Mortality in males treated for an eating disorder—A large prospective study

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Abstract
Objective: To report on the long-term mortality of eating disorders in male inpatients.
Method: Crude mortality rates (CMR) and standardized mortality ratios (SMR) were computed for a large sample of males (147 anorexia nervosa [AN], 81 bulimia nervosa [BN], 110 eating disorder not otherwise specified [ED-NOS]; DSM-IV). In addition, a survival analysis from onset of eating disorder to death or end of observation was computed.
Results: CMR was 12.9% in AN, 11.1% in BN, and 6.4% in ED-NOS. Standardized mortality was significantly elevated in males with AN (SMR = 5.91; 95% confidence interval 3.56–9.23) as well as ED-NOS (SMR = 3.40; 95% confidence interval 1.37–7.01) but not in males with BN (SMR = 1.88; 95% confidence interval 0.86–3.58). Males with AN died sooner after onset of eating disorder than males with BN or ED-NOS.
Discussion: Mortality in male inpatients with eating disorder is high, especially in AN. There is need for developing more effective treatments to achieve better outcome.

KEYWORDS
anorexia nervosa, bulimia nervosa, death, eating disorders, males, standardized mortality ratio

1 | INTRODUCTION

Very little is known on mortality in males with eating disorders (ED). Such knowledge is important for clinicians to be able to inform patients and their loved ones comprehensively on the course and possible outcome of their illness. The majority of individuals treated for ED are females. It is important to stress the seriousness of this illness in males toward policy makers and health insurances lest they dismiss EDs in males as a minor illness of little consequence. This study informs on the worst possible outcome, premature death.

Most studies on mortality in EDs used mixed gender or female only samples. Some studies using mixed gender samples reported mortality separately for males. There are few studies addressing mortality exclusively in males. A recent review of selected outcome studies on anorexia nervosa (AN) in males (Strobel, Quadflieg, Voderholzer, Naab, & Fichter, 2018) reported a total number of 22 deceased out of 553 males included in 21 studies, which allows a rough estimate of overall crude mortality of 4.0% in a heterogeneous group of males. Three deaths (3.1%) occurred in 96 males at less than 5 years follow-up, and 19 of 457 male participants (4.2%) died after more than 9 years. Registry studies included larger samples and results suggest that crude mortality rates (CMR) derived from small-sized studies may underestimate mortality. One study with a mean follow-up time of 17.1 years found 59 of 609 (9.7%) male inpatients with AN having died (Kask et al., 2017). Another study reported 5 of 63 male inpatients with AN (7.9%) having died after a mean 7.8 years (Møller-Madsen, Nystrup, & Nielsen, 1996). For males with bulimia nervosa (BN) and eating disorder not otherwise specified (ED-NOS; we use this term from the DSM-IV [American Psychiatric Association, 1994] as practically all studies, including the present study, were conducted before DSM-5 [American Psychiatric Association, 2013] was published) no such data exist.
Several studies computed standardized mortality ratio (SMR) for males with AN. SMRs were 2.7 after 1 year (Hoang, Goldacre, & James, 2014), 8.2 after 8 years (Møller-Madsen et al., 1996), 8.08 after 10 years (Gueguen et al., 2012), and 4.1 after 17 years (Kask et al., 2017). In two long-term registry studies, mortality in AN patients was nonsignificantly lower than in the reference population. SMR was 0.79 after up to 30 years (Crisp & Collaborators, 2006) and 0.68 after 27 years (Korndörfer et al., 2003). A meta-analysis found lower SMRs in studies which enrolled more males (Keshaviaha et al., 2014).

One registry study reported a nonsignificant SMR of 2.2 in males with BN and a significant SMR of 1.6 in males with ED-NOS after 1 year (Hoang et al., 2014). We assessed mortality in a large prospective clinical sample of former male inpatients.

2 | METHOD

2.1 | Sample

Between January 1985 and February 2017, 360 males (157 AN, 83 BN, and 120 ED-NOS) were treated by inpatient cognitive-behavioral psychotherapy in a hospital with specialized units for EDs in Germany. Patients with acute psychosis or severe alcohol/drug-related disorders were not admitted to treatment. The ED-NOS group included patients with any of four types of ED-NOS described in DSM-IV, page 550: (a) AN with BMI in the normal range (upper limit set at 25); (b) BN with shorter duration or lower frequency of symptoms; (c) Regular use of inappropriate compensatory behavior after consuming small amounts of food at normal weight; (d) Chewing and spitting out food.

The standardized algorithm of the Structured Inventory for Anorexic and Bulimic Eating Disorders Self-rating form (SIAB-S; Fichter & Quadflieg, 2000; available at http://www.klinikum.uni-muenchen.de/Klinik-und-Poliklinik-fuer-Psychiatrie-und-Psychotherapie/de/forschung/forschungsfelder/essstoerungen/evaluation/SIAB/index.html) provided ED diagnoses according to DSM-IV. The SIAB-S questionnaire covers a broad spectrum of ED symptoms, including all symptoms necessary for ED diagnosis in DSM-IV. The diagnostic algorithm is well validated (PPV 0.91). For a more detailed rationale for using the SIAB-S see Fichter, Quadflieg, Crosby, and Koch (2017).

