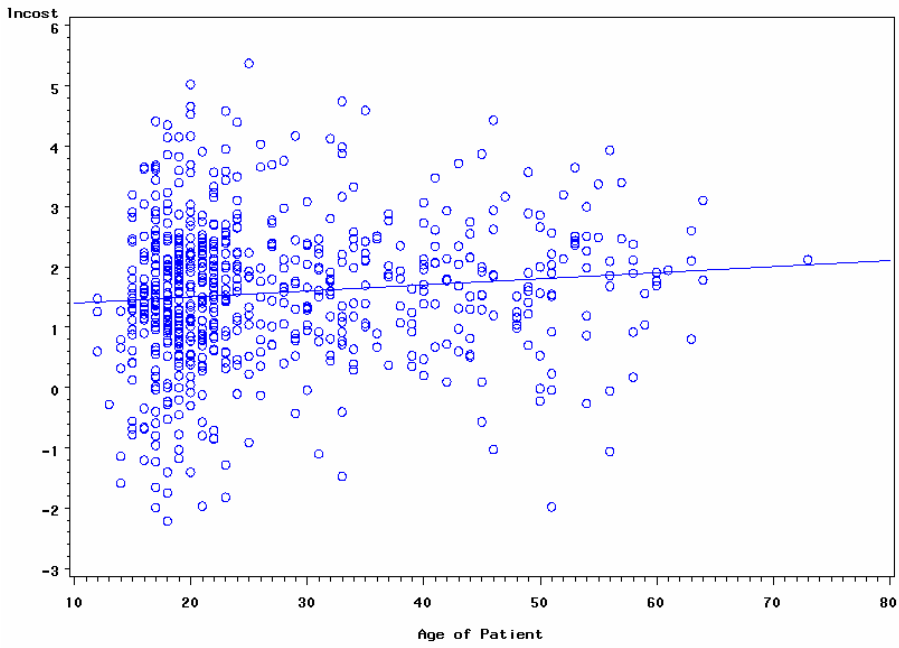


Figure 9: Bivariate scatter plot of natural logarithm of cost and gender (fee-for-service dataset)

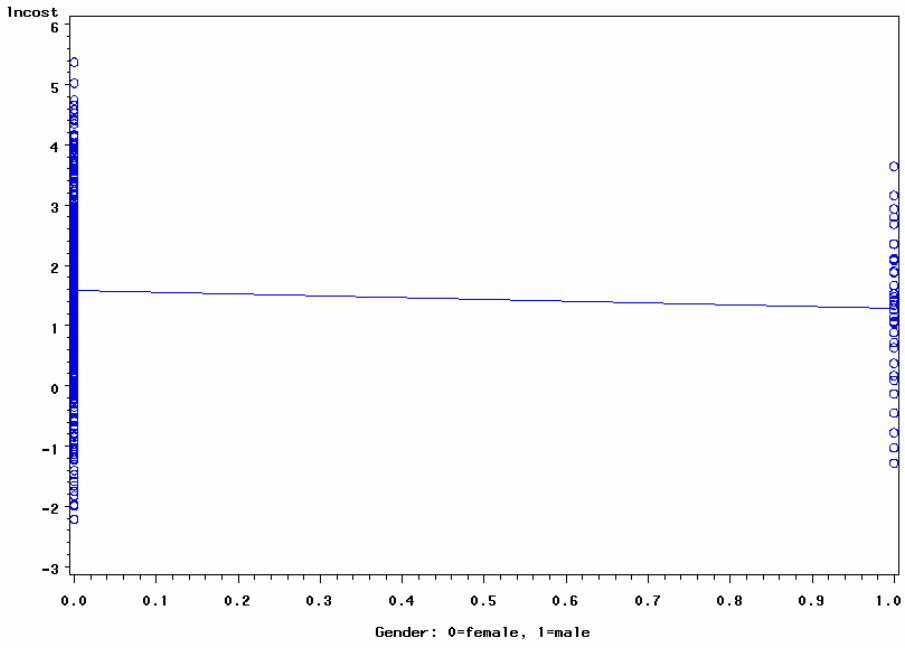


Figure 10: Bivariate scatter plot of natural logarithm of cost and region (fee-for-service dataset)

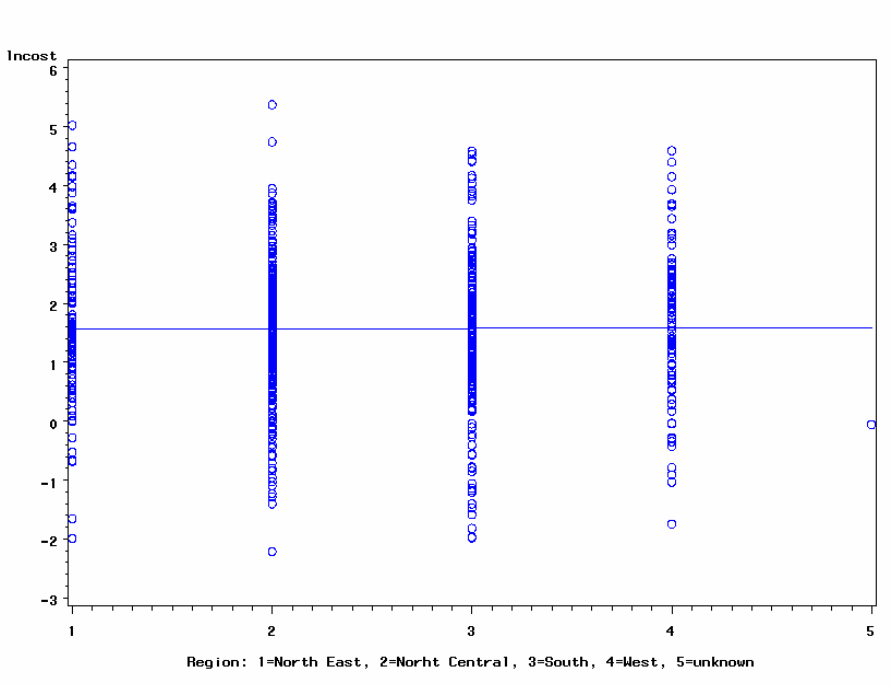


Figure 11: Bivariate scatter plot of natural logarithm of cost and plan type (fee-for-service dataset)

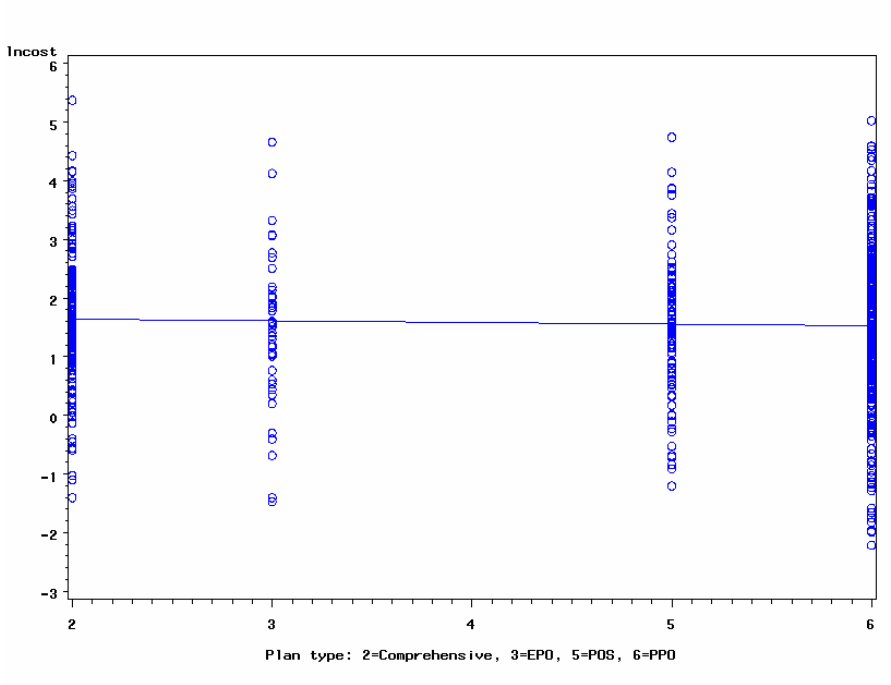
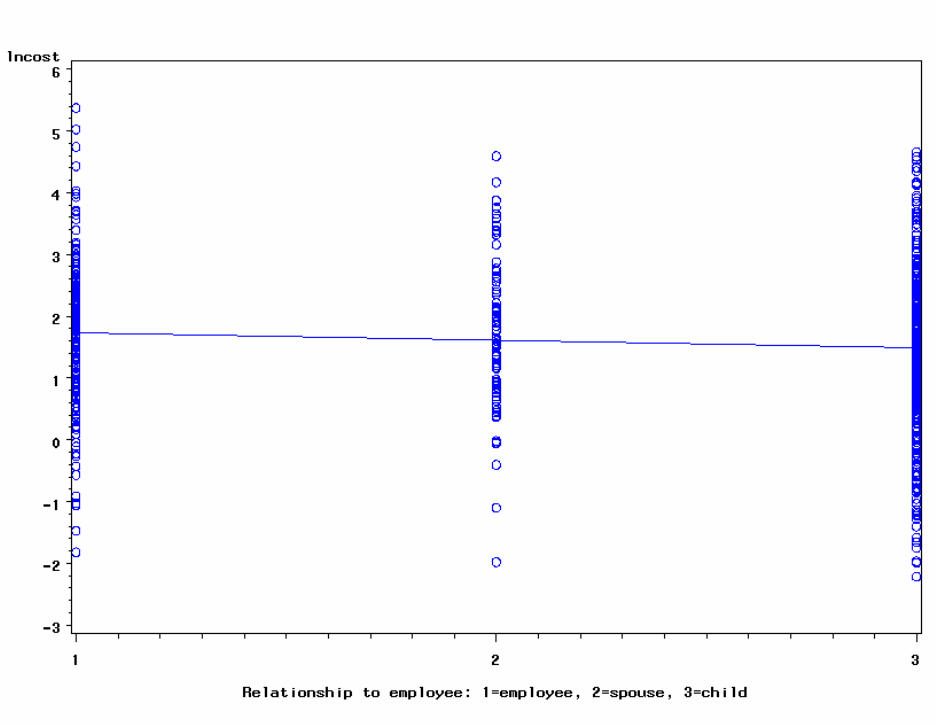


Figure 12: Bivariate scatter plot of natural logarithm of cost and relationship to employee (fee-for-service dataset)



After having graphically confirmed that the normality and linearity assumptions were approximately satisfied by the transformed cost data, an a-priori regression model had to be selected. To assess which variables had a significant impact on the logarithm of costs and might therefore be included in the model as predictors, correlation of the dependent variable with the independent ones was explored.[71] Table 27 demonstrates that number of diagnoses as well as age were significantly positively associated with the logarithm of daily costs ($p < 0.01$), while gender, plan type, and region were not significantly related to the transformed costs. A significant negative association was evident between the logarithm of daily costs and employee relationship, which confirms the association with age, since the coding of employee relationship was inverse to that for age—the numerical code for children was higher than that for employees and spouses (3 versus 1 and 2, respectively). The results of this correlation analysis suggest that number of diagnoses,

[71] Since the purpose of these analyses was to assess potential associations, all categorical variables were analyzed numerically. In the final regression model, dummy variables were used, thereby allowing for interpretation of results.

age, and employee relationship might be relevant predictor variables for the regression model of transformed daily costs.

Table 27: Correlation of the dependent (ln[cost]) and independent variables (fee-for-service dataset)

	Number of diagnoses	Age	Sex*	Plan type†	Relationship to employee‡	Region§
r	0.353	0.104	-0.058	-0.038	-0.095	0.002
p	<0.0001	0.007	0.136	0.326	0.014	0.965

* Male coded as 1, female as 2.
† Comprehensive coded as 2, EPO as 3, POS as 5, and PPO as 6.
‡ Employee coded as 1, spouse as 2, and child as 3.
§ North East coded as 1, North Central as 2, South as 3, West as 4, and 5 as unknown.

The impact of individual explanatory variables on the logarithm of costs was also assessed in univariate linear regression models. As expected, the number of diagnoses was significantly associated with the logarithm of costs ($p < 0.0001$), but this predictor explained only 12.5% of the variation in the response variable (Table 28). In addition, age and employee relationship had a significant impact ($p=0.007$ and $p=0.014$, respectively), but they also accounted only for a small percentage of the variation in the logarithm of costs (r^2 of 0.011 and 0.009, respectively). Gender, plan type, and region were not found to be good predictors (p-value/r^2 of 0.136/0.003, 0.326/0.001, 0.965/0.000, respectively).

Table 28: Univariate linear regression analyses (fee-for-service dataset)

Variable	Parameter estimate	Standard Error	p	r^2
Number of diagnoses	0.462	0.047	<0.0001	0.125
Age	0.010	0.004	0.007	0.011
Relationship to employee	-0.126	0.051	0.014	0.009
Male vs female	-0.309	0.207	0.136	0.003
Plan type	-0.026	0.027	0.326	0.001
Region	0.002	0.051	0.965	0.000

Based on the examination of bivariate scatter plots and the univariate regression models it can be concluded that number of diagnoses, age, and employee relationship appear to have an impact on the logarithm of daily costs.

Since the marginal relationships between transformed costs and each of the explanatory variables are not sufficient to determine the joint relationship between the dependent variable and the different independent variables, interrelationship of predictors was assessed by computing and examining Pearson's correlation matrix. This allowed also determining whether all potential explanatory variables could be included in the multivariate regression model or whether multicollinearity required a reduced model.

The correlation matrix (Table 29) shows that age was strongly and significantly related ($r=–0.75$, $p < 0.0001$) to employee relationship, indicating that only one of these variables should be included in the regression model. In addition, gender was significantly correlated with employee relationship ($p < 0.001$) and with region ($p=0.04$), but the strength of these associations was less than that with age ($r=–0.11$ and $–0.08$, respectively). Further significant, but not strong bivariate correlations were found between type of health insurance and region ($p < 0.0001$, $r=0.18$) and between employee relationship and region ($p=0.05$, $r=–0.07$). Since gender, plan type, and employee relationship were all weakly correlated with region, this might be an indication for the exclusion of region as a predictor variable from the regression model.

Table 29: Correlation matrix of independent variables* (fee-for-service dataset)

	Number diagnoses	Age	Sex†	Plan type‡	Relat. to employee§	Region+
Number diagnoses	1	-0.070 0.069	-0.039 0.315	0.021 0.595	0.039 0.312	0.011 0.776
Age	-0.070 0.069	1	0.087 0.024	-0.035 0.359	-0.747 <0.0001	-0.027 0.484
Sex	-0.039 0.315	0.087 0.024	1	0.005 0.904	-0.108 0.005	-0.079 0.040
Plan type	0.021 0.595	-0.035 0.359	0.005 0.904	1	0.003 0.948	0.179 <0.0001
Relat. to employee	0.039 0.312	-0.747 <0.0001	-0.108 0.005	0.003 0.948	1	-0.076 0.049
Region	0.011 0.776	-0.027 0.484	-0.079 0.040	0.179 <0.0001	-0.076 0.049	1

* In each cell, the first value shows the correlation coefficient, r, and the second (below) the p-value.
† Male coded as 1, female as 2.
‡ Comprehensive coded as 2, EPO as 3, POS as 5, and PPO as 6.
§ Employee coded as 1, spouse as 2, and child as 3.
+ North East coded as 1, North Central as 2, South as 3, West as 4, and 5 as unknown.

The existence of multicollinearity was also confirmed by an analysis of variance inflation factors[72] and of eigenvalues of the correlation matrix of predictor variables[73]. Age and employee relationship were found to have a variance inflation factor of more than $1/(1-r^2)=1.17$ (2.28 and 2.29, respectively),[218] indicating that they were more closely related to other independent variables than to the dependent one. This result concurs with the high bivariate correlation observed between age and employee relationship.

According to the analysis of collinearity, the lowest eigenvalues were 0.79 and 0.25, with associated condition indices[74] of 2.67 and 1.50, respectively. Age and employee relationship were found to be involved in a nearly linear dependency, since about 87% of their variances were associated with the respective eigenvalue. In addition, a linear

[72] Variance inflation factors show how multicollinearity has increased the instability of coefficient estimates; i.e., the variance of the estimated regression coefficient is larger by this factor than if no multicollinearity existed. A variance inflation factor greater than $1/(1-r^2)$ is considered to indicate multicollinearity.
[73] A wide variation in the magnitude of eigenvalues indicates a greater degree of multicollinearity. Eigenvalues of zero indicate exact linear dependencies and very small eigenvalues indicate nearly linear dependencies or high degrees of multicollinearity.
[74] The condition index provides an indication of the severity of multicollinearity.

dependency of plan type and region was apparent with 46% to 58% of the variances of these parameter estimates being associated with the associated eigenvalue.

