Adverse outcomes and mortality in individuals with eating disorder-related electrolyte abnormalities in Ontario, Canada: a population-based cohort study

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See **Comment** page 778

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Summary

Background Individuals with eating disorders are at a higher risk of electrolyte abnormalities than the general population. We conducted the first representative cohort study assessing whether electrolyte abnormalities in people with eating disorders were associated with mortality and physical health outcomes.

Methods This was a retrospective population-based cohort study in Ontario including people aged 13 years or older with an eating disorder and an outpatient electrolyte measure within 1 year (between Jan 1, 2008 and June 30, 2019). An electrolyte abnormality was any of hypokalaemia, hyperkalaemia, hyponatraemia, hypernatraemia, hypomagnesaemia, hypophosphataemia, metabolic acidosis, or metabolic alkalosis. The primary outcome was all-cause mortality. Secondary outcomes were hospitalisation, a cardiac event, infection, acute or chronic kidney disease, fracture, and bowel obstruction. In additional analyses, we examined a younger cohort (<25 years old) and individuals with no previously diagnosed secondary outcome. We involved people with related lived or family experience in the study.

Findings 6163 patients with an eating disorder and an electrolyte measure within 1 year since diagnosis (mean age 26·8 years [SD 17·5]; 5456 [88·5%] female, 707 [11·5%] male; median follow-up 6·4 years [IQR 4–9]) were included. Ethnicity data were not available. The most common electrolyte abnormalities were hypokalaemia (994/1987 [50·0%]), hyponatraemia (752/1987 [37·8%]), and hypernatraemia (420/1987 [21·1%]). Overall, mortality occurred in 311/1987 (15·7%) of those with an electrolyte abnormality versus 234/4176 (5·6%) in those without (absolute risk difference 10·1%; adjusted hazard ratio 1·23 [95% CI 1·03–1·48]). Hospitalisation (1202/1987 [60·5%] *vs* 1979/4176 [47·4%]; 1·35 [1·25–1·46]), acute kidney injury (206/1987 [10·4%] *vs* 124/4176 [3%]; 1·91 [1·50–2·43]), chronic kidney disease (245/1987 [12·3%] *vs* 181/4176 [4·3%]; 1·44 [1·17–1·77]), bone fracture (140/1987 [7·0%] *vs* 167/4176 [4·0%]; 1·40 [1·10–1·78]), and bowel obstruction (72/1987 [3·6%] *vs* 57/4176 [1·4%]; 1·62 [1·12–2·35]) were associated with an electrolyte abnormality, but not infection or a cardiovascular event. Findings were consistent in young individuals (<25 years old) and those without secondary outcomes at baseline, by eating disorder type, and by sex.

Interpretation Electrolyte abnormalities are associated with death and poor physical health outcomes, supporting the importance of monitoring and possible interventions to prevent adverse outcomes. Findings also call for a refinement of the definition of severity of eating disorder and replication of these findings in other jurisdictions.

Funding None.

Introduction

Eating disorders are a complex group of disorders that substantially impair physical health and psychosocial functioning. They are characterised by psychopathology that results in disturbances in eating and related behaviour, and physical health.[1] There are numerous risk factors for the development of eating disorders, however the most credible evidence indicates that early traumatic and stressful events could be risk and precipitating factors.[2] Among eating disorders, anorexia nervosa, bulimia nervosa, binge eating disorder, and other specified eating disorders are the most frequent ones, and other eating disorders are avoidant–restrictive food intake disorder, pica, and rumination disorder.[1] Anorexia nervosa, bulimia nervosa, and binge-eating disorder have a lifetime prevalence of approximately 0·3–0·9% in the USA[3] and are more common among women and adolescents. Globally, the prevalence and burden of eating disorders is often underestimated,[4] and the eating disorders with the largest burden are other specified eating disorders and binge eating disorder.[5] People with eating disorders reach recovery in approximately 46% of cases, and 28% respond to treatment; however, 25% of people with an eating

Research in context

Evidence before this study

We searched PubMed (MEDLINE) on Nov 1, 2023, for publications since database inception with no restriction in language using the terms ("eating disorder" OR "anorexia" OR "bulimia" OR "binge eating disorder" OR "pica" OR "avoid*" OR "restrict*" OR "ruminat*" OR "purge") AND ("electrolyte abnormal*" OR "electrolyte imbalance" OR "electrolyte disorder" OR "hypokalemia" OR "hyperkalemia" OR "hyponatremia" OR "hypernatremia" OR "hypomagnesemia" OR "hypermagnesemia" OR "hypophosphatemia" OR "hyperphosphatemia" OR "hypochloremia" OR "hyperchloremia") AND ("death" or "mortality") and identified 886 articles. We identified several studies which quantified the prevalence of electrolyte abnormalities in a variety of eating disorders and one case–control study which used electrolyte abnormalities as a predictor for the subsequent development of an eating disorder. However, we found no study that identified electrolyte abnormalities in individuals with an eating disorder and tested their association with mortality.