The mixed sample of Fichter and Quadflieg (2016) included a small percentage of males. These males (27 AN, 50 BN, 103 ED-NOS) were included in the present study. Seven males with AN and six males with BN died after participating in follow-up assessment and were included in analysis for mortality and for follow-up (Strobel, Quadflieg, Naab, Voderholzer, & Fichter, under review).

Average age at treatment was 27 years for AN, and 33 years for BN and ED-NOS. Global assessment of functioning scores (American Psychiatric Association, 1994) indicated a severely impaired group of patients (see Table 1 for details). BMI at admission was 15.44 (1.79) in AN patients. This study was approved by the Ethics Committee of the

### TABLE 1  Sample characteristics at the beginning of treatment and posttreatment mortality

<table>
<thead>
<tr>
<th></th>
<th>AN N = 147</th>
<th>BN N = 81</th>
<th>ED-NOS N = 110</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at admission</strong></td>
<td>27.33 (9.90)</td>
<td>33.90 (12.01)</td>
<td>33.08 (11.15)</td>
</tr>
<tr>
<td><strong>Age at onset of ED</strong></td>
<td>20.99 (8.00)</td>
<td>20.59 (10.30)</td>
<td>21.06 (10.40)</td>
</tr>
<tr>
<td><strong>Duration of ED</strong></td>
<td>6.47 (6.92)</td>
<td>13.35 (10.86)</td>
<td>12.39 (11.03)</td>
</tr>
<tr>
<td><strong>Days of index inpatient treatment</strong></td>
<td>84.21 (36.29)</td>
<td>76.40 (38.52)</td>
<td>71.30 (35.52)</td>
</tr>
<tr>
<td><strong>Global assessment of functioning</strong></td>
<td>51.06 (15.29)</td>
<td>55.30 (15.02)</td>
<td>58.68 (14.89)</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of deceased</td>
<td>N = 19</td>
<td>N = 9</td>
<td>N = 7</td>
</tr>
<tr>
<td>Crude mortality rate</td>
<td>12.9%</td>
<td>11.1%</td>
<td>6.4%</td>
</tr>
<tr>
<td>SMR</td>
<td>5.91</td>
<td>1.88</td>
<td>3.40</td>
</tr>
<tr>
<td>(95% confidence interval)</td>
<td>(3.56–9.23)</td>
<td>(0.86–3.58)</td>
<td>(1.37–7.01)</td>
</tr>
<tr>
<td>Age at death</td>
<td>36.87 (16.99)</td>
<td>55.96 (11.54)</td>
<td>48.79 (14.14)</td>
</tr>
<tr>
<td>Years between onset of ED and death</td>
<td>13.71 (8.93)</td>
<td>32.98 (14.88)</td>
<td>31.82 (15.15)</td>
</tr>
<tr>
<td>Years between end of treatment and death</td>
<td>7.18 (7.34)</td>
<td>10.75 (8.32)</td>
<td>11.80 (3.66)</td>
</tr>
</tbody>
</table>

Note. AN = anorexia nervosa; BN = bulimia nervosa; ED-NOS = eating disorder not otherwise specified; ED = eating disorder; SMR = standardized mortality ratio.
Bavarian Medical Association. Patients gave written consent for participation before the beginning of the study.

2.2 | Vital status

Vital status was ascertained for 147 males with AN (93.6%), 81 males with BN (97.6%), and 110 males with ED-NOS (91.7%) primarily through the registration agencies of the patient’s place of residence, close family members or family doctors. All persons living in Germany are required to report their address to the local authorities. These agencies exchange data on residents’ current address, and the local registration agency at the last location of residence is notified of the death of a citizen. After moving away from Germany, no records of the person are updated by the authorities. This was the main reason for failing ascertainment.

2.3 | Statistical analysis

CMR were computed by dividing the number of deaths by the total number of patients with available information on vital status. Dividing the number of the observed deaths by the number of the expected deaths gave the standardized mortality ratio (SMR). The expected number of deaths of the general German population was extracted from the reports of the German Federal Office of Statistics (Federal Office of Statistics, n.d.; accessed on December 6, 2018). A higher number of deaths than expected are indicated by a SMR greater than 1.0. SMRs, and 95% confidence intervals were computed by PAMCOMP software (Taeger, Sun, Keil, & Straif, 2000). A confidence interval including the value one indicates that the number of observed deaths is not significantly (p < .05) different from the number of deaths expected in the general population. Person years are summarized over all participants and reflect the time at risk after discharge from treatment until death or end of observation. Person years were 971 in AN, 724 in BN and 590 in ED-NOS. The Kaplan–Meier method (Chan, 2004) was applied for survival analysis and a log-rank test (Bland & Altman, 2004) compared diagnostic groups. Observation ended with the return of the questionnaire or other contact with the patient, or with the end of observation at December 31, 2012. Survival analysis covered the time from onset of the ED to the end of observation. Age at onset was retrieved from an item in the SIAB-S asking the patient to report the age when their ED began.