Since the initially proposed model, which included all potential explanatory variables, was subject to multicollinearity of independent variables, a regression model with fewer regressors had to be identified. Inclusion of all potential predictors would have resulted in inflated variances of the estimated coefficients,[219] thereby reducing the robustness and predictive power of the model. To identify the optimum subset of independent variables, variable selection according to the adjusted r^2 was applied. This selection method has been found to be superior to automatic step-by-step procedures, like forward, backward, or stepwise selection, which do not guarantee finding the optimum subset of independent variables, might produce less reliable results, and can lead to overstated coefficients and significance levels of t- or F-values.[218;219] The adjusted r^2 rather than the r^2 was chosen as the selection criterion, since the adjusted r^2 is more appropriate for comparing models with different numbers of predictors.[220]

The following independent variables were included in the selection process: age, gender, plan type, employee relationship, region, and number of diagnoses. All categorical variables with three or more categories (i.e., plan type, employee relationship, and region) were entered numerically, since the variable selection process cannot accommodate variables with more than two categories appropriately.[75] However, in the final regression model, dummy variables were created for categorical variables. The selection process identified age, gender, plan type, and number of diagnoses to be the best subset of variables, in that their inclusion resulted in the model with the highest adjusted r^2.

In addition to the selection by adjusted r^2, the Bayesian Information Criterion (BIC or Schwarz criterion) was also observed, which compares various subsets of models based on their lack of fit (residual sum of squares) as well as their complexity (number of terms

[75] The variable selection process would likely only pick one of the dummy variables of a given categorical variable, but not all of them, even though all categories need to be considered to fully reflect the data.

included in the model).[219] The BIC has been shown to provide advantages over the Akaike Information Criterion (AIC), since it is more likely to select the optimal subset of variables and will likely result in a lower-dimensional model.[221;222] The model identified based on the adjusted r^2 criterion was found to have also the lowest BIC, providing additional evidence that the selected model was superior to others. It should be noted that the model selected based on statistical decision criteria included those variables determined a priori to be clinically relevant and uncorrelated with other variables.

In the multivariate regression analysis, plan type and gender were entered as dummy variables to allow for interpretation of results. An inverse transformation of parameter estimates was performed to be able to assess the impact of exploratory variables on the daily costs rather than the natural logarithm of daily costs. The results of the multivariate regression analysis (Table 30) show that only number of diagnoses and age had a significant effect on the dependent variable ($p < 0.001$). The daily per-person cost was estimated to increase by 1.3% with each additional year of age and by 60.2% with each additional diagnosis, assuming all other factors were being held constant. In addition, daily costs were lower in men than women and higher in individuals with comprehensive care than PPO insurance, but these associations were not significant ($p=0.134$ and $p=0.204$, respectively).

The model appeared to be a good fit of the data, as the overall p-value (of the F-statistic) was < 0.0001, indicating a very high chance that at least one of the coefficients would be different from zero. However, only 13.9% of the variance in the transformed costs was explained by the variation in the independent variables of the model (adjusted $r^2=0.139$, $r^2=0.147$).

Table 30: Multivariate regression analysis (fee-for-service dataset)

Variable	Parameter estimate	Standard Error	Exponent (estimate)	p
Intercept	0.568	0.133	1.765	<0.0001
Age	0.013	0.004	1.013	0.0002
Male vs female	-0.290	0.193	0.748	0.134
Comprehensive vs PPO	0.130	0.102	1.139	0.204
POS vs PPO	-0.009	0.123	0.991	0.939
EPO vs PPO	-0.064	0.179	0.938	0.721
Number of diagnoses	0.471	0.047	1.602	<0.0001

* p-value based on t-test.

A posteriori, the fit of the regression model was assessed by checking whether the assumptions underlying linear regression analyses were satisfied; i.e., whether the residuals were independently and identically distributed and were random, normally distributed variables with a mean of zero and a constant variance of σ^2. The statistical assessment of these assumptions demonstrated that the distribution of residuals was normal with a mean of zero, a variance of 1.21, and no extreme skewness (-0.30)[76]. In addition, Student's t-test confirmed the hypothesis that the population mean was zero (p=1.000) and the Shapiro-Wilks statistic indicated that the error terms come from a normal distribution ($p < 0.0001$). The normality of residuals was also apparent in the normality plot (or Q-Q plot), which showed that the distribution of residuals closely followed the straight line of a normal distribution, even though some deviation was apparent for extreme values of residuals (Figure 13).

The scatter plot of the residuals versus predicted values resembled a null plot with an approximately symmetrical distribution of residuals around the horizontal zero line, representing the estimated mean of the residuals (Figure 14). Furthermore, the scatter plot showed that the range of residuals was approximately constant across predicted values, indicating that the regression model was not impacted by heteroscedasticity (unequal distribution of residuals).

[76] Extreme values of skewness are greater than 3 or less than –3.

The assumption of independence of error terms was further assessed by calculating the Durbin-Watson (D-W) statistic, which tests for the existence of a first-order autoregressive process. Since the D-W statistic was close to 2.0 (1.9), a value generally considered indicative of independence of error terms, and since the sample correlation of adjacent residuals was only 0.05, autocorrelation of residuals could be excluded.

Figure 13: Normal probability plot of standardized residuals (fee-for-service dataset)

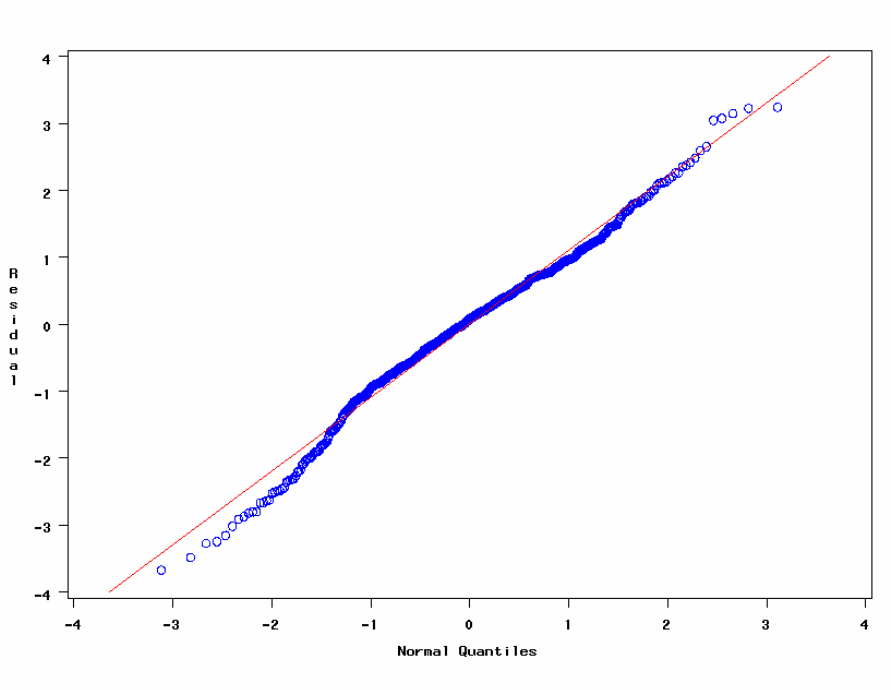
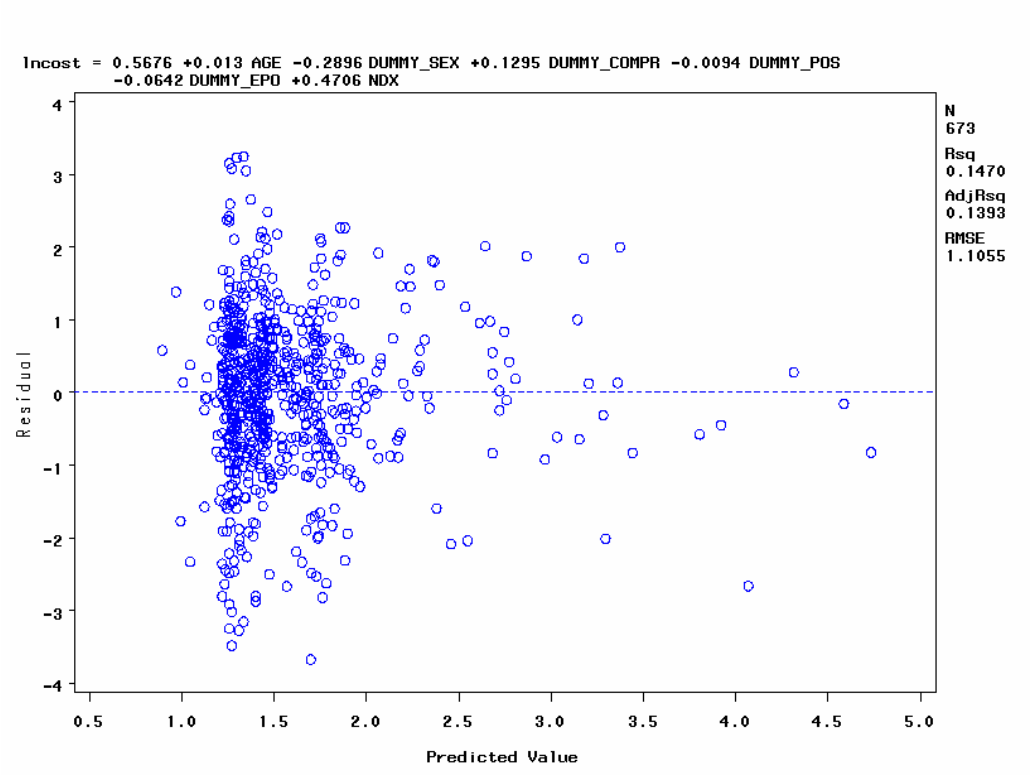


Figure 14: Scatter plot of residuals versus predicted values (fee-for-service dataset)



The robustness of the model was further assessed by determining the influence of the interaction between age and number of diagnoses. Including this interaction term into the regression model reduced the adjusted r^2 of the model only negligibly (0.138 versus 0.139 without the interaction term). Since the term did not have significant impact on the dependent variable, the selected model was robust regarding the interaction between age and number of diagnoses.

Finally, it was assessed whether outliers, visible in the scatter plot of residuals, might have influenced parameter estimates. Altogether 10 outliers were identified by the regression model.[77] The influence of these outliers was assessed by removing them from the dataset and assessing the impact on the estimated model. While parameter estimates for the reduced dataset were nearly the same as for that with outliers, removing the

[77] The standard statistical tool contained in the SAS software package, i.e., the robust regression procedure with detection of outliers via the method of M estimation, was applied.[223] The procedure identifies those observations for which the standardized residuals (the residuals divided by their standard errors) are more than 3 standard deviations away from the mean (zero).[220]

outliers improved the adjusted r^2 from 0.147 to 0.156. Closer examination of the raw data indicated that six of the outliers were patients with two or fewer outpatient visits and no more than one prescription, while the other four were patients who received either very intensive outpatient and/or inpatient treatment and/or very expensive prescriptions for mental disorders. While these were extreme cases, they nevertheless reflect real-life patients who either do not continue with care or who are very severely impacted by their disorder and therefore require expensive treatments. Even though removing the outliers would improve the fit of the model, it would result in a biased view of reality. The original model was therefore chosen as the final one.

3.4.3 Encounter claims

After the cleaning of encounter claims, the dataset contained 7,065 records for 305 patients with bulimia nervosa at least 12 years of age. Since the healthcare enrollment period is critical for the determination of average daily treatment costs, two patients with missing information regarding their start and/or end date of enrollment were excluded. The dataset was thereby reduced to 303 patients with bulimia nervosa and 7,054 encounter claims. These comprised 2,508 outpatient claims incurred by 293 patients, 42 inpatient claims for 20 patients, and 4,504 drug claims for 285 patients.

3.4.3.1 Patient characteristics

Twelve patients were male (3.96%). The distribution of patients by age and other patient baseline characteristics is displayed in Table 31. Nearly two thirds of the patients (62.9%) were younger than 30 years, and about half (49.5%) were the children of the primary beneficiaries: i.e., the employees. The predominant healthcare plan was the HMO (64.0%). About 46% of employees and their dependents were located in the Western region of the U.S.

Table 31: Patient baseline characteristics (encounter dataset)

Patient characteristic	Frequency	Percent
Age group (years):		
• 12–19	99	32.57
• 20–29	92	30.36
• 30–39	54	17.82
• ≥ 40	58	19.14
Relationship to primary beneficiary:		
• Employee	103	33.99
• Spouse	50	16.50
• Child	150	49.50
Plan of healthcare plan:		
• HMO	194	64.03
• POS with capitation	109	35.97
Region:		
• North East	93	30.69
• North Central	34	11.22
• South	37	12.21
• West	139	45.87

Abbreviations: HMO = Health Maintenance Organization; POS = Point Of Service

In addition to treatment for bulimia nervosa, patients had also received healthcare services for a variety of other conditions. The frequency distribution of number of diagnoses per patient was similar to that for the fee-for-service dataset: based on only primary diagnoses of claims, 87% of patients were treated for one condition, while the remainder had received treatment for one or two additional conditions (Table 32). If all primary and secondary diagnoses were considered, approximately 18% of patients had received treatment in relation to two or more conditions.

Table 32: Number of diagnoses per patient (based on primary and/or secondary diagnoses in the encounter dataset)*

Number of diagnoses per patient	Primary diagnosis		Primary & secondary diagnoses	
	Number of patients	Percent of patients	Number of patients	Percent of patients
1	265	87.46	249	82.18
2	34	11.22	25	8.25
3	4	1.32	16	5.28
4			5	1.65
5			6	1.98
9			2	0.66
Total	**303**	**100.00**	**303**	**100.00**

* Each diagnosis was counted only once per patient. Outpatient and inpatient claims may contain up to 4 secondary diagnoses in addition to the primary diagnosis.

Table 33 shows the frequency of primary and secondary diagnoses by ICD-9 class and ICD-9 code, as recorded in the original claims data, with each diagnosis being counted only once per patient. The most prevalent comorbidities or complications of patients with bulimia nervosa based on all diagnoses as well as primary diagnoses only were symptoms concerning nutrition, metabolism, and development (28 and 27 patients, respectively), and episodic mood disorders (13 and 11 patients, respectively). All of the 303 patients had been treated primarily for bulimia nervosa at least once.

Table 33: Frequency of diagnoses per patient* (based on all diagnoses [ALL DX] and primary diagnoses only [1° DX] in the encounter dataset)

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	All DX (%)	1° DX (n)	1° DX (%)
3. Endocrine, nutritional, and metabolic diseases, and immunity disorders			**8**		**1**	
272		Disorder of lipid metabolism	1	0.33		
	272.0	Pure hypercholesterolemia	1	0.33		
276		Disorders of fluid, electrolyte, and acid-base balance	3	0.99	1	0.33
	276.5	Volume depletion	1	0.33		
	276.8	Hypokalemia	2	0.66	1	0.33
278		Obesity and other hyperalimentation	3	0.99	1	0.33
	278.00	Obesity – unspecified	2	0.66		
	278.01	Morbid obesity	1	0.33	1	0.33
285		Other and unspecified anemias	1	0.33		
	285.9	Anemia – unspecified	1	0.33		
5. Mental disorders			**353**		**307**	
293		Transient mental disorder due to conditions classified elsewhere	1	0.33		
	293.84	Anxiety disorder in conditions classified elsewhere	1	0.33		
296		Episodic mood disorders	13	4.29	11	3.63
	296.20	Major depressive disorder, single episode – unspecified	1	0.33	1	0.33
	296.23	Major dep. dis., single episode – severe, w/o mention of psychotic beh.	2	0.66	2	0.66
	296.30	Major depressive disorder, recurrent episode – unspecified	1	0.33	1	0.33
	296.32	Major depressive disorder, recurrent episode – moderate	1	0.33	1	0.33
	296.33	Major dep. dis., recurrent epi. – severe, w/o mention psychotic beh.	3	0.99	2	0.66
	296.34	Major dep. dis., recurrent epi. – severe, with psychotic beh.	1	0.33	1	0.33

Table 33 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	All DX (%)	1° DX (n)	1° DX (%)
	296.41	Bipolar I disorder, most recent/current episode – mild	1	0.33	1	0.33
	296.7	Bipolar I disorder, most recent/current episode – unspecified	2	0.66	2	0.66
	296.80	Bipolar disorder – unspecified	1	0.33		
300		Anxiety, dissociative and somatoform disorders	3	0.99		
	300.15	Dissociative disorder or reaction – unspecified	1	0.33		
	300.4	Dysthymic disorder	2	0.66		
301		Personality disorders	4	1.32		
	301.83	Borderline personality disorder	3	0.99		
	301.9	Unspecified personality disorder	1	0.33		
303		Alcohol dependence syndrome	2	0.66	1	0.33
	303.00	Acute alcoholic intoxication – unspecified	1	0.33		
	303.91	Other or unspecified alcohol dependence – continuous	1	0.33	1	0.33
304		Drug dependence	1	0.33		
	304.80	Combinations of drug dependence excluding opioid type drug – unspec.	1	0.33		
305		Nondependent abuse of drugs	6	1.98		
	305.20	Cannabis abuse – unspecified	3	0.99		
	305.21	Cannabis abuse – continuous	1	0.33		
	305.90	Other, mixed, or unspecified drug abuse – unspecified	1	0.33		
	305.91	Other, mixed, or unspecified drug abuse – continuous	1	0.33		
307		Special symptoms or syndromes, not elsewhere classified	313	103.30	291	96.04
	307.1	Anorexia nervosa	8	2.64	3	0.99
	307.50	Eating disorder – unspecified	2	0.66		
	307.51	Bulimia nervosa	303	100.00	288	95.05