Added value of this study

To our knowledge, this is the first study to assess and find that any electrolyte abnormality within 1 year of eating disorder diagnosis was associated with increased risk of mortality. We found that electrolyte abnormalities were also associated with hospitalisation, chronic kidney disease, bone fracture, bowel obstruction, and acute kidney injury. Importantly, there was no association found between electrolyte abnormalities and infection or a cardiovascular disease event.

Implications of all the available evidence

Electrolyte disturbances in people with newly diagnosed eating disorders might be a direct or indirect marker of the severity of the eating disorder, prompting further medical evaluation to reduce the risk of premature mortality, and certain physical health conditions. These findings have implications for clinical practice (clinicians could use findings of this work in psychoeducational activity with people living with eating disorders), future monitoring guidelines (electrolytes and associated outcomes should be monitored to delay death and non-cardiovascular complications), and can inform a refinement in the definition of severity of eating disorders, which is currently largely based on BMI and frequency of compensatory behaviour of binge episodes.

disorder develop a chronic course, 26% need hospitalisation, and 26% relapse after recovery.[6] Evidence clearly supports first-line treatment options for bulimia nervosa and binge eating disorder, yet for adults with anorexia nervosa there is no clear evidence-based outpatient treatment.[7]

Eating disorders are associated with significant morbidity[8] and mortality.[9] People with anorexia nervosa are reported to have the second-highest premature mortality of any psychiatric disorder (second to opioid use disorder),[10] whereby they are approximately 5-times more likely to die from any cause and 18-times more likely to die by suicide than the general population.[11] Variables associated with increased mortality include severe malnourishment, severe underweight, inadequate access to treatment, and physical complications.[6] Particularly, people with eating disorders have been shown to be at increased risk of several adverse health outcomes such as mortality,[10] hospitalisation,[12] chronic kidney disease,[13] acute kidney injury,[13] bone fractures,[14] bowel obstruction,[15] and cardiovascular disease events.[16] It is therefore imperative to identify risk factors for mortality and adverse health outcomes in people with eating disorders.

Electrolyte abnormalities are common in people with eating disorders, which largely stem from abnormal eating patterns and recurrent purging behaviours.[17] In the inpatient setting, a study of 1026 adult patients with an eating disorder found that 265/1026 (25·8%) had hypokalaemia and 144/1026 (14·0%) had hyponatraemia at the time of admission.[18] These electrolyte abnormalities might predispose individuals with eating disorders to adverse and fatal health consequences.[19]

A recent case-control study used outpatient electrolyte abnormalities as a predictor for the subsequent diagnosis of an eating disorder;[20] however, to our knowledge, no study has investigated if electrolyte abnormalities in people with eating disorder are associated with mortality. We conducted a cohort study which aimed to determine if the presence of any electrolyte abnormality within 1 year of eating disorder diagnosis was associated with mortality or other adverse health outcomes in people with an eating disorder.

Methods

Study design and participants

We conducted a population-level, retrospective cohort study of individuals aged 13 years or older in Ontario, Canada from Jan 1, 2008 to June 30, 2019 using linked databases held at ICES. Ontario is Canada's largest province with approximately 15 million residents.[13] ICES captures data on all Ontario residents who undergo a health-care encounter, including health-care visits, laboratory tests, hospitalisations, eating disorder visits, and vital statistics. ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyse health-care and demographic data, without consent, for health system evaluation and improvement. The use of data in this project was authorised under

See Online for appendix

section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. The reporting of this study follows the STROBE checklist (appendix p 3).[14,15]

We included Ontario residents with a diagnosis of eating disorder on a hospitalisation or emergency department record, and an outpatient electrolyte test between Jan 1, 2008, and June 30, 2019. As Canada is an entirely public health-care system, we captured and linked government databases with complete coverage for demographics, health-care encounters, and laboratory values in Ontario. The electrolyte test had to be within 1 year (latest date June 30, 2020) of the eating disorder diagnosis (ie, index diagnosis). Follow-up began from the index date (first abnormal electrolyte measure for the exposed group or first electrolyte measure for the unexposed group) until death, emigration, loss of eligibility for Ontario Health Insurance Plan, or study end on June 30, 2022. We excluded people with invalid data or data that could not be linked, individuals younger than 13 years at index, or people with an eating disorder diagnosis before index eating disorder diagnosis. Eating disorders included anorexia nervosa, bulimia nervosa, eating disorder not otherwise specified (EDNOS), and possible combinations of these diagnoses as identified using ICD codes (appendix p 6). We used ICD coding definitions previously examined in ICES data that were identified as accurate in identifying eating disorders.[21] As a comparison, we measured differences in baseline characteristics between people with an electrolyte test (abnormality or not) and no electrolyte test within the first year.