3 | RESULTS

Average length of follow-up was 6.61 (SD 5.78; range 1–30) years in AN, 8.94 (SD 6.63; range 1–31) in BN and 5.36 (SD 4.17; range 1–23) in ED-NOS. Nineteen males with AN (12.9%), nine males with BN (11.1%) and seven males (6.4%) with ED-NOS died. SMRs were significantly (p < .05) elevated in AN and ED-NOS but not in BN. Mortality in males with AN was nearly six-times higher than in the male reference population. Age at death was lowest in AN (37 years) and highest in BN (56 years) although age at onset was similar in all diagnostic groups (Table 1, lower part).

3.1 | Survival analysis

Figure 1 shows the cumulative survival from the onset of ED. Long-term survival after onset of ED was shorter in males with AN compared to BN ($\chi^2 = 7.31; p = .007$) and ED-NOS ($\chi^2 = 8.96; p = .003$). BN and ED-NOS did not differ ($\chi^2 = 0.001; p = .975$).

4 | DISCUSSION

To the best of our knowledge, our study presents the largest prospective clinical follow-up sample on mortality in eating disordered male inpatients. We assessed crude and standardized mortality in males separately for AN, BN or ED-NOS. In addition, we analyzed the time from onset of ED to death or end of observation. Compared to the reference population, mortality was elevated in males with AN, but not in males with BN or ED-NOS. Long-term survival from onset of ED was shorter in AN than in BN or ED-NOS.

In our study, males with AN (age at treatment 27 years) had a CMR of 13% and a SMR of 5.91 after an average 7 years of follow-up. Gueguen et al. (2012) reported also a CMR of 13% and a somewhat higher SMR of 8.2 after 10 years in adult male inpatients with AN. Age at treatment was similar to our sample (26.6 years). The registry study of Møller-Madsen et al. (1996) reported on male inpatients with AN after 8 years. Compared to our study, CMR was lower (8%) and SMR was higher (9.2). Age at death was 25 years, lower than the 37 years in our AN sample. Thus our study and previous studies underscore that mortality is elevated in males with AN.

After 9 years the nonsignificant SMR was 1.88 in our BN sample (age at treatment 34 years). In a registry study, Hoang et al. (2014) reported a nonsignificant SMR of 2.2 in males with BN of all ages.
after 1 year. SMR was much higher for males aged 25–44 years (13.0; not significant) than in our sample. In our ED-NOS sample (age at treatment 33 years) the SMR after 5 years was 3.4. Hoang et al. (2014) reported a lower SMR of 1.6 for males with ED-NOS of all ages and a higher, nonsignificant SMR of 6.3 for males with ED-NOS aged 25–44 years. These results suggest no elevated mortality in males with BN. For males with ED-NOS results are more equivocal with some indications for elevated mortality.

Survival analysis suggested a shorter time from onset to death in males with AN compared to males with BN or ED-NOS. As the length of follow-up differed between diagnostic groups, this result should be interpreted cautiously. However, a survival analysis reported by Gueguen et al. (2012) found a shorter 3-year survival time in males with AN compared to females after discharge from treatment. Similarly, Møller-Madsen et al. (1996; page 456) concluded that "male [AN] patients seem to die early in the course of their disease". Males with ED tend to be more reluctant to seek treatment for an ED (Griffiths et al., 2015). Possibly treatment is less effective after symptoms have become more advanced and chronic. This would indicate a need for prevention programs tailored for males.

Limitations of our study include: (a) ED diagnoses at admission were made by using the self-rating SIAB-S. However, for all ED diagnoses we applied the well-validated and empirically based standardized diagnostic algorithms for the SIAB-S. The use of self-report for diagnosis is discussed more extensively in Quadflieg and Fichter (in press). (b) ED diagnoses were made at treatment but not over the further course of symptoms after discharge. (c) Our samples derived from one hospital and from inpatients only. We have no evidence how this affects generalizability of our findings.

Our study has several strengths: (a) Our sample size was large for a study on males with ED. (b) All ED diagnoses including ED-NOS were defined strictly according to one diagnostic system (DSM-IV). (c) We not only reported sample size-dependent crude mortality, but also mortality comparable to the general population of the same sex and age. (d) Ascertainment of vital status was very high (92–98%). Ascertainment rate is rarely reported in the ED literature. Keel et al. (2003) reported an ascertainment rate of 95% in a female sample with AN and BN.

## 5 Conclusion

Mortality in ED is high in males. Compared to males in the general population, males with AN carry a sixfold higher risk of premature death. Clinical practitioners should be aware that EDs in males can be a deadly disease which needs careful attention and intensive therapy. Further research should aim at collecting large clinical samples to allow definitions of meaningful subsamples for identifying risk factors for premature death.

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## Conflict of Interest

None.

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