Table 33 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	All DX (%)	1° DX (n)	1° DX (%)
309		Adjustment reaction	4	1.32	2	0.66
	309.0	Adjustment disorder with depressed mood	2	0.66	2	0.66
	309.4	Adjustment disorder with mixed disturbance and depressed mood	1	0.33		
	309.81	Posttraumatic stress disorder	1	0.33		
311	311	Depressive disorder, not elsewhere classified	6	1.98	2	0.66
8. Diseases of the respiratory system			**1**			
465		Acute upper respiratory infections of multiple or unspecified sites	1	0.33		
	465.9	Unspecified site	1	0.33		
9. Diseases of the digestive system			**2**		**1**	
530		Diseases of esophagus	1	0.33		
	530.19	Other esophagitis	1	0.33		
535		Gastritis and duodenitis	1	0.33	1	0.33
	535.50	Unspecified gastritis and gastroduodenitis, w/o mention of obstruction	1	0.33	1	0.33
10. Diseases of the genitourinary system			**2**		**1**	
626		Disorders of menstruation & other abnormal bleeding female genital tract	2	0.66	1	0.33
	626.0	Absence of menstruation	1	0.33		
	626.1	Scanty or infrequent menstruation	1	0.33	1	0.33

Table 33 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	All DX (%)	1° DX (n)	1° DX (%)
11. Complications of pregnancy, childbirth, and the puerperium			**6**		**2**	
646		Other complications of pregnancy, not elsewhere classified	1	0.33	1	0.33
	646.83	Other unspec. compl. of preg., delivered w mention of postpartum cond.	1	0.33	1	0.33
648		Other current conditions in the mother classifiable elsewhere, but complicating pregnancy, childbirth, or the puerperium	4	1.32	1	0.33
	648.41	Mental disorders, delivered, w or w/o mention of antepartum condition	1	0.33		
	648.43	Mental disorders, antepartum condition or complication	1	0.33		
	648.91	Other current conditions classifiable elsewhere, delivered w or w/o mention of antepartum condition	1	0.33	1	0.33
	648.93	Other current cond. classifiable elsewhere, antepartum condition/compl.	1	0.33		
654		Abnormality of organs and soft tissues of pelvis	1	0.33		
	654.21	Previous Caesarean delivery, delivered, w or w/o mention of antepartum condition	1	0.33		
13. Diseases of the musculoskeletal system and connective tissue			**1**			
724		Other and unspecified disorders of back	1	0.33		
	724.2	Lumbago	1	0.33		
16. Symptoms, signs, and ill-defined conditions			**32**		**28**	
780		General symptoms	1	0.33	1	0.33
	780.2	Syncope and collapse	1	0.33	1	0.33
783		Symptoms concerning nutrition, metabolism, and development	28	9.24	27	8.91
	783.0	Anorexia	1	0.33	1	0.33
	783.1	Abnormal weight gain	1	0.33	1	0.33
	783.21	Loss of weight	1	0.33		
	783.6	Polyphagia	25	8.25	25	8.25

Table 33 continued

ICD-9 class	ICD-9 code	Description of ICD-9 code	All DX (n)	All DX (%)	1° DX (n)	1° DX (%)
784		Symptoms involving head and neck	1	0.33	1	0.33
	784.0	Headache	1	0.33	1	0.33
787		Symptoms involving digestive system	1	0.33		
	787.03	Vomiting alone	1	0.33		
789		Other symptoms involving abdomen and pelvis	1	0.33		
	789.09	Abdominal pain – other specified site	1	0.33		
17. Injury and poisoning			**3**		**2**	
913		Superficial injury of elbow, forearm, and wrist	1	0.33		
	913.8	Other and unspecified superficial injury without mention of infection	1	0.33		
965		Poisoning by analgesics, antipyretics, and antirheumatics	1	0.33	1	0.33
	965.1	Salicylates	1	0.33	1	0.33
969		Poisoning by psychotropic agents	1	0.33	1	0.33
	969.0	Antidepressants	1	0.33	1	0.33
V. Supplementary classification of factors influencing health status and contact with health services			**7**		**1**	
	V12.71	Peptic ulcer disease	1	0.33		
	V13.01	Urinary calculi	1	0.33		
	V60.0	Lack of housing	1	0.33		
	V61.20	Counseling for parent-child problem, unspecified	1	0.33		
	V65.3	Dietary surveillance and counseling	2	0.66		
	V70.3	Other medical examination for administrative purposes	1	0.33	1	0.33

* Each diagnosis was counted only once per patient. Outpatient and inpatient claims may contain up to 4 secondary diagnoses in addition to the primary one.

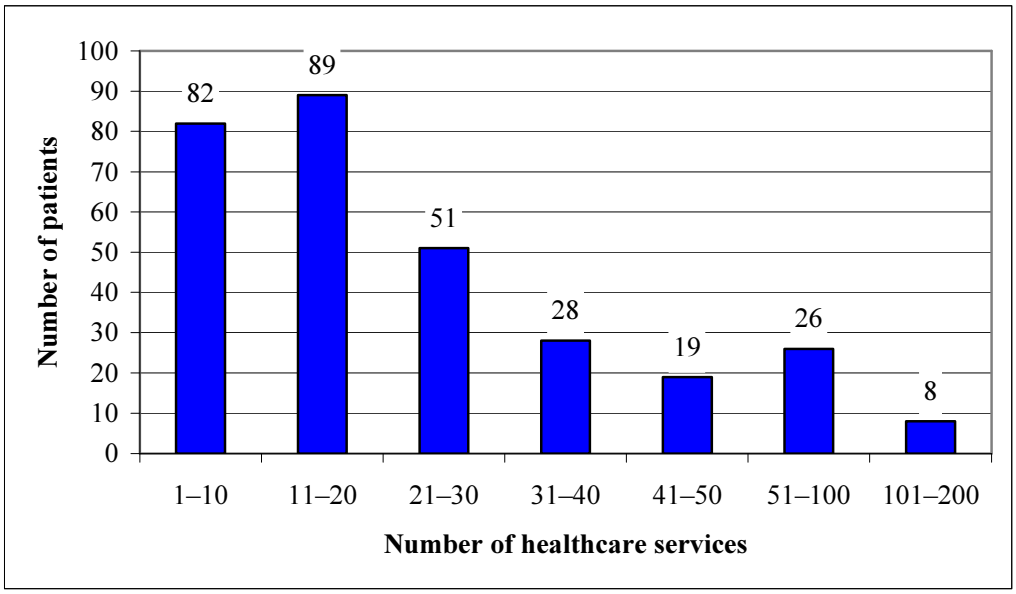
Abbreviation: DX = diagnosis

3.4.3.2 Healthcare utilization

As for the fee-for-service dataset, the utilization of healthcare services by patients with encounter claims was explored in terms of the number and types of resources used. Costs incurred due to treatment are described in section 3.4.3.3.

Throughout the year 2002, patients used on average 24.75 outpatient, inpatient, and pharmaceutical services, with a minimum of 1 and a maximum of 168. While more than half of the patients received between one and 20 services (56.4%), fewer than 3% used more than 100 (Figure 15).

Figure 15: Number of healthcare services* used per patient (encounter dataset)



* Healthcare services include outpatient and inpatient services as well as prescriptions.

As in the fee-for-service dataset, information regarding the procedure code, the place of service, the provider type, or the service type was either not applicable or missing for many claims. Therefore, results reported in the following tables reflect only a subset of all healthcare services, which might not be representative for the entire patient population with encounter claims.

Table 34 shows that among the claims containing information about the place of service (i.e., those with non-missing information), the most frequent site was the office (80.2% of

patients and 63.8% of services), followed by the outpatient hospital (11.6% of patients and services). The average number of claims for services in physician offices and outpatient hospital facilities were 7.9 and 9.9 per patient per year, respectively.

Table 34: Frequency of places of service (encounter dataset)

Code	Place of service	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
11	Office	243	80.20	7.85	1,908	63.83
21	Inpatient hospital	21	6.93	5.29	111	3.71
22	Outpatient hospital	35	11.55	9.89	346	11.58
23	ER – hospital	10	3.30	2.30	23	0.77
25	Birthing center	1	0.33	3.00	3	0.10
51	Inpatient psychiatric facility	8	2.64	13.00	104	3.48
52	Psychiatric facility, partial hospitalization	7	2.31	10.43	73	2.44
81	Independent laboratory	9	2.97	4.67	42	1.41
95	Outpatient (NEC)	35	11.55	6.74	236	7.90
99	Other unlisted facility	6	1.98	23.83	143	4.78
Total					**2,989**	**100.00**

Abbreviations: NEC = Not Elsewhere Classified; no. = number; ER = Emergency Room
* Each patient can have visited different places of service or at none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 303 and 100%, respectively.
† The mean/patient reflects the average number of times a patient visited the respective place of service.
‡ The total number of services reflects the overall number of times the respective place of service was used by all patients included in the analysis.
§ The total percent shows the overall distribution of the utilization of places of service by all patients.

The predominant healthcare providers were the psychiatrist (43.2% of patients and 33.7% of services) and the supportive therapist (23.4 % of patients and 22.0% of services; Table 35). Patients received on average 7.6 and 9.1 services from psychiatrists and supportive therapists, respectively, during the year.

Table 36 demonstrates that the most frequent group of procedures was other psychiatric services (71.6% of patients and 60.1% of services), while according to Table 37, individual psychiatric therapy was the most prevalent type of service (51.8% of patients and 38.2% of services), which patients received an average of 7.2 times per year.

Table 35: Frequency of provider types (encounter dataset)

Code	Provider type	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
1	Acute care hospital	49	16.17	4.69	230	7.81
10	Birthing center	1	0.33	3.00	3	0.10
20	Mental health/chemical dependency (NEC)	6	1.98	26.50	159	5.40
21	Mental health facility	8	2.64	6.13	49	1.66
40	Other facility (NEC)	6	1.98	15.67	94	3.19
170	Pathology	1	0.33	13.00	13	0.44
200	Medical doctor - MD (NEC)	16	5.28	3.56	57	1.94
204	Internal medicine (NEC)	11	3.63	2.27	25	0.85
206	Multi-specialty physician group	6	1.98	12.67	76	2.58
220	Emergency Medicine	5	1.65	2.40	12	0.41
240	Family practice	17	5.61	3.29	56	1.90
250	Cardiovascular disorder/ cardiology	1	0.33	2.00	2	0.07
275	Gastroenterology	1	0.33	1.00	1	0.03
365	Psychiatry	131	43.23	7.58	993	33.72
400	Pediatrician (NEC)	15	4.95	1.93	29	0.98
410	Pediatric specialist (NEC)	1	0.33	3.00	3	0.10
458	Child psychiatry	1	0.33	2.00	2	0.07
810	Dietician	8	2.64	12.88	103	3.50
822	Nursing services	3	0.99	2.00	6	0.20
853	Therapists (supportive)	71	23.43	9.11	647	21.97
860	Psychologist	30	9.90	10.60	318	10.80
930	Laboratory	12	3.96	5.58	67	2.28
Total					**2,945**	**100.00**

Abbreviations: NEC = Not Elsewhere Classified; no. = number; dep. = dependency

* Each patient can have been treated by different provider types or by none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 303 and 100%, respectively.

† The mean/patient reflects the average number of times a patient visited the respective provider type.

‡ The total number of services reflects the overall number of times the respective provider type was visited by all patients included in the analysis.

§ The total percent shows the overall distribution of the utilization of provider types by all patients.

Table 36: Frequency of procedure groups (encounter dataset)

Code	Procedure group	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
31	Venipucture (blood draw)	18	5.94	1.11	20	0.77
101	Office visits, new patient	11	3.63	1.09	12	0.46
104	Office visits, established patient	55	18.15	3.40	187	7.23
111	ER visit, new patient	10	3.30	1.40	14	0.54
120	Consultation	5	1.65	2.20	11	0.43
129	Other medical services	1	0.33	4.00	4	0.15
133	Preventive medical services	2	0.66	6.00	12	0.46
135	Psychotherapy, individual	2	0.66	6.00	12	0.46
136	Psychotherapy, family	26	8.58	3.12	81	3.13
137	Psychotherapy, group	41	13.53	8.98	368	14.22
139	Other psychiatric services	217	71.62	7.17	1,555	60.11
150	Other ENT services (nonsurgical)	1	0.33	1.00	1	0.04
155	EKG	6	1.98	1.33	8	0.31
169	Other nonsurgical pulmonary services	3	0.99	3.00	9	0.35
177	Other neurology services	5	1.65	1.40	7	0.27
190	Case Management Services	3	0.99	2.33	7	0.27
197	Specimen handling	1	0.33	1.00	1	0.04
199	All other medical procedures	13	4.29	8.23	107	4.14
202	X-ray, chest	1	0.33	1.00	1	0.04
210	CAT scan, head & neck	1	0.33	1.00	1	0.04
303	Lab test, organ/disease panel	29	9.57	1.62	47	1.82
306	Routine urinalysis	5	1.65	1.40	7	0.27
307	Other urinalysis	1	0.33	1.00	1	0.04
311	Thyroid function test (RIA)	7	2.31	1.71	12	0.46
312	Thyroid function test (non-RIA)	2	0.66	1.00	2	0.08
313	Other radio-immunoassays (RIA)	3	0.99	1.00	3	0.12
319	Other chemical/toxicology tests	17	5.61	4.12	70	2.71
331	Blood count, automated	15	4.95	1.33	20	0.77
334	Blood tests, sedimentation rate	1	0.33	1.00	1	0.04
349	Immunology tests	4	1.32	1.00	4	0.15
363	Bacterial culture, urine	1	0.33	2.00	2	0.08
Total					**2,587**	**100.00**

Abbreviations: no. = number; ER = emergency room; ENT = ear, nose and throat;
EKG = electrocardiogram; CAT = computerized axial tomography; RIA = radio-immunoassays

* Each patient can have received different procedure groups or none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 303 and 100%, respectively.
† The mean/patient reflects the average number of times a patient received the respective procedure group.
‡ The total number of services reflects the overall number of times the respective procedure group was used by all patients included in the analysis.
§ The total percent shows the overall distribution of the utilization of procedure groups by all patients.

Table 37: Frequency of service types (encounter dataset)

Code	Service type	No. of patients*	Percent of patients*	Mean/ patient†	Total no.‡	Total percent§
1	Surgery (NEC)	14	4.62	1.07	15	0.51
50	Physician attendance	83	27.39	2.94	244	8.30
60	Room and board (NEC)	13	4.29	16.92	220	7.49
61	Intensive care unit	1	0.33	1.00	1	0.03
68	All inclusive – room/board/ ancillary	4	1.32	1.25	5	0.17
69	Other room charges	1	0.33	1.00	1	0.03
75	Ancillary/facility services (NEC)	4	1.32	1.25	5	0.17
76	Clinic (NEC)	2	0.66	1.50	3	0.10
77	Emergency services	4	1.32	1.00	4	0.14
81	Inpatient pharmacy/IV	2	0.66	1.50	3	0.10
85	Diagnostic services (NEC)	6	1.98	2.17	13	0.44
86	Diagnostic lab	41	13.53	5.29	217	7.39
87	Diagnostic radiology	2	0.66	3.50	7	0.24
88	Computerized axial tomography scan	2	0.66	1.00	2	0.07
91	Electrocardiogram	6	1.98	1.33	8	0.27
101	Psychiatric (NEC)	49	16.17	6.86	336	11.44
102	Substance abuse (NEC)	1	0.33	1.00	1	0.03
104	Psychiatric day/night care	2	0.66	17.50	35	1.19
105	Psychiatric exam/testing	89	29.37	1.35	120	4.08
106	Individual psychiatric therapy	157	51.82	7.15	1,123	38.22
107	Group psychiatric therapy	64	21.12	6.98	447	15.21
110	Therapies & treatments NEC	2	0.66	5.00	10	0.34
131	Health education	11	3.63	10.00	110	3.74
155	Drugs (NEC)	1	0.33	5.00	5	0.17
161	Hearing	1	0.33	1.00	1	0.03
190	State imposed surcharges	1	0.33	2.00	2	0.07
Total					**2,938**	**100.00**

Abbreviations: NEC = Not Elsewhere Classified; no. = number; IV=intravenous therapy
* Each patient can have received different service types or none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 303 and 100%, respectively.

† The mean/patient reflects the average number of times a patient received the respective service type.
‡ The total number of services reflects the overall number of times the respective service type was used by all patients included in the analysis.
§ The total percent shows the overall distribution of the utilization of service types by all patients.

Among the admissions of patients with bulimia nervosa, the predominant DRG codes were for psychoses (2.6% of patients and 41.7% of hospitalizations) and other mental disorder diagnoses (1.3% of patients and 16.7% of hospitalizations; Table 38).