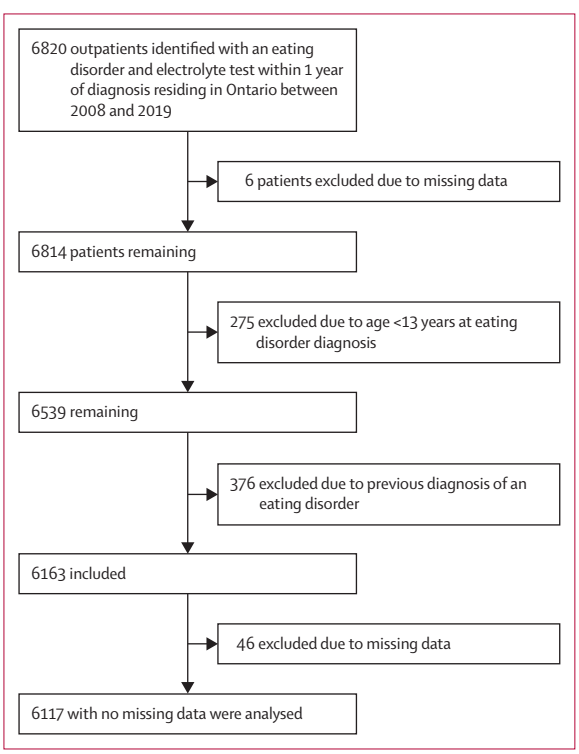

Figure 1: **Study profile**

Procedures

We ascertained baseline characteristics and outcome data from de-identified, linked databases housed at ICES. Demographic and vital status information was obtained from the Ontario Registered Persons Database, Postal Code Conversion File, and census data. Diagnostic and procedural information from all hospitalisations was determined using the Canadian Institute for Health Information Discharge Abstract Database. Diagnostic information from emergency department visits was obtained from the National Ambulatory Care Reporting System and day surgery visits from the Same Day Surgery dataset. Information was also obtained from the Ontario Health Insurance Plan database, which contains all health claims for inpatient and outpatient physician services. Whenever possible, we defined baseline characteristics and outcomes using validated codes (see appendix pp 5, 6, 9) for data sources and diagnostic codes for study cohort definition, exposure, and outcomes. Laboratory information is contained in the Ontario Laboratory Information System which captures laboratory tests for individuals in Ontario. These datasets were linked using unique encoded identifiers and analysed at ICES. The databases were complete for all other variables used except for rural residence and neighbourhood income quintile, for which data were missing for less than 0·75% of individuals.

The primary study exposure group included individuals with the presence of an outpatient electrolyte abnormality defined as any of the following: hypokalaemia (serum potassium ≤3·5 mmol/L), hyperkalaemia (serum potassium ≥5·5 mmol/L), hyponatraemia (serum sodium ≤135 mmol/L), hypernatraemia (serum sodium ≥145 mmol/L), hypomagnesaemia (serum magnesium ≤0·60 mmol/L), hypophosphataemia (serum phosphate ≤0·80 mmol/L), metabolic acidosis (serum bicarbonate ≤22 mmol/L), or metabolic alkalosis (serum bicarbonate ≥30 mmol/L). Only outpatient electrolyte measurements were included (appendix p 6).

Outcomes

The primary study outcome was all-cause mortality. Secondary outcomes were hospitalisation, cardiovascular disease event (ie, acute coronary syndrome, congestive heart failure, stroke, or atrial fibrillation), infection, acute kidney injury or chronic kidney disease, fracture, or bowel obstruction.

Demographic covariates encompassed age, sex, year, neighbourhood income quintile, geographical region, and urban or rural living status derived from postal code data. Comorbidities diagnosed within 5 years pre-index, such as asthma, chronic kidney disease, chronic obstructive pulmonary disorder, congestive heart failure, Crohn's disease or colitis, diabetes, myocardial