Table 38: Frequency of DRGs among all admissions* (encounter dataset)

Code	DRG	No. of patients†	Percent of patients†	Total no.‡	Total percent§
296	Nutritional & miscellaneous metabolic disorders with complication, age > 17 years	1	0.33	1	4.17
371	Caesarean section without complication	1	0.33	1	4.17
383	Other antepartum diagnoses with medical complication	1	0.33	1	4.17
426	Depressive neuroses	3	0.99	3	12.50
428	Disorders of personality and impulse control	2	0.66	2	8.33
430	Psychoses	8	2.64	10	41.67
431	Childhood mental disorders	1	0.33	1	4.17
432	Other mental disorder diagnoses	4	1.32	4	16.67
451	Poisoning & toxic effects of drugs, age 0–17 years	1	0.33	1	4.17
Total				**24**	**100.00**

* Each DRG refers to one unique admission.
† Each patient can have been hospitalized multiple times or not at all; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 303 and 100%, respectively.
‡ The total number of DRGs reflects the overall number of times the respective DRG was recorded as the primary reason for a hospitalization.
§ The total percent shows the overall distribution of DRGs among all hospitalizations.

With regard to drugs, the most frequently prescribed were for the central nervous system (55.8% of patients and 51.2% of prescriptions), followed by hormones and synthetic substitutes (34.3% of patients and 15.1% of prescriptions; Table 39). Patients received these medications for an average of 294 days and 212 days, respectively, during the year.

Table 39: Frequency of therapeutic groups (encounter dataset)[*]

Code	Therapeutic Group	No. of patients*	Percent of patients*	Days/ patient[†]	Total no.[‡]	Total percent[§]
01	Antihistamines and combinations	23	7.59	81.35	92	1.75
02	Anti-infective agents	101	33.33	42.04	487	9.27
04	Autonomic drugs	65	21.45	59.09	232	4.42
06	Blood forming/coagulating agents	2	0.66	130.50	10	0.19
07	Cardiovascular agents	13	4.29	291.15	89	1.69
08	Central nervous system	169	55.78	294.45	2,689	51.21
09	Contraceptive cream/foam/ devices	1	0.33	2.00	2	0.04
10	Dental agents	3	0.99	35.67	7	0.13
13	Electrolytic, caloric, water	13	4.29	207.15	73	1.39
15	Antituss/expector/ mucolytic	15	4.95	17.53	33	0.63
16	Eye, ear, nose, throat	24	7.92	43.67	74	1.41
17	Gastrointestinal drugs	45	14.85	139.80	212	4.04
20	Hormones & synthetic substitutes	104	34.32	211.75	791	15.06
21	Immunosuppressants	1	0.33	540.00	22	0.42
25	Serums, toxoids, vaccines	1	0.33	60.00	2	0.04
26	Skin & mucous membrane	59	19.47	42.34	308	5.87
27	Smooth muscle relaxants	4	1.32	192.50	21	0.40
28	Vitamins & combinations	9	2.97	66.00	40	0.76
29	Unclassified agents	17	5.61	103.35	65	1.24
30	Devices & non-drug items	2	0.66	45.50	2	0.04
Total					**5,251**	**100.00**

* Each patient can have received different therapeutic groups of drugs or none of them; therefore, the sum of the number of patients and the sum of the percentages of patients do not equal 303 and 100%, respectively.

† The days/patient reflect the average number of days a patient received the respective therapeutic group prescribed.

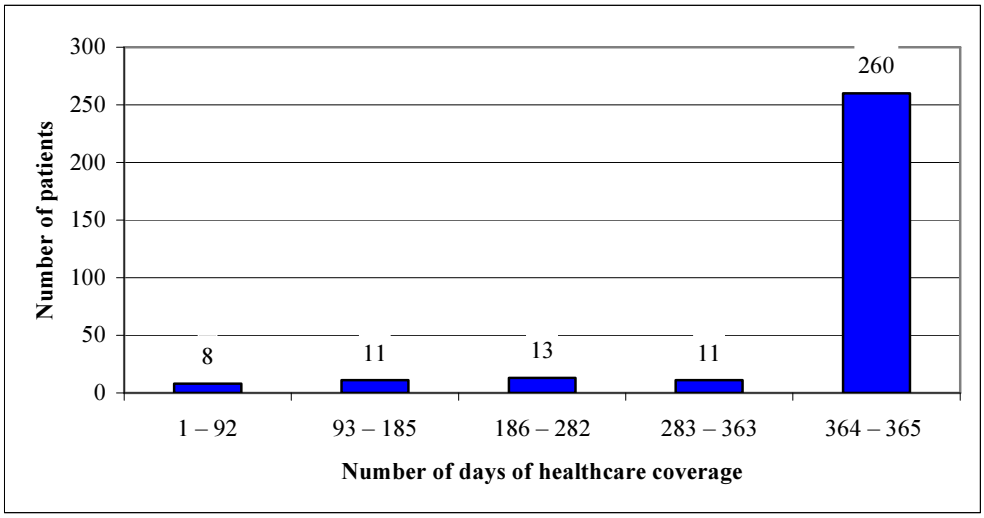
‡ The total number reflects the overall number of days the respective therapeutic group of drugs was prescribed for all patients included in the analysis.

§ The total percent shows the overall distribution of the utilization of therapeutic groups, based on the number of days prescribed.

3.4.3.3 Total cost of illness

By analogy to the fee-for-service claims, the cost of bulimia nervosa was analyzed on a per patient per day basis, since the time period of enrollment, and therefore health insurance coverage, varied between patients (Figure 16). The majority (86%) were enrolled in a healthcare plan throughout 2002, while only 6% had less than half a year of enrollment in either an HMO or a POS with capitation plan.

Figure 16: Distribution of patients by number of days of healthcare coverage (encounter dataset)



For the main analysis, the mean daily costs of patients aged at least 12 years with encounter claims for bulimia nervosa in 2002 were determined based on the approximated costs, as described in 3.3.2.2. In a secondary analysis, daily costs were also calculated according to the information contained in the original claims—i.e., without cost approximation and with inclusion of zero payments.

Average approximated costs are shown in Table 40. The average daily gross payment to providers across all claims, irrespective of whether or not the specific cost was incurred by the patient, was $11.61 per patient, while the net payment by insurers was on average $7.41 per patient. Mean daily costs to patients were $1.22 and $0.14 for copayments and

deductibles, respectively, and the average payment by third party payers was $0.09. Results were virtually identical for the subset of patients incurring the respective costs.

As costs and expenses for most encounter claims were approximated by mean fee-for-service equivalents, the estimates for the net payment, copayment, deductible, and COB did not necessarily add up to the estimated gross payment for each encounter claim.

Table 40: Approximated average daily cost per patient (encounter dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
All patients							
Gross payment	303	11.61	4.84	0.53	29.95	0.04	657.69
Net payment	303	7.41	3.40	0.35	14.75	0.00	607.96
COB	303	0.09	0.00	0.00	0.04	0.00	21.32
Copayment	303	1.22	0.89	0.08	3.34	0.00	17.30
Deductible	303	0.14	0.07	0.00	0.48	0.00	3.62
Patients incurring the respective cost							
Gross payment	303	11.61	4.84	0.53	29.95	0.04	657.69
Net payment	301	7.46	3.47	0.37	14.75	0.03	607.96
COB	236	0.12	0.00	0.00	0.08	0.00	21.32
Copayment	301	1.23	0.89	0.08	3.34	0.00	17.30
Deductible	296	0.15	0.07	0.01	0.48	0.00	3.62

Table 41 shows that, based on all 303 patients, the approximated average daily gross payment per patient was higher for outpatient claims ($4.94) and drug claims ($4.03) than inpatient claims ($2.65). Since these results include patients who did not receive the respective service, the lower mean daily cost per patient for inpatient services reflects the infrequent admission of patients with bulimia nervosa. In contrast, considering only patients who received the respective type of service, the estimated mean daily costs were $40.11 for inpatient services compared to $5.11 and $4.28 for outpatient services and pharmaceuticals, respectively.

Table 41: Approximated average daily cost per patient (encounter dataset; in US$, 2002)

Cost variable	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
All patients							
Outpatient services	303	4.94	1.03	0.12	9.01	0.00	656.60
Inpatient services	303	2.65	0.00	0.00	14.87	0.00	283.58
Drugs	303	4.03	2.38	0.00	13.29	0.00	50.92
Patients incurring the respective cost							
Outpatient services	293	5.11	1.12	0.15	9.02	0.04	656.60
Inpatient services	20	40.11	24.09	6.35	213.85	6.35	283.58
Drugs	285	4.28	2.66	0.13	14.13	0.01	50.92

* The mean is based on the approximated daily gross payment.

In a secondary analysis, daily costs per patient were determined based on the payment information contained in the original claims records. Since financial information in encounter claims underestimates the costs of healthcare services, these unadjusted mean costs provide a conservative estimate of the costs of bulimia nervosa. Accordingly, unadjusted mean daily gross payments and net payments per patient were lower than the equivalent approximated costs (Table 42). Mean daily gross and net payments averaged across all patients were lower than the corresponding results for only patients incurring the respective costs.

Table 42: Unadjusted average daily cost per patient (encounter dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
All patients							
Gross payment	303	5.96	4.49	0.06	17.72	0.00	94.75
Net payment	303	3.19	3.06	0.00	12.72	0.00	90.81
COB	303	0.00	0.00	0.00	0.00	0.00	0.07
Copayment	303	0.78	0.53	0.07	2.24	0.00	6.45
Deductible	303	0.02	0.00	0.00	0.00	0.00	1.10
Patients incurring the respective cost							
Gross payment	289	6.25	3.18	0.36	21.68	0.01	94.75
Net payment	175	5.52	2.87	0.21	19.54	0.06	90.81
COB	1	0.07	0.07	0.07	0.07	0.07	0.07
Copayment	303	0.78	0.53	0.07	2.24	0.00	6.45
Deductible	11	0.57	0.55	0.03	1.10	0.03	1.10

As with the results of the main analysis, unadjusted average daily costs were found to be higher for outpatient services and drugs than for inpatient services if all claims and patients were included, but the converse if only patients incurring the respective costs were considered (Table 43). As expected, unadjusted average daily costs were much lower than approximated costs.

Table 43: Unadjusted average daily cost per patient (encounter dataset; in US$, 2002)

Cost variable	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
All patients							
Outpatient services	303	2.14	0.75	0.00	7.77	0.00	66.42
Inpatient services	303	1.02	0.00	0.00	1.81	0.00	67.70
Drugs	303	2.80	1.02	0.00	11.77	0.00	38.85
Patients incurring the respective cost							
Outpatient services	293	2.22	0.76	0.00	7.92	0.00	66.42
Inpatient services	20	15.39	12.55	0.00	59.12	0.00	67.70
Drugs	285	2.98	1.24	0.02	11.81	0.00	38.85

* The mean is based on the unadjusted daily gross payment.

3.4.3.4 Sensitivity analyses and univariate analyses

i) Cost of illness based on claims with a primary diagnosis of bulimia nervosa

In a sensitivity analysis, the costs directly attributable to bulimia nervosa were assessed by including only those claims with the respective primary diagnosis. This reduced the dataset to 2,368 outpatient and inpatient encounter claims, which were incurred by 288 patients.

Similarly to the analysis of all claims, the main analysis was based on approximated costs, while in a secondary analysis mean costs were calculated according to the financial information contained in the original claims records. Table 44 shows that the approximated average daily cost per patient was about 50% lower compared to that for all claims due the exclusion of claims without a primary diagnosis of bulimia nervosa and those of prescription claims. The average daily gross payment per patient was $5.78 and the payments by insurers, patients, and third parties were on average $4.27, $0.60, and $0.10, respectively.

Table 44: Approximated average daily cost per patient based on outpatient and inpatient claims with a primary diagnosis of bulimia nervosa - all patients (encounter dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	288	5.78	1.11	0.15	9.62	0.04	656.60
Net payment	288	4.27	0.79	0.09	6.23	0.00	607.19
COB	288	0.10	0.00	0.00	0.04	0.00	21.32
Copayment	288	0.46	0.16	0.02	1.56	0.00	16.99
Deductible	288	0.14	0.06	0.01	0.48	0.00	3.61

The unadjusted mean gross payment to providers and the net payment by insurers were much lower: $2.25 and $1.21, per day per patient, respectively (Table 45). As discussed above, the unadjusted mean daily gross payment reflects a minimum estimate of the cost of bulimia nervosa.

Table 45: Unadjusted average daily cost per patient based on outpatient and inpatient claims with a primary diagnosis of bulimia nervosa - all patients (encounter dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	288	2.25	0.75	0.00	7.60	0.00	66.42
Net payment	288	1.21	0.02	0.00	4.56	0.00	64.58
COB	288	0.00	0.00	0.00	0.00	0.00	0.07
Copayment	288	0.28	0.08	0.00	1.11	0.00	5.45
Deductible	288	0.02	0.00	0.00	0.00	0.00	1.10

ii) Cost of illness based on all patients at least 18 years of age

Mean daily costs were also determined for the subgroup of patients at least 18 years of age, limiting the analysis to 241 patients. Results were very similar to those for all patients: the approximated mean daily gross payment was $11.05 in patients at least 18 years of age compared to $11.61 for all 303 patients with encounter claims (Table 46). Approximated mean payments by insurers were also similar: $8.02 per patient at least 18 years of age versus $7.41 for all 303 patients.

Table 46: Approximated average daily cost per patient at least 18 years of age, all diagnoses and patients (encounter dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	241	11.05	4.95	0.70	22.48	0.10	657.69
Net payment	241	8.02	3.51	0.38	14.75	0.00	607.96
COB	241	0.11	0.00	0.00	0.04	0.00	21.32
Copayment	241	1.26	0.94	0.09	3.27	0.00	17.30
Deductible	241	0.15	0.15	0.00	0.48	0.00	3.62

With regard to unadjusted mean costs, results were also comparable for patients at least 18 years of age (Table 47) and those 12 years or older: for instance, mean daily gross payments were $5.58 and $5.96 for patients at least 18 and 12 years, respectively.

Table 47: Unadjusted average daily cost per patient at least 18 years of age, all diagnoses and patients (encounter dataset; in US$, 2002)

Cost variable	N	Mean	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
Gross payment	241	5.58	3.09	0.13	16.37	0.00	94.75
Net payment	241	3.20	0.49	0.00	12.00	0.00	90.81
COB	241	0.00	0.00	0.00	0.00	0.00	0.00
Copayment	241	0.79	0.56	0.08	2.22	0.00	6.45
Deductible	241	0.02	0.00	0.00	0.00	0.00	0.96

iii) Univariate analyses of patient characteristic

In addition, univariate analyses were performed to assess descriptively whether patients' baseline characteristics could have an impact on the average approximated daily cost, as determined based on all patients and all claims. Results demonstrate that the mean daily cost per patient tended to be slightly higher for females than males (Table 48), was lower for children and employees than spouses (Table 49), lower for point of service plans with capitation than HMOs (Table 50), and higher in the Northeast and West than the North Central and South regions of the U.S. (Table 51). These findings mirror in part those of the fee-for-service dataset with the exception of cost differences between employees, spouses, and children. Contrary to the results of the univariate analyses of the fee-for-service dataset, average daily costs were slightly lower in employees than children, which may be explained by a correlation of the variable 'relationship with employee' with the patient's age. The lower average daily costs in patients with a capitated POS is likely explained by the disincentives for physicians to provide resource-intensive care, given that they are paid on a per-patient basis.

Table 48: Approximated daily cost by gender - all patients (encounter dataset; in US$, 2002)

Gender	N	Mean*	Median	5th percentile	95th percentile	Minimum	Maximum
Male	12	10.29	3.99	0.64	51.45	0.64	51.45
Female	291	11.67	4.87	0.52	29.95	0.04	657.69

* Mean refers to approximated daily gross payment.

Table 49: Approximated daily cost by relationship to employee - all patients (encounter dataset; in US$, 2002)

Relationship to employee	N	Mean*	Median	5th percentile	95th percentile	Minimum	Maximum
Employee	103	7.80	5.26	0.87	20.56	0.46	56.38
Spouse	50	24.21	6.23	1.04	29.95	0.46	657.69
Child/other	150	10.05	3.83	0.39	35.94	0.04	283.58

* Mean refers to approximated daily gross payment.

Table 50: Approximated daily cost by type of healthcare plan - all patients (encounter dataset; in US$, 2002)

Plan type	N	Mean*	Median	5th percentile	95th percentile	Minimum	Maximum
HMO	194	13.50	4.86	0.58	39.83	0.12	657.69
POS with capitation	109	8.23	4.72	0.46	23.42	0.04	170.50

* Mean refers to approximated daily gross payment.

Table 51: Approximated daily cost by region - all patients (counter dataset; in US$, 2002)

Region	N	Mean*	Median	5th percentile	95th percentile	Minimum	Maximum
Northeast	93	14.39	4.72	0.62	29.26	0.39	657.69
North Central	34	9.03	4.59	1.04	39.83	0.95	52.78
South	37	8.41	3.33	0.33	13.59	0.10	170.50
West	139	11.25	5.33	0.53	35.94	0.04	283.58

* Mean refers to approximated daily gross payment.

Approximated daily costs appeared to increase with the number of comorbidities per patient, as they were higher for patients with three or more comorbidities than those with one or two diagnoses (Table 52). However, there were too few patients to detect a trend.

Table 52: Approximated daily cost by number of diagnoses - all patients (encounter dataset; in US$, 2002)

Number of diagnoses	N	Mean*	Median	5th per-centile	95th per-centile	Mini-mum	Maxi-mum
1	249	8.78	4.64	0.52	17.84	0.04	657.69
2	25	7.94	3.62	0.62	29.26	0.34	52.78
3	16	48.99	14.67	0.58	283.58	0.58	283.58
4	5	29.14	39.83	4.32	51.45	4.32	51.45
5	6	23.03	20.60	7.31	48.57	7.31	48.57
9	2	32.73	32.73	29.95	35.52	29.95	35.52

* Mean refers to approximated daily gross payment.