	No electrolyte abnormality (n=4176)	Electrolyte abnormality (n=1987)	Total (N=6163)	Standardised difference	Standardised difference after propensity score overlap weighting
Age, years	24·04 (15·29)	32·56 (20·20)	26·78 (17·49)	0·476	0·000
Sex					
Female	3743 (89·6%)	1713 (86·2%)	5456 (88·5%)	0·105	0·000
Male	433 (10·4%)	274 (13·8%)	707 (11·5%)	0·105	0·000
Index year					
2008	76–80*	32–36*	112 (1·8%)	0·023	0·000
2009	194 (4·6%)	64 (3·2%)	258 (4·2%)	0·073	0·000
2010	185 (4·4%)	67 (3·4%)	252 (4·1%)	0·055	0·000
2011	215 (5·1%)	93 (4·7%)	308 (5·0%)	0·022	0·000
2012	396 (9·5%)	136 (6·8%)	532 (8·6%)	0·096	0·000
2013	412 (9·9%)	177 (8·9%)	589 (9·6%)	0·033	0·000
2014	486 (11·6%)	215 (10·8%)	701 (11·4%)	0·026	0·000
2015	395 (9·5%)	222 (11·2%)	617 (10·0%)	0·056	0·000
2016	458 (11·0%)	242 (12·2%)	700 (11·4%)	0·038	0·000
2017	449 (10·8%)	258 (13·0%)	707 (11·5%)	0·069	0·000
2018	524 (12·5%)	291 (14·6%)	815 (13·2%)	0·061	0·000
2019	361 (8·6%)	185 (9·3%)	546 (8·9%)	0·023	0·000
2020	21–25*	1–5*	26 (0·4%)	0·041	0·000
Nearest neighbourhood income quintile (within CMA/CA)					
Not reported	31 (0·7%)	15 (0·8%)	46 (0·7%)	0·001	0·000
First	741 (17·7%)	435 (21·9%)	1176 (19·1%)	0·104	0·000
Second	719 (17·2%)	364 (18·3%)	1083 (17·6%)	0·029	0·000
Third	783 (18·8%)	348 (17·5%)	1131 (18·4%)	0·032	0·000
Fourth	876 (21·0%)	391 (19·7%)	1267 (20·6%)	0·032	0·000
Fifth	1026 (24·6%)	434 (21·8%)	1460 (23·7%)	0·065	0·000
Rural living situation					
Not reported	24 (0·6%)	12 (0·6%)	36 (0·6%)	0·004	0·000
No	3717 (89·0%)	1781 (89·6%)	5498 (89·2%)	0·02	0·000
Yes	435 (10·4%)	194 (9·8%)	629 (10·2%)	0·022	0·000
Yearly LHIN					
Central	538 (12·9%)	317 (16·0%)	855 (13·9%)	0·087	0·000
Central East	433 (10·4%)	222 (11·2%)	655 (10·6%)	0·026	0·000
Central West	165 (4·0%)	86 (4·3%)	251 (4·1%)	0·019	0·000
Champlain	336 (8·0%)	139 (7·0%)	475 (7·7%)	0·04	0·000
Erie St. Clair	106 (2·5%)	49 (2·5%)	155 (2·5%)	0·005	0·000
Hamilton Niagara Haldimand Brant	567 (13·6%)	184 (9·3%)	751 (12·2%)	0·136	0·000
Mississauga Halton	343 (8·2%)	134 (6·7%)	477 (7·7%)	0·056	0·000
North East	248 (5·9%)	81 (4·1%)	329 (5·3%)	0·085	0·000
North Simcoe Muskoka	207 (5·0%)	86 (4·3%)	293 (4·8%)	0·03	0·000
North West	59 (1·4%)	26 (1·3%)	85 (1·4%)	0·009	0·000
South East	193 (4·6%)	89 (4·5%)	282 (4·6%)	0·007	0·000
South West	324 (7·8%)	254 (12·8%)	578 (9·4%)	0·166	0·000
Toronto Central	396 (9·5%)	215 (10·8%)	611 (9·9%)	0·044	0·000
Waterloo Wellington	261 (6·3%)	105 (5·3%)	366 (5·9%)	0·041	0·000
Number of hospitalisations in the last 2 years	1·02 (1·46)	1·45 (2·27)	1·16 (1·77)	0·227	0·000
Previous health-care visit for mental health	3461 (82·9%)	1493 (75·1%)	4954 (80·4%)	0·191	0·000
Outpatient psychiatry visit	2702 (64·7%)	1280 (64·4%)	3982 (64·6%)	0·006	0·000
Asthma	675 (16·2%)	326 (16·4%)	1001 (16·2%)	0·007	0·000
Chronic kidney disease	83 (2·0%)	113 (5·7%)	196 (3·2%)	0·193	0·000
Chronic obstructive pulmonary disease	120 (2·9%)	155 (7·8%)	275 (4·5%)	0·221	0·000

(Table 1 continues on next page)

	No electrolyte abnormality (n=4176)	Electrolyte abnormality (n=1987)	Total (N=6163)	Standardised difference	Standardised difference after propensity score overlap weighting
(Continued from previous page)					
Congestive heart failure	84 (2·0%)	115 (5·8%)	199 (3·2%)	0·196	0·000
Crohn's disease or colitis	66 (1·6%)	46 (2·3%)	112 (1·8%)	0·053	0·000
Diabetes	230 (5·5%)	272 (13·7%)	502 (8·1%)	0·280	0·000
Myocardial infarction	13 (0·3%)	17 (0·9%)	30 (0·5%)	0·072	0·000
Liver disease	164 (3·9%)	139 (7·0%)	303 (4·9%)	0·135	0·000
Depression	1376 (33·0%)	501 (25·2%)	1877 (30·5%)	0·171	0·000
Anxiety	1097 (26·3%)	480 (24·2%)	1577 (25·6%)	0·049	0·000
Personality disorder	250 (6·0%)	142 (7·1%)	392 (6·4%)	0·047	0·000
Substance misuse	346 (8·3%)	241 (12·1%)	587 (9·5%)	0·127	0·000
Eating disorder type (on index hospitalisation or emergency department visit)					
Anorexia and bulimia	24 (0·6%)	15–19*	39–43*	0·039	0·000
Anorexia and bulimia and EDNOS	0 (0·0%)	1–5*	1–5*	0·045	0·000
Anorexia and EDNOS	88 (2·1%)	29 (1·5%)	117 (1·9%)	0·049	0·000
Anorexia only	927 (22·2%)	436 (21·9%)	1363 (22·1%)	0·006	0·000
Bulimia and EDNOS	32 (0·8%)	14 (0·7%)	46 (0·7%)	0·007	0·000
Bulimia only	611 (14·6%)	325 (16·4%)	936 (15·2%)	0·048	0·000
EDNOS only	2494 (59·7%)	1163 (58·5%)	3657 (59·3%)	0·024	0·000

Data are mean (SD) or n (%) unless otherwise stated. CMA=census metropolitan area. CA=census area. EDNOS=eating disorder not otherwise specified. LHIN=local health integration networks. *Cell sizes with <6 individuals (or if back calculation would lead to another cell size <6) are suppressed as per ICES policy.

Table 1: **Baseline characteristics**

infarction, liver disease, depression, anxiety, personality disorder, or substance misuse, were included. Eating disorder type (anorexia nervosa, bulimia nervosa, EDNOS, or combination), number of hospitalisations, previous hospital-based health-care visits for a mental disorder diagnosis, or a previous psychiatry ambulatory visit (all within the previous 2 years) were included (appendix p 6).

We involved people with related lived or family experience in the study design and implementation.

Statistical analysis

To examine the association between the exposure and the primary outcome, we used overlap propensity score-weighted Cox proportional hazards models. The overlap propensity weights included all covariates previously described. Density plots of the propensity scores pre-weighting and post-weighting were visually examined. The proportional hazards assumption was examined by including an interaction term with time and our exposure in the model. For models examining the secondary outcomes, death was handled as a competing event using Fine and Gray sub-distributional hazard models.[22] We conducted all analyses using SAS Enterprise Guide, version 8.3 (SAS Institute, Cary, NC, USA). The 95% CI that did not overlap with 1·0 and two-sided p-values less than 0·05 were interpreted as statistically significant. We used a complete case analysis approach (as missing data were low [<0·75%]).

We conducted a subgroup analysis by restricting the population to those with a maximum age of 24 years at cohort entry because 82·4% of patients with eating disorders have onset before the age of 25 years.[23] We conducted a sensitivity analysis whereby we excluded people with a previous diagnosis of a cardiovascular disease event (ie, acute coronary syndrome, congestive heart failure, stroke, or atrial fibrillation), infection, acute kidney injury, chronic kidney disease, fracture, or bowel obstruction before the index date, when considering each of these outcomes. A lookback window of 1 month was used for infection and 5 years for the remainder of the secondary outcomes. We tested the interaction between our primary model (death) and eating disorder types (anorexia nervosa, bulimia nervosa, and EDNOS) and any electrolyte abnormality. We also analysed the association with sex.

Results

Of 6820 eligible people living in Ontario identified with an ICD-defined eating disorder and electrolyte test within 1 year of diagnosis, 6163 (90·4%) participants met the inclusion criteria, of whom we analysed 6117 with no missing data (figure 1). Most patients were diagnosed with an EDNOS (3657/6163 [59·3%]), followed by anorexia nervosa (1363/6163 [22·1%]), and bulimia nervosa (936/6163 [15·2%]). Of the 6163 included patients, 1987 (32·2%) had any electrolyte abnormality within 1 year of an eating disorder diagnosis. The

numbers of participants with each electrolyte abnormality were as follows: hyperkalaemia (132/1987 [6·6%]), hypokalaemia (994/1987 [50·0%]), metabolic alkalosis (171/1987 [8·6%]), metabolic acidosis (172/1987 [8·7%]), hypernatraemia (420/1987 [21·1%]), hyponatraemia (752/1987 [37·8%]), hypomagnesaemia (65/1987 [3·3%]), and hypophosphataemia (196/1987 [9·9%]).

Mean age was 26·8 years (SD 17·5), with the majority being female (5456/6163 [88·5%]; table 1). Ethnicity data were not available. The median follow-up time was 6·35 years (IQR 4–9). Individuals with an electrolyte abnormality had a higher mean number of previous hospitalisations in the past 2 years than individuals without an electrolyte abnormality, and a higher proportion had a history of chronic kidney disease, chronic obstructive pulmonary disease, congestive heart failure, Crohn's disease or colitis (2·3% *vs* 1·6%), diabetes, myocardial infarction, liver disease, and substance misuse (table 1). A higher proportion of people without an electrolyte abnormality had a previous health-care visit for mental health and a history of depression. There was no statistically significant difference in diagnosed eating disorder type, asthma, anxiety, or personality disorder between people with an electrolyte abnormality and people without an electrolyte abnormality. After overlap weighting, standardised differences for all the covariates were <0·1. There were statistically significant differences at baseline in people with any electrolyte test (abnormality or not) versus no electrolyte test within the first year (appendix pp 12–14). Briefly, standardised differences greater than 0·1 indicated that people included in the study had an older age at index eating disorder diagnosis, more frequently had no or greater than three previous admissions, had more frequent physical comorbidities, and had less frequent mental health visits despite no differences in frequency of mental health diagnoses compared with people with an eating disorder not included in this study.

A total of 545 (8·8%) of 6163 participants died during follow-up (table 2). Among people with an electrolyte abnormality, 311 (15·7%) of 1987 died compared with 234 (5·6%) of 4176 people without an electrolyte abnormality (absolute risk difference=10·1). People with electrolyte abnormalities within 1 year of an eating disorder diagnosis demonstrated increased mortality in both the adjusted (figure 2A; p=0·0100) and unadjusted (figure 2B; p<0·0001) Kaplan–Meier plots. This was consistent in time to event models after weighting (adjusted hazard ratio [aHR] 1·23 [95% CI 1·03–1·48]).