Potential predictor variables of the approximated mean daily cost per patient were further assessed in multiple linear regression analyses.

3.4.3.5 Regression analyses

As with the fee-for-service data, regression analyses were only performed for the whole dataset, since the approximated mean daily cost per patient, which was assumed to be the best estimate of the cost of bulimia nervosa, was very similar for those at least 12 years of age and those 18 years or older.

The same explanatory variables as for fee-for-service analyses were selected a priori, with the only difference being that plan type referred to the categories HMO and POS with capitation. Since the steps of the regression analysis were identical to those described in section 3.4.2.5, only main results are reported here. In general, findings were similar to those of the fee-for-service dataset, even though statistical power was less due to the smaller patient population.

Since the distribution of daily costs was severely skewed (skewness 12.19, kurtosis 170.80) and deviated from that of a normal curve (Figure 17), the response variable was transformed by applying the natural logarithm of daily costs. The distribution of transformed costs was approximately normal (skewness 0.01, kurtosis 1.51), even though some outliers were visible at the upper and lower tail ends of the Q-Q plot (Figure 18).

Figure 17: Normality test – normal probability plot of daily cost and theoretical normal distribution (encounter dataset)

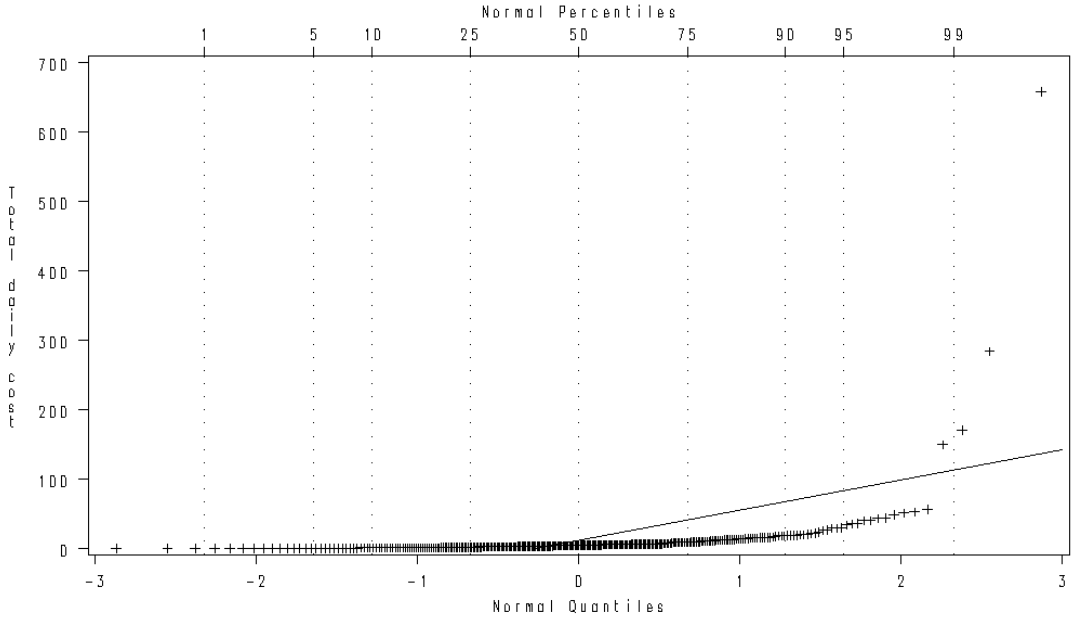
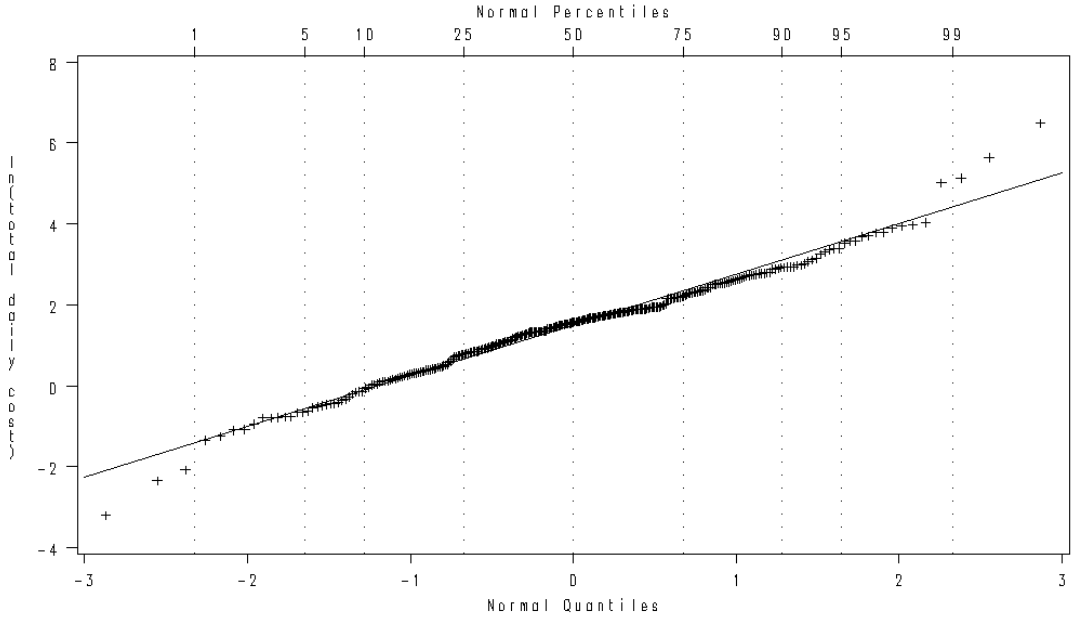


Figure 18: Normality test – normal probability plot of natural logarithm of daily cost and theoretical normal distribution (encounter dataset)



Examination of the bivariate scatter plots confirmed that the linearity assumption was met by the transformed cost data. Based on an assessment of the scatter plots, the correlation matrix of dependent and independent variables, and the results of univariate regression models (Table 53), number of diagnoses, age, and potentially employee relationship were identified as potential predictor variables, since they had an impact on the logarithm of daily costs. However, employee relationship showed only borderline significance in the univariate regression analysis (p=0.057).

Table 53: Univariate linear regression analyses (encounter dataset)

Variable	Parameter estimate	Standard Error	p	r^2
Number of diagnoses	0.388	0.067	<0.0001	0.100
Age	0.023	0.006	0.0001	0.048
Relationship to employee	-0.151	0.080	0.059	0.012
Male vs female	0.010	0.370	0.978	0.000
POS with capitation vs HMO	-0.058	0.050	0.250	0.004
Region	0.023	0.055	0.670	0.001

The correlation matrix of dependent variables demonstrated that age was strongly and significantly related to employee relationship (Table 54). In addition, age was significantly correlated with plan type and region. Further significant associations were found between plan type and region, plan type and employee relationship, gender and region, as well as between number of diagnoses and employee relationship, but of these correlations, only that between region and plan type was strong.

Table 54: Correlation matrix of independent variables* (encounter dataset)

	Number diagnoses	Age	Sex†	Plan type‡	Relat. to employee§	Region+
Number diagnoses	1	-0.105 0.068	-0.024 0.680	-0.083 0.151	0.124 0.031	0.012 0.833
Age	-0.105 0.068	1	0.064 0.269	-0.206 0.0003	-0.687 <0.0001	0.221 0.0001
Sex	-0.024 0.680	0.064 0.269	1	-0.082 0.156	0.003 0.964	0.131 0.022
Plan type	-0.083 0.151	-0.206 0.0003	-0.082 0.156	1	0.215 0.0002	-0.418 <0.0001
Relat. to employee	0.124 0.031	-0.687 <0.0001	0.003 0.964	0.215 0.0002	1	-0.099 0.086
Region	0.012 0.833	0.221 0.0001	0.131 0.022	-0.418 <0.0001	-0.099 0.086	1

* In each cell, the first value shows the correlation and the second one (below it) the p-value.
† Male coded as 1, female as 2.
‡ Comprehensive coded as 2, EPO as 3, POS as 5, and PPO as 6.
§ Employee coded as 1, spouse as 2, and child as 3.
+ North East coded as 1, North Central as 2, South as 3, West as 4, and 5 as unknown.

In addition to an examination of the correlation matrix, the existence of multicollinearity was confirmed by the computation of variance inflation factors and eigenvalues of the correlation matrix of predictor variables, which also indicated a close relationship between age and employee relationship and between plan type and region.

The optimum subset of independent variables for the regression model was selected according to the adjusted r^2 criterion. The best model, which included only age and number of diagnoses, was found to also have the lowest BIC.

The results of the selected regression model, which are presented in Table 55, demonstrate that daily costs increased by 3% with each additional year of age and by 52% with each additional diagnosis. The model was a good fit of the data; however, only 15.94% of the variance in the transformed daily costs was explained by the variation in the two independent variables.

Table 55: Multivariate regression analysis (encounter dataset)

Variable	Parameter estimate	Standard Error	Exponent (estimate)	p
Intercept	0.167	0.197	1.18	0.398
Age	0.027	0.006	1.03	<0.0001
Number of diagnoses	0.420	0.065	1.522	<0.0001

* p-value based on t-test.

The same a-posteriori checks of the selected regression model were performed as for the fee-for-service data. By statistical criteria as well as by graphical examination of the Q-Q plot (Figure 19) it was confirmed that the distribution of residuals was close to normal. In addition, there was no indication of heteroscedasticity, since the scatter plot of residuals versus predicted values (Figure 20) demonstrated an approximately equal variance of residuals across the range of predicted values. Autocorrelation of residuals was also excluded (Durbin-Watson statistic of 2.05).

Figure 19: Normal probability plot of standardized residuals (encounter dataset)

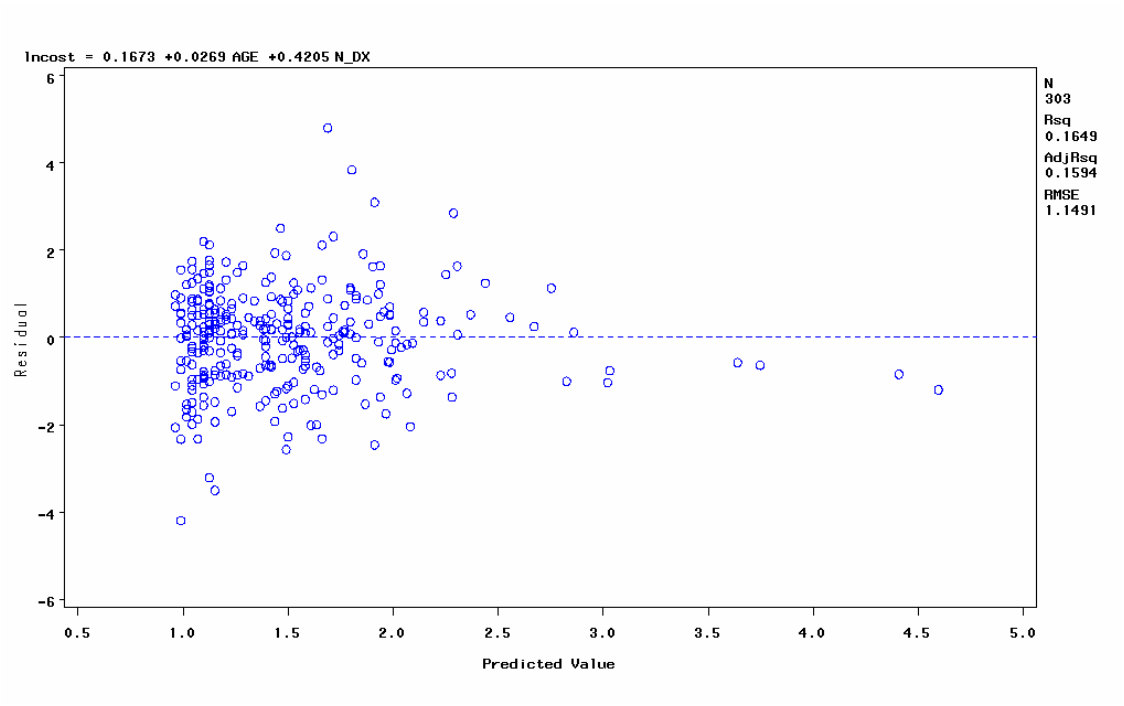
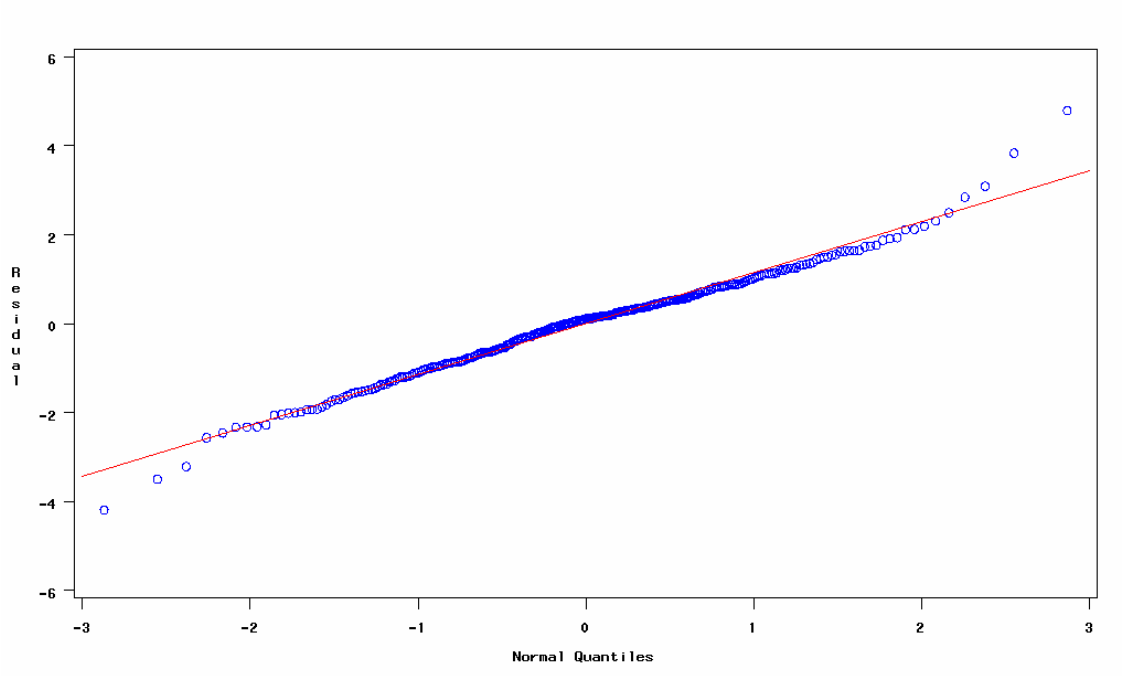


Figure 20: Scatter plot of residuals versus predicted values (encounter dataset)



Unlike the analysis of the fee-for-service data, the model based on the encounter data was influenced by the interaction term between age and number of diagnoses, even though this term did not reach statistical significance (p=0.08). Adding the term to the model led to an improvement of the adjusted r^2 (0.165 versus 0.159 without the interaction term) and the model with the interaction was therefore chosen as the final model, as it represented a better fit of the data (Table 56).

The interpretation of the interaction term is best described by an example: To compare the costs between two patients 30 and 20 years of age, respectively, both having three diagnoses, the estimate of the log(cost) obtained from the model for age=20 and number of diagnoses=3 is subtracted from that for age=30 and number of diagnoses=3; the result is then exponentiated to get an estimate of the ratio of costs for the 30-year-old patient over that of the 20-year-old patient; i.e., 1.11[78]. This result indicates that costs were 11% higher for each additional 10 years of age or they were about 1% higher for each additional year of age when comparing two patients, both having three diagnoses. Similarly, costs can be estimated to be 44%[79] higher for a patient 30 years of age with two diagnoses than for a patient 30 years of age with only one diagnosis.

Table 56: Multivariate regression analysis with interaction term (encounter dataset)

Variable	Parameter estimate	Standard Error	Exponent (estimate)	p
Intercept	-0.170	0.276	0.844	0.539
Age	0.040	0.009	1.041	<0.0001
Number of diagnoses	0.664	0.154	1.943	<0.0001
Interaction age and number of diagnoses	-0.010	0.006	0.991	0.083

* p-value based on t-test

Since the residual plot contained some outliers, their impact on the model was also assessed. Altogether, five outliers were identified. Removing these from the dataset only

[78] Assuming number of diagnoses=3, the exponent of the difference in costs between a patient 30 years of age and one 20 years of age is calculated as: exp[(-0.170+0.040*30+0.664*3-0.010*30*3)-(-0.170+0.040*20+0.664*3-0.010*20*3)] =1.111.

[79] Assuming age=30, the exponent of the difference in costs between a patient with two diagnoses versus one is calculated as: exp[(-0.170+0.040*30+0.664*2-0.010*30*2)- (-0.170+0.040*30+0.664*1-0.010*30*1)] =1.439.

led to a small improvement of the adjusted r^2 (0.166), but the interaction term was no longer significant (p=0.180). Three of the identified outliers referred to patients incurring very low costs (two patients with two laboratory tests each and one patient with one group psychiatric therapy), while for the other two patients treatment costs were very high (one patient was hospitalized for mental disorders and one patient had very extensive outpatient hospital care). Even though the reduced model would improve the fit of the model slightly, there was no indication that approximated costs for outliers were unrealistic, and the model with the interaction term based on 303 patients was therefore chosen as the final one.

4 Extrapolation

To estimate the burden of bulimia nervosa to payers in the U.S., national healthcare costs were predicted based on the average yearly cost per patient, the estimated prevalence of the disorder, as well as information about the size and insurance status of the U.S. population. The extrapolation of per-patient costs to the U.S. population was performed according to the following steps: first, the prevalence of bulimia nervosa in the adult population was estimated based on the literature presented in Chapter 2; then, the number of affected persons in the U.S. was calculated; finally, annual costs were projected by applying mean fee-for-service costs per patient. Since all these steps were subject to assumptions, the cost of illness is presented as a range, extending from the minimum to the maximum estimated burden to payers.

The two most recent epidemiological studies providing evidence on the prevalence of bulimia nervosa in the adult U.S. population are those by Klaplow et al (2002) and Johnson et al (2001).[57;61] Both were conducted in patients in primary care, but the study by Klaplow et al included men and women, while the study by Johnson et al focused on women only. In general practice attendees younger than 65 years and at least 65 years old, Klaplow et al found DSM-IV-based prevalence rates of 1.0% and 0.0%, respectively. Johnson et al reported prevalence rates for five age groups of adult women in primary and obstetric care, with an average rate of 0.9% across all age groups. Since this study provided prevalence rates for different age groups and since it included a validation of the patient's self-reported bulimic behavior by the physician, it was used as the primary reference to estimate the number of people suffering from bulimia nervosa in the U.S. The availability of age-specific prevalence rates was considered to be important, as age has been shown to be predictive of risk for bulimia nervosa. It should be noted that the prevalence may have been underestimated in the survey by Johnson et al if some outpatients did not disclose their disordered eating attitudes to avoid being diagnosed and treated; the rate of 0.9% in adult women is therefore likely a conservative estimate.

The overall prevalence in Johnson et al's survey concurs with results of other studies in adult female populations. In the absence of further evidence on the DSM-IV- or DSM-III-R-based prevalence in U.S. adult populations, findings from Johnson et al were compared with those reported in other industrialized countries. For example, Götesdam et al found a DSM-III-R-based prevalence of 0.7% in women in Norway,[81] while Kinzl et al and Westenhöfer et al reported slightly higher DSM-IV-based rates of 1.5% and 1.1% for Austria and Germany, respectively.[65;71] These three studies were conducted in general population samples and relied on patients' self-reported bulimic behavior only, while Johnson et al's estimates were derived from outpatients, whose responses to questionnaires were reviewed by the treating physician. Although results are therefore not directly comparable, they nevertheless lend support to the assumption that the prevalence in the general U.S. population may be similar to that in outpatients in the survey by Johnson et al.

Since the study by Johnson et al (2001) included only women, the prevalence of bulimia nervosa in men had to be estimated based on other available data sources. In their literature review, Carlat et al reported a prevalence ratio of 1:10 in men and women.[156] Assuming this ratio would be representative for outpatients and the general population, 0.09% of adult men were predicted to suffer from bulimia nervosa in the U.S. This is a conservative estimate, as studies included in the literature review by Carlat et al have likely underestimated the prevalence in men due to the fact that men are even less likely than women to seek treatment or disclose disordered eating behaviors.

The prevalence estimate of 0.09% in men is lower than that reported by other researchers, further supporting its conservative nature. Since no evidence is available from recent studies in adult men in the U.S., the prevalence estimate was compared with results reported for other industrialized countries. For example, Hay et al found a prevalence of 0.2% in adult men in Australia,[38] while according to Kinzl et al and Götesdam et al the prevalence in men in Austria and Germany was 0.5% and 1.1%, respectively (all estimates based on DSM-IV).[65;71]

For the purpose of estimating the number of affected people and the cost of bulimia nervosa in the U.S., prevalence rates in women as reported by Johnson et al as well as a 1:10 prevalence ratio in men and women were applied. It was assumed that estimates derived from a sample of female outpatients would be representative of the total female population, including those not seeking healthcare and/or not having health insurance. In addition, it was assumed that the prevalence ratio in men and women was constant across age groups.

Table 57 presents the prevalence rates that were the basis for estimating the number of people with bulimia nervosa in the U.S. in 2002.

Table 57: Prevalence estimates of bulimia nervosa in adults in the U.S., by age and gender (2002)

Age group (years)	Prevalence (%)	
	Women	**Men**
18–25	0.9	0.09
26–35	1.3	0.13
36–45	1.0	0.10
46–55	0.9	0.09
56–99	0.3	0.03
Overall	**0.9**	**0.09**

* The prevalence in women based on survey by Johnson et al (2001);[61] the prevalence in men was assumed to be 10% of that in women.

Information on the U.S. population by age and insurance status was obtained from the Annual Social and Economic Supplement (ASEC) of the Current Population Survey (CPS).[224] The sample of the ASEC household survey (approximately 78,000 households) represents the civilian non-institutionalized population, with results adjusted to apply to the national population on the basis of age, race, sex, and ethnic origin.[225] Generally, one respondent from each household provides information on all individuals who reside within the same household. In the ASEC, private health insurance is defined as coverage by a plan provided through an employer or union or purchased by an individual from a

private company. Government health insurance includes the federal programs Medicare, Medicaid, and military healthcare, the State's Children's Health Insurance Program, and individual state health plans. For the year 2002, Table 58 shows the distribution of the U.S. population by gender, age group, and type of medical insurance.

Table 58: U.S. population by gender, age, and insurance status (in thousands)* (2002)[224]

Age group (years)	Total	Private or government insurance								Not covered
		Total insured	Private insurance			Government insurance				
			Total private	Employment based	Direct purchase	Total gov.	Medicaid	Medicare	Military	
Men										
18–24	13,834	9,288	8,270	6,817	764	1,498	1,055	86	425	4,546
25–34	19,564	13,936	12,899	12,049	1,095	1,438	846	219	465	5,628
35–44	21,733	17,530	16,223	15,276	1,376	1,872	1,087	447	588	4,203
45–54	19,606	16,778	15,379	14,383	1,485	2,050	966	700	699	2,828
55–64	13,166	11,602	10,189	9,256	1,353	2,303	690	1,124	836	1,564
≥65	14,528	14,422	9,195	5,685	4,056	13,870	1,088	13,804	1,250	106
Total ≥18	**102,431**	**83,556**	**72,155**	**63,466**	**10,129**	**23,031**	**5,732**	**16,380**	**4,263**	**18,875**
Women										
18–24	13,604	10,022	8,292	6,612	802	2,240	1,854	97	354	3,583
25–34	19,679	15,538	13,593	12,751	1,003	2,506	1,955	236	457	4,141
35–44	22,341	18,762	17,017	15,904	1,441	2,368	1,641	434	533	3,578
45–54	20,627	17,870	16,344	15,234	1,602	2,295	1,261	683	652	2,757
55–64	14,233	12,277	10,608	9,250	1,718	2,578	1,082	1,268	646	1,957
≥65	19,706	19,554	11,490	5,897	6,080	18,943	2,195	18,827	1,008	152
Total ≥18	**110,190**	**94,023**	**77,344**	**65,648**	**12,646**	**30,930**	**9,988**	**21,545**	**3,650**	**16,168**

Source: Annual Social and Economic Supplement (ASEC) of the Current Population Survey (CPS)

* An individual can have more than one type of coverage during the year.

Based on gender- and age-specific prevalence rates of bulimia nervosa (Table 57) and ASEC population counts (Table 58), it was estimated that 81,212 adult men and 889,133 adult women suffered from bulimia nervosa in 2002 (Table 59). These estimates take the age-specific prevalence estimates (Table 57) into account. Using instead average prevalence estimates across all age groups (0.9% and 0.09% in men and women, respectively), 92,188 men and 991,710 women would be estimated to have suffered from bulimia nervosa in 2002. These calculations assume that prevalence was similar in outpatients and the general population.

Since individuals with medical insurance are more likely to visit a physician, get diagnosed, and incur bulimia-related healthcare costs than those without any healthcare coverage, the number of prevalent cases was also determined for the population with private or public insurance. Based on insurance rates reported in the ASEC survey (Table 59), and using age-specific prevalence estimates, it was estimated that 62,587 adult men and 677,473 adult women suffered from bulimia nervosa in 2002; the corresponding numbers using average prevalence estimates across age groups were 75,200 and 846,207, respectively.

Table 59: Estimated number of adults with bulimia nervosa in the U.S. – total and insured population (2002)

Age group (years)	Prevalent cases (estimates)				
	ASEC-based		Insurance coverage (2001) (%)		SIPP-based
	Total	Insured	ASEC	SIPP*	Insured
Men					
18–25	12,451	8,359	71.9	74.2	8,627
26–35	25,433	18,117	76.6	79.2	18,732
36–45	21,733	17,530	83.9	84.8	17,718
46–55	17,645	15,100	86.9	87.5	15,204
56–99	3,950	3,481	86.9	89.9	3,601
Total†	**81,212**	**62,587**			**63,882**
Overall‡	**92,188**	**75,200**	**85.4**	**85.9**	**75,641**
Women					
18–25	122,436	90,198	71.9	74.2	93,083
26–35	255,827	201,994	76.6	79.2	208,850
36–45	223,410	187,620	83.9	84.8	189,633
46–55	185,643	160,830	86.9	87.5	161,940
56–99	101,817	36,831	86.9	89.9	38,102
Total†	**889,133**	**677,473**			**691,609**
Overall‡	**991,710**	**846,207**	**85.4**	**85.9**	**851,161**

Abbreviations: ASEC = Annual Social and Economic Supplement; SIPP = Survey of Income and Program Participation

* Monthly averages.

† Sum of individual age groups.

‡ Assuming general prevalence of 0.9% in women and 0.09% in men, without age differentiation.

According to prior research, health insurance coverage is generally underreported by the ASEC for a number of reasons, the main one being the retrospective nature of the survey, which asks respondents in February to April about their health insurance status during the previous calendar year.[225] It has been suggested that the ASEC more closely approximates the number of people insured at a specific point in time during the year than the number of people insured for the entire year.

Information on healthcare coverage of U.S. citizens is also available from the Survey of Income and Program Participation (SIPP), a longitudinal household survey in which each individual provides information on a 4-monthly basis. To obtain yearly estimates, at least

four surveys (waves) have to be combined. While the main advantage of the SIPP is the shorter recall period of 4 months, results are limited due to a smaller sample size (27,500 to 35,000 persons in waves in 2001). Based on a comparison of 2001 health insurance coverage rates, as reported in the ASEC and the SIPP surveys, it has been shown that ASEC respondents underreported government health insurance of 6 months duration or less as well as private insurance of 8 months or less.[226]

To account for underreporting of healthcare coverage in the ASEC, the estimated number of bulimic individuals with medical insurance was adjusted according to SIPP-based coverage rates. Since the SIPP survey was not conducted in 2002, the ratio of coverage according to ASEC and SIPP in 2001 was used as an adjustment factor. It was assumed that this factor was for each age group the same for men and women, as information on age-specific insurance coverage was only available for both genders combined. The adjusted estimate of the number of medically insured individuals with bulimia nervosa was slightly higher than that derived from ASEC insurance coverage rates: 63,882 adult men and 691,609 adult women were predicted to have suffered from this eating disorder in 2002, based on age-specific prevalence estimates (75,641 and 851,161, respectively, based on average estimated prevalence; Table 59).

Since the per-person cost of bulimia nervosa refers to patients in the MedStat Commercial Claims and Encounters Database, which contains only data from private insurers, the number of bulimic cases was estimated separately for the populations with private and with government-funded health insurance, following the same approach as for the overall population (Table 60). According to SIPP coverage rates, an estimated 58,723 to 67,779 adult men and 614,907 to 726,532 adult women with private health insurance suffered from bulimia nervosa in 2002.

Table 60: Estimated number of adults with bulimia nervosa in the U.S. in 2002, by type of medical insurance

Age group	Prevalent cases (estimates)—private insurance			
	ASEC-based	Adjustment factors 2001 (%)		SIPP-based
	Insured	ASEC	SIPP*	Insured
Men				
18–25	7,443	62.3	64.9	7,754
26–35	16,769	69.6	71.7	17,275
36–45	16,223	77.5	78.3	16,390
46–55	13,841	80.0	81.3	14,066
56–99	3,057	75.9	80.4	3,238
Total†	**57,333**			**58,723**
Overall‡	**64,940**	**70.9**	**74.0**	**67,779**
Women				
18–25	74,628	62.3	64.9	77,742
26–35	176,709	69.6	71.7	182,041
36–45	170,170	77.5	78.3	171,927
46–55	147,096	80.0	81.3	149,486
56–99	31,824	75.9	80.4	33,711
Total†	**600,427**			**614,907**
Overall‡	**696,096**	**70.9**	**74.0**	**726,532**

Abbreviations: ASEC = Annual Social and Economic Supplement; SIPP = Survey of Income and Program Participation

* Monthly averages.

† Sum of individual age groups.

‡ Assuming general prevalence of 0.9% in women and 0.09% in men, without age differentiation.

Since only bulimics visiting a healthcare professional are likely to get diagnosed and treated, as a more conservative estimate the number of prevalent cases was also predicted based on the population with healthcare coverage and at least on physician visit throughout the year. Only the SIPP, but not the ASEC, collected information on healthcare utilization and reported for the year 2001 the percentage of persons who visited a doctor at least once.[227]

The number of prevalent cases with healthcare coverage was adjusted by the probability of at least one yearly doctor visit according to the SIPP (Table 61), assuming healthcare-seeking behavior was similar in 2002 as in 2001. In addition, it was assumed that women and men did not differ regarding their likelihood of visiting a doctor, as no gender-specific information was available. Since this assumption is unlikely satisfied in clinical practice, the total predicted number of bulimic cases is a more reliable estimate than the split by gender. Based on the population with private health insurance and having visited a doctor at least once, the estimated number of cases was 487,437 (42,458 men and 444,979 women).

Table 61: Estimated number of insured adults with bulimia nervosa and at least 1 doctor visit in the U.S. in 2002, by type of medical insurance

Age group	With at least 1 doctor visit in 2001 (SIPP)[227] (%)	Estimated prevalent cases	
		With private or public insurance	With private insurance
Men			
18–25	64.50	5,564	5,001
26–35	70.40	13,187	12,161
36–45	70.40	12,474	11,539
46–55	79.50	12,088	11,182
56–99	79.50	2,863	2,574
Total*		**46,175**	**42,458**
Overall†	**73.10**	**55,293**	**49,546**
			Women
18–25	64.50	60,039	50,144
26–35	70.40	147,031	128,157
36–45	70.40	133,501	121,036
46–55	79.50	128,743	118,842
56–99	79.50	30,291	26,800
Total*		**499,605**	**444,979**
Overall†	**73.10**	**622,199**	**531,095**

Abbreviation: SIPP = Survey of Income and Program Participation
* Sum of individual age groups.
† Assuming general prevalence of 0.9% in women and 0.09% in men without age differentiation.

Since the 2002 MarketScan population was generally representative of the non-elderly population with private health insurance, the average fee-for-service per-patient cost,

determined in Chapter 3, was used to predict the cost of bulimia nervosa to payers. Assuming each of the estimated 487,437 prevalent cases with private insurance who visited a doctor at least once incurred mean annual costs of $3,577, the total annual burden of bulimia nervosa, including its complications and comorbidities, amounted to $1.7 billion ($1,743,562,149) in 2002.

However, the burden to payers could have been much higher. If all adult men (81,212) and adult women (889,133), predicted to have suffered from bulimia nervosa (Table 59), would have been diagnosed and treated, irrespective of their healthcare coverage and healthcare seeking behavior, the annual cost of bulimia nervosa would have been $3.5 billion ($3,470,852,525) in 2002. This projection assumes that the average fee-for-service per-patient cost was representative for the overall population.

If only the costs directly attributable to bulimia nervosa—i.e., outpatient and inpatient treatment with a primary diagnosis of bulimia nervosa—were considered, the annual burden would have been between $1.0 billion[80] and $2.1 billion[81], based on a yearly per-patient fee-for-service cost of $2,113. Since this estimate does not take the costs of medications into account, which are a main component of the treatment of bulimia nervosa, it severely underestimates the costs to payers.

The above calculations of the cost of bulimia nervosa implicitly assumed that the average fee-for-service cost could be generalized to the U.S. population. Since the Northeast region of the U.S. was underrepresented in the Commercial Claims and Encounters Database, extrapolation of the average per-patient cost to the general population might have resulted in a biased estimate. However, region was not identified as a significant predictor of the per-patient cost, and predicted national costs would therefore only be biased if individuals in the Northeast differed from those in other regions in terms of age and number of comorbidities—significant predictors of the per-patient costs.