For the secondary outcomes, we found that patients with any outpatient electrolyte abnormality within 1 year of eating disorder diagnosis were at higher risk (compared with patients without any outpatient electrolyte abnormality) of hospitalisation (60·5% [1202/1987] *vs* 47·4% [1979/4176]; aHR 1·35, [95% CI 1·25–1·46]), acute kidney injury (10·4% [206/1987] *vs* 3·0% [124/4176]; 1·91 [1·50–2·43]), chronic kidney disease (12·3% [245/1987] *vs* 4·3% [181/4176]; 1·44 [1·17–1·77]), bone fracture (7·0% [140/1987] *vs* 4·0% [167/4176]; 1·40 [1·10–1·78]), and bowel obstruction (3·6% [72/1987] *vs* 1·4% [57/4176]; 1·62 [1·12–2·35]), but were not at increased risk of infection (0·99 [0·94–1·06]) or a cardiovascular disease event (1·04 [0·82–1·32]; table 2).

In adjusted analyses of patients younger than 25 years at cohort entry, any outpatient electrolyte abnormality within 1 year of eating disorder diagnosis was associated with an increased risk of death (aHR 1·79 [95% CI 1·05–3·05]; table 3). For the secondary outcomes, we found that patients with any outpatient electrolyte abnormality within 1 year of eating disorder diagnosis were at a higher risk of

	No electrolyte abnormality (n=4176)	Electrolyte abnormality (n=1987)	Total (N=6163)	Absolute risk difference (crude %)	HR (95% CI)
Death	234 (5·6%)	311 (15·7%)	545 (8·8%)	10·1	1·23 (1·03–1·48)
Any hospitalisation					
No event	2153 (51·6%)	722 (36·3%)	2875 (46·6%)	..	..
Event	1979 (47·4%)	1202 (60·5%)	3181 (51·6%)	13·1	1·35 (1·25–1·46)*
Death (competing event)	44 (1·1%)	63 (3·2%)	107 (1·7%)	..	..
Cardiovascular disease event					
No event	3860 (92·4%)	1602 (80·6%)	5462 (88·6%)	..	..
Event	148 (3·5%)	170 (8·6%)	318 (5·2%)	4·9	1·04 (0·82–1·32)
Death (competing event)	168 (4·0%)	215 (10·8%)	383 (6·2%)	..	..
Infection					
No event	437 (10·5%)	173 (8·7%)	610 (9·9%)	..	..
Event	3707 (88·8%)	1746 (87·9%)	5453 (88·5%)	-1·0	0·99 (0·94–1·06)
Death (competing event)	32 (0·8%)	68 (3·4%)	100 (1·6%)	..	..
Chronic kidney disease					
No event	3818 (91·4%)	1528 (76·9%)	5346 (86·7%)	..	..
Event	181 (4·3%)	245 (12·3%)	426 (6·9%)	8·0	1·44 (1·17–1·77)
Death (competing event)	177 (4·2%)	214 (10·8%)	391 (6·3%)	..	..
Bone fracture					
No event	3794 (90·9%)	1567 (78·9%)	5361 (87·0%)	..	..
Event	167 (4·0%)	140 (7·0%)	307 (5·0%)	3·0	1·40 (1·10–1·78)
Death (competing event)	215 (5·1%)	280 (14·1%)	495 (8·0%)	..	..
Bowel obstruction					
No event	3903 (93·5%)	1637 (82·4%)	5540 (89·9%)	..	..
Event	57 (1·4%)	72 (3·6%)	129 (2·1%)	2·2	1·62 (1·12–2·35)
Death (competing event)	216 (5·2%)	278 (14·0%)	494 (8·0%)	..	..
Acute kidney injury					
No event	3864 (92·5%)	1567 (78·9%)	5431 (88·1%)	..	..
Event	124 (3·0%)	206 (10·4%)	330 (5·4%)	7·5	1·91 (1·50–2·43)*
Death (competing event)	188 (4·5%)	214 (10·8%)	402 (6·5%)	..	..

Data are n (%) unless otherwise stated. HR=hazard ratio. *Proportional hazard assumption violation for any hospitalisation and acute kidney injury outcomes, please refer to appendix (p 11) for time-dependent estimates.

Table 2: **Association between electrolyte abnormalities, death, and adverse health outcomes in people with an eating disorder**

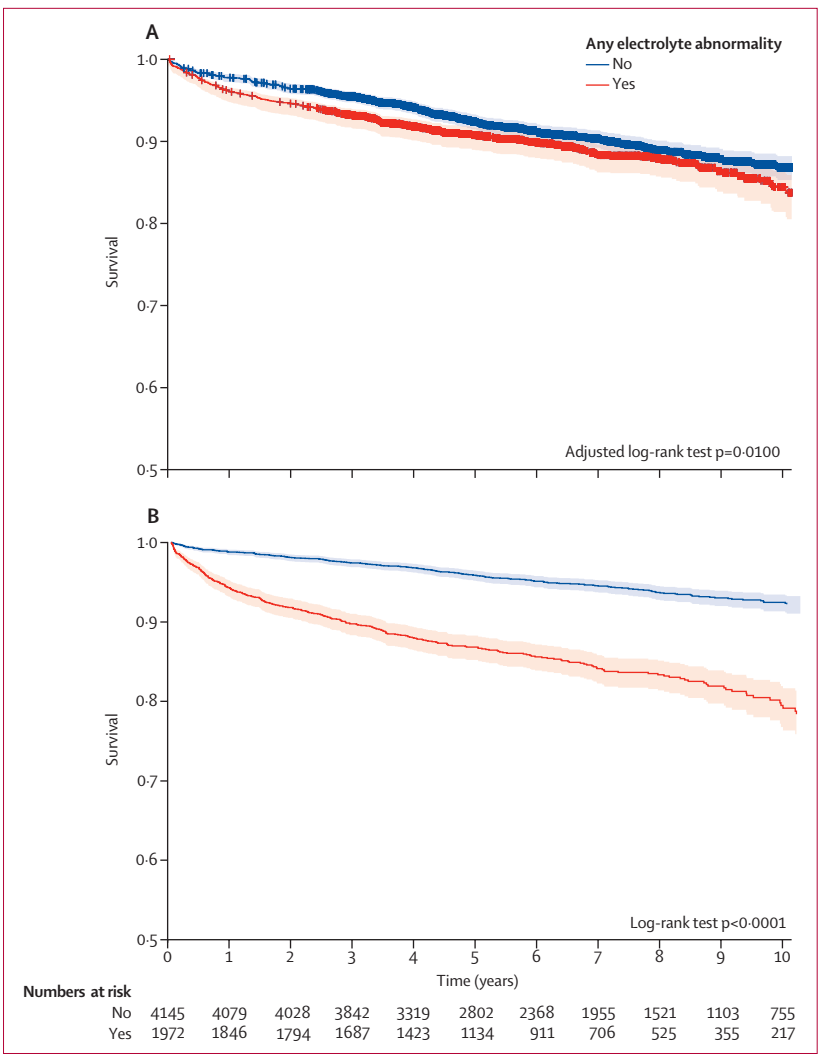

Figure 2: **Weighted (adjusted; A) and unweighted (B) Kaplan–Meier plots for the survival over time in people with an eating disorder with and without an electrolyte abnormality**
Shaded areas represent 95% CI.

hospitalisation (1·42 [1·28–1·57]) and acute kidney injury (2·69 [1·62–4·46]), but were not at an increased risk of a cardiovascular disease event (1·01 [0·49–2·11]), infection (1·01 [0·93–1·09]), chronic kidney disease (1·39 [0·83–2·32]), fracture (1·42 [0·97–2·09]), or bowel obstruction (1·65 [0·76–3·56]). The risk of electrolyte abnormalities associated hospitalisation and cardiovascular disease events associated with electrolyte abnormalities changed over time, and occurred predominantly in the first 3 years following diagnosis (appendix p 11).

In the sensitivity analyses excluding people with secondary outcomes present at baseline, any outpatient electrolyte abnormality within 1 year of eating disorder diagnosis was associated with an increased risk of acute kidney injury (aHR 1·70 [95% CI 1·29–2·23]), chronic kidney disease (1·52 [1·16–1·98]), bone fracture (1·38 [1·08–1·77]), or bowel obstruction (1·62 [1·06–1·08]), but not with an increased risk of a cardiovascular disease event (1·21 [0·88–1·67]) or infection (0·99 [0·93–1·06]). There was no statistically significant association (p=0·89) when testing the interaction between our primary model (death) and eating disorder types (anorexia nervosa, bulimia nervosa, and EDNOS) and any electrolyte abnormality. No differences emerged by sex (p=0·51).

Discussion

To our knowledge, this is the first study to assess if outpatient electrolyte abnormalities in people with eating disorders were associated with mortality and physical health complications. In this population-based cohort of 6163 individuals with an eating disorder, we found 32% had an outpatient electrolyte abnormality within 1 year of an eating disorder diagnosis and this was associated with a higher risk of all-cause mortality. Electrolyte abnormalities were also associated with multiple serious physical health conditions, including hospitalisation, acute kidney injury, chronic kidney disease, bone fracture, and bowel obstruction. These findings largely persisted when focusing on young individuals (<25 years old) and people with no previous history of our selected physical health conditions. Our findings suggest clinical vigilance, monitoring, and therapeutic intervention of electrolyte abnormalities in individuals with eating disorders could improve clinical outcomes.

Our findings are consistent with previous studies from populations without an eating disorder. For instance, a cohort study found that electrolyte abnormalities in adult patients who presented to the emergency department were associated with increased morbidity and mortality.[24] Particularly, hyponatraemia and hypokalaemia were associated with 58% and 73% increased risk of in-hospital mortality, respectively. Furthermore, an abnormally increased level of electrolytes substantially increased mortality, with the risk of mortality increasing with electrolyte abnormality severity.[24] Our study expands the association between electrolyte abnormalities and clinical outcomes in a relatively young cohort of individuals at high risk due to having an eating disorder. Importantly, even after controlling for potential source of bias and excluding participants with secondary outcomes at baseline, sensitivity analyses confirmed the association between electrolyte abnormalities and adverse health outcomes.