[80] $1,029,954,381: assuming each of the estimated 487,437 prevalent cases with private insurance who visited a doctor at least once incurred annual costs of $2,113.
[81] $2,050,338,985: assuming all 970,345 predicted cases were treated and incurred mean annual costs of $2,113.

Cost estimates derived from encounter claims were not used to estimate the burden of bulimia nervosa in the U.S., as unadjusted costs did not reflect true healthcare costs, and approximated costs, which were based on fee-for-service equivalents, were similar to those derived from fee-for-service claims.

Implicitly, the above calculations assumed that costs would be similar in patients identified by ICD-9 diagnoses as in those meeting the DSM-IV criteria. This assumption was necessary because prevalence estimates were derived from a study using the DSM-IV criteria, while per-patient costs were estimated from the MedStat database, which is based on ICD-9 codes. Even though the DSM-IV criteria for bulimia nervosa are more restrictive than the ICD-9 criteria, it can be assumed that patients meeting the ICD-9 criteria and being treated for bulimia nervosa also meet the strict DSM-IV criteria, as insurance companies likely only authorize treatments for severe bulimic cases; i.e., those binging and purging at least twice per week.

It should be noted that the cost of illness was estimated based on the point prevalence of bulimia nervosa, even though a more accurate approach would have been to use the period prevalence; i.e., the point prevalence plus the annual incidence. However, since evidence on the incidence is scant, the point prevalence was used instead, leading to an underestimate of the number of prevalent cases and the burden to payers.

In summary, the estimated cost of bulimia nervosa to payers in the U.S. was at least $1.0 billion in 2002, if only outpatient and inpatient treatment costs directly attributable to bulimia nervosa and only the population with private insurance and likely having visited a physician at least once were taken into account. However, the burden to payers could have been much higher ($1.7 billion) if the costs of complications and comorbidities of bulimia nervosa were considered. Assuming all predicted bulimia nervosa sufferers, irrespective of insurance status and healthcare seeking behavior, had been diagnosed and received treatment, the costs could have amounted to $3.5 billion. Since most cases

currently go untreated, this estimate would not be expected to reflect actual healthcare costs in 2002, but rather to indicate potential future costs.

5 Discussion

5.1 Summary of findings

Epidemiology

Since the formal recognition of bulimia nervosa as a distinct eating disorder in 1980, numerous research articles have been published on its epidemiology. As described in the literature review presented in Chapter 2, prevalence estimates have decreased from 8% to 13% in surveys conducted in the 1980s to approximately 1% in studies in the late 1990s and the beginning of the 21st century. However, no conclusions regarding a time trend can be drawn from these findings, since the diagnostic criteria for bulimia nervosa became more stringent over time. It has been proposed that, had the DSM-III-R criteria been used in earlier studies instead of the DSM-III criteria, the prevalence might have ranged from 1% to 4%.[1] Furthermore, different methods of case ascertainment (i.e., self-reported symptoms in earlier surveys versus clinical interviews in more recent studies) and different populations (i.e., students versus general population samples) might have resulted in a spurious decline in estimated prevalence.

According to the DSM-IV criteria, the prevalence of bulimia nervosa is approximately 1% in Western countries, with women being at much higher risk than men. Studies in the clinical setting have generally resulted in higher prevalence estimates than surveys in the community, indicating that results from clinical samples may not always be generalizable. In addition, higher prevalence rates have been found in students than in general population samples, which is likely explained by age differences between study populations, since risk for bulimia nervosa is age dependent.

It has also been shown that bulimia nervosa is not uncommon in non-Western countries and that individuals of different racial and ethnic groups may be vulnerable to the influence of Western beauty standards, particularly when the culture-of-origin is devalued. In addition to age and gender, limited evidence exists for other potential risk factors for the development of bulimia nervosa, including sexual orientation, specific comorbidities (e.g., diabetes), engagement in athletic activities, and military service.

Evidence on the lifetime prevalence of bulimia nervosa is currently scant and subject to limitations of respective studies, including respondent age at assessment, respondents' recall bias, and use of convenience samples. In Caucasian women, the lifetime prevalence can be assumed to be at least 2%, although this is a very conservative estimate. Estimates of the incidence of bulimia nervosa are also limited and findings reported in the literature vary widely. Since most studies have relied on case registers, they were only able to account for diagnosed cases and therefore provided minimum estimates of the incidence of bulimia nervosa.

With an approximate DSM-IV-based prevalence of 1.0% in adult women and men in the U.S., the prevalence of this eating disorder is similar to that of obsessive-compulsive disorders and agoraphobia (about 1.0% and 0.8% of American adults, respectively), but much lower than that of certain other mental disorders, such as bipolar disorder (2.6%), panic disorder (2.7%), generalized anxiety disorder (3.1%), major depressive disorder (6.7%), or mood disorder (9.5%).[228] Although bulimia nervosa may be considered a relatively rare condition compared to many other chronic mental disorders, it is nevertheless of great concern to society, as it affects mainly young people and may lead to serious complications. Bulimia nervosa differs in this regard from some other mental disorders, since it is not only associated with psychological, but also physical morbidity, requiring separate treatment approaches, and thereby potentially leading to higher overall costs.

Resource utilization and per-patient treatment costs

The cost of illness analysis in Chapter 3 demonstrates the burden of bulimia nervosa to payers: insurance companies, patients, and third party payers. In patients with private employer-based health insurance, the total annual fee-for-service per-patient costs, including inpatient, outpatient, and drug treatment of bulimia nervosa as well as its complications and comorbidities, were estimated at $3,577, of which $1,865 were directly attributable to inpatient and outpatient care of bulimia nervosa. Pharmaceutical services accounted for 42% of the total costs, while inpatient and outpatient care

contributed 25% and 33%, respectively. Since payments recorded in encounter claims provide an underestimate of costs, fee-for-service equivalents were used to approximate treatment costs for patients with encounter claims, leading to an estimated $4,238 annually per patient, of which $2,113 were directly attributable to the outpatient and inpatient treatment of bulimia nervosa.

Based on a comparison with cost-of-illness estimates of other mental disorders reported in the literature, the per-patient costs of bulimia nervosa appear to be either similar or lower. For example, an analysis of claims data from employer-sponsored healthcare plans reported for the years 2001 to 2002 annual costs of $2,036 and $596 per patient with bipolar and other mental disorders, respectively, if only costs directly attributable to mental disorders were taken into account.[229] As with the costs of bulimia nervosa, total costs including those of comorbidities were found to be much higher: $5,435 and $4,141 per patient with bipolar disorder and other mental disorders, respectively. The estimated annual costs of bulimia nervosa were much lower than those of depression alone and depression with comorbid alcoholism, which—based on 1996 to 2000 data from the MedStat database—amounted to $4,718 and $8,380, respectively.[230] In addition, the estimated per-person treatment costs of bulimia nervosa were less than those reported for anxiety disorders ($6,475 among persons with employer-sponsored healthcare coverage)[231] and schizophrenia ($8,747 in patients with private health insurance)[232].

Even though results of different cost-of-illness studies may not be directly comparable due to differences in methodologies and databases used, the indirect comparison nevertheless demonstrates that the per-patient costs of bulimia nervosa in 2002 were relatively low. However, it has to be considered that bulimia nervosa is likely underdiagnosed and undertreated, perhaps more so than other mental disorders. The undertreatment of bulimia nervosa becomes evident if healthcare utilization of patients in the MedStat database is compared with current treatment recommendations.

The American Psychiatric Association (APA) recommends a comprehensive treatment plan, which should include the treatment of medical complications and psychiatric comorbidities of bulimia nervosa. Specifically the guideline states that:[7;12]

- Psychosocial interventions, including cognitive behavioral psychotherapy, interpersonal, behavioral, psychodynamic, and psychoanalytic approaches in individual and/or group format, either alone or in combination, as well as family or couples therapy, should be chosen on the basis of the comprehensive evaluation of the individual patient.
- Nutritional counseling and rehabilitation may be useful as an adjunct to other treatments.
- Antidepressants, especially selective serotonin reuptake inhibitors (SSRIs), may be prescribed as a component of an initial treatment program and should be continued for at least 9 to 12 months, preferably in combination with psychotherapeutic interventions.
- Inpatient treatment should be considered for cases with severe disabling symptoms not responding to outpatient treatment.
- Bright light therapy and self-help programs or support groups may be effective in some patients.

Treatment guidelines have also been published for specific subgroups of patients (e.g., adolescents[233]) as well as by other international organizations, such as the National Institute of Clinical Excellence (NICE).[234] Contrary to the APA guideline, which leaves the determination of the treatment plan mainly up to the clinician, the NICE guideline is more specific. For example, NICE recommends cognitive behavioral therapy of at least 16 to 20 sessions over 4 to 5 months as a routine treatment, and states that no drugs other than antidepressants should be prescribed for bulimia nervosa.

Of the bulimic patients with fee-for-service and encounter claims in the MedStat database, 80% and 78%, respectively, had at least once in 2002 a claim with a procedure

code for a psychosocial intervention[82], with of a mean annual frequency of 9.7 and 8.5 per patient, respectively. According to the information on service types, 78% and 71% received psychological treatment[83] at least once, with a mean annual frequency of 9.9 and 8.8 per patient, respectively. These results demonstrate that 20% to 29% of patients did not get any psychosocial care and that among those who received these treatments the average number of sessions was much lower than what is currently recommended by NICE.

In addition, only very few patients received advice from a dietician or health educator (about 1% and 3% of patients with fee-for-service and encounter claims, respectively), and monitoring of patients' laboratory values occurred infrequently (only 13–14% of patients had one or more laboratory services). Inpatient treatment was also generally rare, with only 7% and 6% of patients in the fee-for-service and encounters dataset, respectively, being hospitalized for a reason that could be indicative of the treatment of bulimia nervosa[84].

In contrast, approximately 67% and 70% of patients in the fee-for-service and encounter datasets, respectively, received antidepressants for an average duration of 244.2 (168.0) and 244.8 (191.2) days per year, respectively. Based on these findings it can be concluded that pharmacological therapy was the norm in 2002, while most bulimic patients received less than the recommended level of psychiatric outpatient care, especially in terms of the number of therapy sessions as well as nutritional counseling. This undertreatment can be predicted to increase long-term healthcare costs, since bulimia nervosa is associated with serious complications, likely to require costly interventions.

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[82] The following procedure groups were included: individual psychotherapy, family psychotherapy, group psychotherapy, psychiatric advice (non-patient), and other medical psychiatric services.

[83] The following service types were included: individual psychiatric therapy, group psychiatric therapy, and psychiatric/substance therapy not specified.

[84] The following DRGs were considered to be potentially indicative of the treatment of bulimia nervosa: procedure with principal diagnosis of mental illness, depressive neurosis, other neurosis, disorders of personality and impulse control, psychoses, childhood mental disorders, and other mental disorder diagnoses.

Even though the cost-of-illness analysis accounted only for treatments paid by insurance companies, it is unlikely that the treatment gap was filled by patients paying for therapies out-of-pocket. The undertreatment of bulimia nervosa may be due to disincentives for providers to prescribe therapies and for patients to seek care. For example, psychological treatments often require pre-authorization by insurance companies, increasing the workload for providers, and, if approved, are limited in terms of the number of therapy sessions. In addition, patients usually have to pay high copayments and deductibles. The direct economic burden of bulimia nervosa would therefore be expected to be much higher if patients were treated according to recommended standards of care.

Other studies have also reported on the insufficient treatment of bulimia nervosa in the U.S. For example, a review of inpatient records of an Eating Disorder Program in New York found that between 1984 and 1998 the average length of stay decreased, while in parallel the percentage of patients with managed private health insurance increased.[235] The authors conclude that due to high inpatient costs, pressure has been applied by managed care companies to reduce the length of stay in an attempt to contain costs. The impact of shorter inpatient stays on patients' recovery has not been fully assessed yet. It can be hypothesized that the likelihood of a relapsing course of bulimia nervosa is increased, since prior research has shown that patients who had practiced and adopted normal eating behaviors during an inpatient program were less likely to relapse after discharge.[236]

As an alternative to inpatient care, residential treatment program offering longer-term intensive care are available in the U.S., but they frequently require a significant financial contribution from the patient. Based on a national survey, the average length of treatment in residential programs was estimated at 83 days with an average cost per day of $956, leading to average per-case costs of $79,348.[237] The fact that these treatment programs have more than tripled in the past decade is alarming, since it indicates a shift of the financial burden from insurance companies to patients and their families, who often have to pay the majority of costs of residential treatment programs.

Cost-of-illness in the U.S.

To predict the overall medical cost of bulimia nervosa to payers in the U.S., a prevalence-based approach was applied. Assuming an overall prevalence of 0.9% in women and 0.09% in men, an estimated 0.5 to 1.0 million adults suffered from bulimia nervosa in 2002 (Chapter 4). If all bulimic individuals with private health insurance who visited a physician at least once had been diagnosed, treated and incurred average per-patient costs of $3,577, the total burden of bulimia nervosa would have been $1.7 billion, with $1.0 billion directly related to the outpatient and inpatient treatment of bulimia nervosa. These findings are of importance, not only because they allow a comparison with the burden of other disorders, but also because they can be used by decision makers as a guide for health resource allocation and financial planning.

Since bulimia nervosa is a relatively rare disorder, its overall cost to payers can be expected to be lower than that of many other mental disorders. For example, the direct costs in 1990 of affective disorders, depression, and schizophrenia have been estimated at $10.5 to $19.2 billion, $12.4 billion, and $17.3 million, respectively, with an overall cost for mental disorders of $67.0 billion.[238] Even though the cost of bulimia nervosa appears low compared to those of other mental disorders, it has to be taken into consideration that this eating disorder is frequently underdiagnosed and undertreated. Costs to all payers could be much higher, if all cases—irrespective of insurance coverage and health care seeking behavior—would be diagnosed and treated. In this scenario, assuming per-patient costs of $3,577, the direct cost in 2002 would have been $3.5 billion, of which $2.1 billion would have been directly attributable to the outpatient and inpatient therapy of bulimia nervosa.

Only two previous studies provided estimates of the costs of bulimia nervosa. Striegel-Moore et al performed a cost-of-illness analysis in 1995 and reported average annual per-patient outpatient and inpatients costs of $3,012 ($2,962 in women and $3,885 in men),[13] while in 2002 respective costs were only $1,865. This may be due to differences in healthcare service utilization; for example, 12.5% of the patients in 1995 received inpatient treatment compared to 6% to 7% of patients with fee-for-service and encounter

claims, respectively, in 2002. In addition, the average annual number of outpatient treatments was 15.6 in women and 9.1 in men (weighted average of 15.2 days) in 1995, which was slightly higher than the average number of psychological treatments received in 2002 (9.9 and 8.8 in patients with fee-for-service and encounter claims, respectively).

Even though no final conclusions can be drawn due to differences in study methodologies applied, the comparison with findings by Striegel-Moore et al seems to at least indicate that the intensity of treatment of bulimia nervosa has not improved and might even have deteriorated between 1995 and 2002. Unlike this study, Striegel-Moore et al did not take into account the costs of drug treatments and those of complications and comorbidities of bulimia nervosa, and therefore their findings provided an underestimate of the total costs of bulimia nervosa.

The only other published cost-of-illness study used benefit payments by insurance companies to estimate the treatment costs of bulimia nervosa in Germany.[14] Similarly to the approach in this study, results were projected to the national level based on prevalence data reported in the literature. However, Krauth et al were able to include only inpatient treatment and care in rehabilitation or convalescence centers as direct costs, and comparison with the results of this study is therefore limited. While the average duration of inpatient treatment was much higher in Germany than in the U.S. (45.5 days vs 13.2 and 15.7 days per patient with fee-for-service and encounter claims, respectively, per year), average treatment costs (€11,700 per case in 1998) did not differ greatly from the annual inpatient costs in this study (mean inpatient costs of $10,997 in 55 patients). These results demonstrate the more intensive inpatient treatment of bulimic patients in Germany as well as lower daily costs of inpatient care in Germany than in the U.S.

Krauth et al estimated also the indirect costs due to inability to work and mortality based on benefit data provided by pension insurance schemes and published evidence on mortality rates. They reported indirect costs 10 times higher than direct costs; the projected direct and indirect costs in 1998 were estimated at €10 and €114 million, respectively. However, the majority of the indirect costs were due to mortality (€112

million), and results should therefore be interpreted with caution, since evidence regarding an increased mortality risk in bulimic patients is still scant.

Current evidence seems to indicate an increased probability of premature death in patients with bulimia nervosa, but the exact rate is unclear. Nielson et al (1998) found inconclusive results in his first meta-analysis,[239] while in an updated version the authors reported an overall standardized mortality ratio (SMR)[85] of 7.4 (95% CI: 2.9–14.9) based on studies with 5 to 11 years of follow-up.[240] However, if all published follow-up studies of bulimia nervosa cohorts, not just those reporting an SMR, were taken into account, the estimated overall SMR would have been 1.6 (95% CI: 0.8–2.7).[15] It can therefore be concluded that subjects with bulimia nervosa are at an increased risk of premature death compared to healthy people of the same age and gender. However, the extent of this risk is currently unclear; it could either be moderate (about 1.6 times increased risk) or severe (about 7 times).

Factors influencing per-patient costs

Another finding of this research was that age and comorbidity (i.e., number of unique diagnoses per patient) significantly impacted the per-patient costs. Based on the analysis of fee-for-service claims, costs increased by 1.3% with each additional year of age and by 60.2% with each additional diagnosis. These results could indicate that more severe cases incur higher costs, since older patients are likely to represent chronic cases—assuming an average age of onset of about 18 years—and patients with several diagnoses may suffer from complications of the eating disorder.

Psychological comorbidity of a personality disorder or history of mood disorders as well as a poor functional assessment have previously been found to be predictors of treatment utilization, demonstrating that bulimic patients with more severe symptoms received more treatments.[241] In addition, the findings from this analysis are corroborated by those of a study in patients with anxiety disorders, which found that patient demographics (age,

[85] SMR = number of deaths observed in a sample to number of deaths expected in the population, correcting for age, sex, and duration of follow-up

gender, region of residence, and type of insurance coverage, as well as medical and psychiatric comorbidities, quantified by the number of unique ICD-9 diagnoses) impacted treatment costs.[231] While in the study of patients with anxiety disorders all of these variables were found to be significant predictors of the per-patient costs, this study of bulimic patients identified only age and number of diagnoses as independently significant, which might be due to the much smaller patient sample (782 patients with bulimia nervosa versus 6,497 with anxiety disorders).

5.2 Methodological considerations

One of the main strengths of this research was the comprehensive assessment of evidence on the prevalence and incidence of bulimia nervosa since its formal recognition as a disorder, thereby providing a global perspective of the epidemiological burden. Another advantage was that the per-patient costs of bulimia nervosa were estimated based on a large, geographically diverse patient sample and included not only inpatient, outpatient, and drug treatments of bulimia nervosa, but also treatment of its complications and psychiatric comorbidities, thereby overcoming limitations of previous cost-of-illness studies. In addition, since the database analysis provided an assessment of the quantity of healthcare services received by patients, results can be used to evaluate whether patients received an adequate level of care.

However, this study is also subject to several limitations. The literature review focused on manuscripts published in English or German and the search was limited to articles indexed in Medline and Embase. Unpublished research as well as papers published in other languages or in journals not listed in these databases may have therefore been missed. Even though it was attempted to minimize publication bias by conducting extensive hand searches of reference lists of identified articles, underrepresentation of research conducted in developing countries and published in other languages cannot be excluded. With regard to the U.S., however, the literature should completely reflect the available and published epidemiological evidence.

The projection of the number of cases in the U.S. assumed that the overall prevalence of 0.9% in adult women reported by Johnson et al would be representative for the whole female U.S. population. However, age-specific rates derived from a sample of outpatients are unlikely to be generalizable. Götesdam et al and Kinzl et al found the highest prevalence in women in the community aged 18 to 29 years and less than 25 years in Sweden and Austria, respectively, while in Johnson et al's survey the highest prevalence occurred in those aged 26 to 35 years. This may be explained by the fact that women in this age group, who are seeking obstetric care, could be at a higher risk of bulimia nervosa, since eating disorders may lead to fertility problems.[12] The estimated overall number of female bulimic cases is therefore a more reliable estimate than the breakdown by age groups.

A further limitation of this research is that results of the Commercial Claims and Encounters database are not necessarily generalizable to the overall U.S. population, since the regional distribution of the MedStat population was different from that of the U.S. However, after adjustment for other variables, region was not found to be a significant predictor of the per-patient costs of bulimia nervosa and estimates of the cost to payers in the U.S. are therefore unlikely to be biased by the non-representative regional distribution of the patient sample.

Since costs were derived from a database of patients with employer-sponsored healthcare plans, the estimated per-patient costs may not be generalizable to patients with public or no medical insurance. This was addressed by providing a range for the national cost of bulimia nervosa, with the minimum referring to patients with private insurance and the maximum being based on the total U.S. population. Nevertheless, the burden to payers may have been overestimated if patients in the MedStat database being diagnosed with and actively seeking help for bulimia nervosa were more severe cases than bulimic individuals in the community.

In addition, the total per-patient costs of bulimia nervosa may represent an overestimate, since the costs of all comorbidities were included and no incremental cost analysis was

performed. Therefore, an analysis of claims with a primary diagnosis of bulimia nervosa was performed, which provides an estimate of the costs directly attributable to this eating disorder. It should be noted that other claims included in the estimate of total per-patient costs but not in that of costs directly attributable to bulimia nervosa were either for primary diagnoses closely related to bulimia (e.g., polyphagia, 64 and 25 patients in the fee-for-service and encounter datasets, respectively), or psychiatric comorbidities (e.g., mental disorders other than bulimia nervosa, 39 and 19 patients), or complications of the eating disorder (e.g., nutritional and metabolic disorders, 3 and 2 patients; gastrointestinal diseases, 3 and 1 patient[s]). It can therefore be assumed that the majority of the total per-patient costs were either directly or indirectly related to bulimia nervosa.

Since drug claims are not linked to diagnoses, the inclusion of all drug costs for patients with bulimia nervosa could have resulted in an overestimation of the total per-patient costs. Currently, only fluoxetine is approved by the Food and Drug Administration (FDA) for the treatment of bulimia nervosa, but other antidepressants as well as other pharmacotherapies have been studied in clinical trials and used in clinical practice.[12;242] In the Medstat patient sample, about 50% to 51% of the treatment days were prescribed for drugs in the therapeutic group of central nervous system agents, which indicates that a large portion of drug costs was likely related to the treatment of bulimia nervosa or its psychiatric comorbidities.

An inherent limitation of claims database analyses is the lack of an independent validation of diagnoses. The use of diagnostic codes to identify cases is not as rigorous as a formal diagnostic assessment and may have resulted in nonidentification of cases, especially as bulimia nervosa is a relatively new disorder with diagnostic criteria changing over time. In addition, cases may have not been identified if clinicians recorded other diagnostic codes to avoid the often disadvantageous reimbursement of this eating disorder. This could have lead to non-inclusion of costs of bulimia nervosa and an underestimate of the cost of illness directly related to bulimia nervosa. The results from the main cost-of-illness analysis, which included all claims for patients with bulimia nervosa, might therefore be a better estimate of the true treatment costs.

Another limitation of claims databases is that information on outcome measures (e.g., patients' quality of life or psychosocial functioning) are not available. These variables could therefore not be assessed in the multivariate analyses. Predictors of the per-patient costs other than age and number of diagnoses are likely important, since the model could not account for all the variances in costs, indicating that other, unmeasured factors also had an impact.

This cost-of-illness study was based on payments reported in claims and therefore reflects the costs to payers, but not those to society, since the opportunity costs of healthcare resources were likely different from payments negotiated between insurance companies and providers. Furthermore, the total direct costs of bulimia nervosa could not be estimated, as claims databases contain only information on healthcare resources paid for by insurance companies, but not by government, social services, or patients.

In addition, the indirect costs of bulimia nervosa due to absenteeism, disability, or premature death could not be assessed. These could be as high as 10 times the direct costs according to the analysis by Krauth et al.[14] Finally, the costs of bulimia nervosa did not include costs related to impaired health-related quality of life. However, these costs have rarely been estimated in other burden-of-illness studies, since they are difficult to measure.

5.3 Implications

Even though numerous research articles have been published on the epidemiology, risk factors, and complications of bulimia nervosa since 1980, public attention to this eating disorder has only recently increased, especially due to reports in the mass media about celebrities suffering from eating disorders.

Even today, many bulimic individuals receive inadequate or no treatment. Different factors likely account for this undertreatment of bulimia nervosa, including the

unwillingness of sufferers to seek care, the underdiagnosis of cases by physicians, and the lack of affordable treatment options. To improve the level of care and thereby reduce the health burden of bulimia nervosa, it is necessary to address the different barriers to treatment.

A previous study of an ethnically diverse group of women with eating disorders found that only 57% ever sought help, and of these, only 14% received treatment.[243] The main reported barriers to seeking care were system-related: financial difficulties and lack of insurance (59% and 48% of participants, respectively). Person-level barriers were also frequently stated as reasons for not making healthcare contact (e.g., 35% feared to be labeled and 31% felt ashamed). Even though this study was not specifically focused on bulimia nervosa, findings nevertheless indicate potential reasons for the underdiagnosis and undertreatment of bulimia nervosa, which affect not only the U.S., but also countries in Europe.[31;61]

Since bulimic individuals are often afraid of being stigmatized, it is important to increase the awareness and knowledge of physicians and the general public about this disorder, including the recognition of eating disorders as treatable illnesses. Similarly to obesity, bulimia nervosa is often considered a lifestyle condition rather than a medical disorder that can be severe and potentially life threatening. While other addictions (e.g., alcoholism, drug abuse, and smoking) are usually considered to be treatable dependencies for which healthcare resources are therefore made available, eating disorders, including bulimia nervosa, do not yet receive the same level of attention, either from healthcare decision makers or the public.

It is also important that physicians of different specialties (e.g., dentists, dermatologists, and gynecologists) are familiar with the signs and symptoms of bulimia nervosa, thereby allowing for an earlier diagnosis and referral for treatment of cases presenting in clinical practice. In addition, healthcare resources for the treatment of bulimia nervosa have to be made available. While specialized eating disorder centers exist in many countries, they are generally running at capacity limits with long waiting lists for potential

patients.[6;244;245] Furthermore, the number of healthcare professionals experienced in the treatment of eating disorders is limited, which might be due to the fact that this is still a less lucrative medical specialty. It can be assumed that existing outpatient and inpatient facilities and staffing levels in the U.S. are insufficient to treat all patients predicted to have suffered from bulimia nervosa in 2002. This is of concern, because the early diagnosis and treatment of bulimic individuals may prevent a chronic course of the eating disorder and reduce the probability of complications.

However, the provision of healthcare services alone is not sufficient to improve the level of treatment, since healthcare needs to be accessible and affordable. Ironically, most health insurance companies cover the treatment and prevention of complications of common physical chronic diseases, but they have not yet adapted a similar approach for mental disorders like bulimia nervosa. Since insurance companies are more likely to reimburse treatments that have been shown to be effective, safe, and cost-effective in the long term, further evidence needs to be generated on therapies for bulimia nervosa. Compared to other mental disorders, clinical studies assessing different therapies for bulimia nervosa are still limited, which may have led to a general reluctance of health insurance companies to pay for the treatment of bulimia nervosa. Effective treatment options have the potential to lead to cost offsets and potentially cost savings for payers.[246]

Compared to Western countries, the availability of specialized treatment facilities is likely even more limited in developing and non-Western countries. This is of concern, since evidence indicates that bulimia nervosa exists also in modernizing countries in Asia, Eastern Europe, and Latin America, and the prevalence in these countries might even rise in the future.

5.4 Suggestions for future research

Several aspects of the burden of bulimia nervosa have been evaluated in this thesis, but due to the reliance on published evidence on the prevalence and incidence and the limitations of claims databases, some aspects could not be addressed. This section outlines potential areas for future research.

Even though the prevalence and incidence of bulimia nervosa has been researched extensively, there is still limited evidence from well-designed prospective observational studies in representative community samples. These would be required to allow for a more accurate assessment of healthcare services required to address current treatment needs of bulimic individuals as well as potential future demands for healthcare. In addition, further research should include broader population samples, including both genders, all age groups, and different ethnicities, cultures and countries.

Since the risk of morbidity and mortality attributable to bulimia nervosa is largely unknown, long-term epidemiological studies are needed. These would not only provide the basis for a more accurate evaluation of the total burden of illness, but could also be used to evaluate treatment programs in terms of their effectiveness at preventing morbidity and mortality. In addition, longitudinal studies could be used to identify contributing factors of bulimia nervosa and to separate them from consequences of the disorder. Finally, long-term studies would allow for an evaluation of time trends in the incidence as well an assessment of the lifetime prevalence of bulimia nervosa, estimates of which are still limited.

While some research has been generated on the risk factors of bulimia nervosa, there are still evidence gaps. Among others it is important to identify the sociocultural stressors involved in the development of bulimia nervosa and to assess how they interact with a person's genetic predisposition and psychological characteristics. Respective findings could then be used to develop treatment and prevention approaches targeted for specific at-risk groups.

To fully determine the burden of bulimia nervosa to all payers requires a comprehensive assessment of the resource use of patients with bulimia nervosa, including non-healthcare costs (e.g., social services, and patients' and caregivers' out-of-pocket expenses). In addition, the short-term and long-term costs of complications attributable to bulimia nervosa should be researched more thoroughly. Assuming evidence on the risk of

complications attributable to bulimia nervosa will be generated, a decision modeling approach could be used to predict total costs.[247]

Currently, very little is known about the indirect costs of bulimia nervosa, including the educational and occupational impact of this eating disorder. While indirect costs of other mental disorders have been researched in different studies, those of bulimia nervosa are limited to evidence from one study in Germany. In addition to an assessment of the indirect costs, the intangible costs of bulimia nervosa also have to be estimated. Even though quality of life costs are difficult to determine, efforts should be made to quantify the psychosocial burden on patients and caregivers, for example with willingness-to-pay studies. Very limited evidence suggests that the subjective burden on family members may be higher than the objective burden.[19]

Since this study did not permit any conclusions regarding reasons for the undertreatment of patients with bulimia nervosa, further research is needed to explore barriers to care and evaluate strategies to overcome these. In addition, the current level of healthcare provision—i.e., the resources available for the treatment of bulimic individuals—has to be assessed, so that the need for additional resources can be determined.

To reduce the medical and health burden of bulimia nervosa on patients and payers will require effective treatment options that improve the outcome of this eating disorder in the short as well as the long term. This implies that existing treatment options need to be fully assessed in terms of their efficacy–safety profiles and their long-term benefits, and that new therapies should be developed and assessed appropriately.

Addressing the research needs outlined above would require a significant investment. In the fiscal year 2005, the budget spent by the National Institute of Mental Health (NIMH) on Eating Disorders Research was $21.8 million or 1.53% of the total NIMH budget,[248] of which about $14 million were related to research in anorexia nervosa.[249] Funding available for bulimia nervosa was much less than for other mental disorders such as Alzheimer's disease ($656 million) and schizophrenia ($353 million). It can be estimated

that the NIMH spent between $8 and $16[86] on bulimia nervosa research per person with this eating disorder, much lower than the per-patient investment for Alzheimer's and schizophrenia, at $146 and $147, respectively (assuming a prevalence of 4.5 and 2.4 million Americans, respectively[228]).

Current NIMH research in bulimia nervosa focuses on interventional studies, including pharmaceutical as well as psychological therapies, and the etiology of this eating disorder.[250] However, only a limited number of new studies are initiated per year and many suffer from small sample sizes, an exclusion of men, and a short follow-up. For example, one ongoing study compares the efficacy of a new outpatient treatment approach with treatment-as-usual in 280 patients over a 6-week time period with a 6-month follow-up,[251] while another assesses guided self-help treatment versus usual clinical care in 200 patients over a 3-month period with a 6-month follow-up.[252] While most other ongoing NIMH-funded research activities are done in small population samples, one recent observational study deserves mentioning, since it is expected to enroll 2,420 7- to 17-year-old patients with the objective of evaluating the safety and effectiveness of 3 months of antidepressant therapy.

Compared with other mental disorders, the number of well-designed interventional and long-term follow-up studies in bulimia is very limited. Further research should assess existing and novel psychological and pharmaceutical treatment options, including multidisciplinary approaches, in broad ranges of patients in clinical practice, to determine differential efficacy by age, sex, race, ethnicity, and cultural group, and should include a follow-up of several years. Future studies should also include an assessment of outcomes like the impact on patients' quality of life and family burden. In addition, factors contributing to this eating disorder need to be determined, thereby enabling the development of prevention programs. Finally, for both future treatment and outcome studies, researchers should address issues of statistical power, research design, and

[86] A maximum of $21.80 million minus $14.00 million of NIMH research funds could have been spent on eating disorders other than anorexia nervosa. Assuming between 0.5 and 1.0 million adults suffer from bulimia nervosa, the research dollars spent on this eating disorder amount to a maximum of $7.80 to $15.60 per affected person.

appropriateness of statistical analyses, since the literature on the treatment efficacy and outcomes of bulimia nervosa is of variable quality.[253]

5.5 Final conclusion

Since industry-sponsored research is currently scant, it can be concluded that more public funds will be required to address existing research gaps in a timely manner. However, the availability of safe and effective treatment options alone is not sufficient to reduce the burden of bulimia nervosa, since they also have to be accessible and affordable. For years, many U.S. health plans provided limited or no mental health benefits and often subcontracted benefits to behavioral health service companies, thereby separating them from the general health plans and making a multidisciplinary treatment approach difficult. Although this system is slowly changing, with most U.S. states having passed some form of mental health parity law to require insurers to provide some benefits for mental and general medical healthcare, few states provide full parity of coverage for mental and physical illnesses, and to date only 12 states mandate healthcare coverage for eating disorders.[254] The U.S. system therefore still has a long way to go to improve adequate reimbursement for care and access to therapies at a sufficient level and for a long enough time period.

Increased access to treatments and expanded insurance coverage, together with additional evidence on the short- and long-term effectiveness and safety of existing and novel treatment approaches are key to reduce the health burden of bulimia nervosa. However, implementation of these will require the recognition of bulimia nervosa as a treatable illness, not a choice, and the reduction of other barriers to treatment, especially the stigma associated with the disorder.

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