There are various biological mechanisms which could explain the link between electrolyte abnormalities and the various physical health complications observed. First, potassium and magnesium abnormalities predispose patients to cardiac arrhythmias. Second, sodium and phosphate alterations increase the risk of cognitive impairment and seizures. Third, hyponatraemia is known to have a direct negative affect on the metabolism and integrity of the bone through osteoclast formation and increased resorptive activity; which leads to an increased risk of both osteoporosis and fracture.[25] Fourth,

electrolyte abnormalities (particularly disorders in potassium, calcium, magnesium, or bicarbonate) might contribute to hypoperistalsis, leading to eventual bowel obstruction.[26] Fifth, recurrent binging, restricting, and purging behaviours might result in dehydration and subsequent electrolyte abnormalities that can lead to recurrent acute kidney injury, which is associated with progressive chronic kidney disease over time.[27] Lastly, due to the previously mentioned increase in morbidity, people with an eating disorder would be at a higher risk for requiring more immediate medical attention through hospitalisation.

People with an early-stage eating disorder might not suffer from complications such as chronic kidney disease, fracture, or bowel obstruction which can result from prolonged illness and electrolyte abnormalities. When the analysis was focused on younger patients (ie, <25 years old), the risks of hospitalisation and acute kidney injury remained statistically significantly increased in people with electrolyte abnormalities, calling for a careful comprehensive assessment of eating disorder severity and monitoring of kidney functioning. Electrolyte abnormalities leading to hospitalisation and acute kidney injury can be due to extreme dietary restriction including restriction of fluids or an extreme severity of purging, even in the absence of a low BMI. The criteria that determine severity in eating disorders in the DSM-5 are largely based on BMI in anorexia nervosa, frequency of compensatory behaviours in bulimia nervosa, and frequency of binge episodes in binge eating disorder.[28]

This work has three main policy implications. First, electrolyte abnormalities could be considered as one of the severity criteria in DSM. Second, these results inform primary care providers and specialists working in outpatient settings to carefully monitor electrolytes in people with eating disorders, and not just rely on BMI, or frequency of compensatory behaviours and binge episodes. The UK National Institute for Health and Care Excellence guidelines provide little guidance, generally advising to assess electrolyte imbalances in those with eating disorders and to correct abnormalities found; however, there is no mention of the associated outcomes such as morbidity or mortality.[29] Our findings build upon the Medical Emergencies in Eating Disorders guidelines which discuss the medical risk and provide shared information for treatment in emergency situations.[30] Third, the results can be translated into psychoeducation material to be co-developed with patients with lived experience.

This study has several limitations. First, due to the observational nature of this work, we cannot confirm a causal relationship between outpatient electrolyte abnormalities and death or adverse health outcomes. Second, the data sources did not allow us to determine the type of clinician who made the diagnosis of an eating disorder in our cohort, and atypical eating disorder presentations might not be formally recognised. However, the definition of eating disorder based on administrative health data has been used previously.[21] Third, in Ontario comprehensive medication data are only available for people 65 years or older, or people receiving disability pension, which did not allow us to account for psychotropics, laxatives, or diuretics which could cause or contribute to electrolyte disturbances. Fourth, despite our large cohort size, we were limited by the number of events in examining in detail analysis by electrolyte abnormality type or severity. This reduces our ability to determine which electrolyte abnormality or thresholds for abnormality are more likely to lead to mortality or adverse health outcomes. Fifth, our data did not allow us

	No electrolyte abnormality (n=3073)	Electrolyte abnormality (n=1023)	Total (N=4096)	Absolute risk difference (crude %)	HR (95% CI)
Death	37 (1·2%)	26 (2·5%)	63 (1·5%)	1·3	1·79 (1·05–3·05)
Any hospitalisation					
No event	1684 (54·8%)	459 (44·9%)	2143 (52·3%)	..	..
Event	1381 (44·9%)	557 (54·4%)	1938 (47·3%)	9·5	1·42 (1·28–1·57)*
Death (competing event)	8 (0·3%)	7 (0·7%)	15 (0·4%)	..	..
Cardiovascular disease event					
No event	3013 (98·0%)	989 (96·7%)	4002 (97·7%)	..	..
Event	27 (0·9%)	11 (1·1%)	38 (0·9%)	0·2	1·01 (0·49–2·11)*
Death (competing event)	33 (1·1%)	23 (2·2%)	56 (1·4%)	..	..
Infection					
No event	342 (11·1%)	101 (9·9%)	443 (10·8%)	..	..
Event	2725 (88·7%)	915 (89·4%)	3640 (88·9%)	0·7	1·01 (0·93–1·09)
Death (competing event)	6 (0·2%)	7 (0·7%)	13 (0·3%)	..	..
Chronic kidney disease					
No event	2989 (97·3%)	976 (95·4%)	3965 (96·8%)	..	..
Event	48 (1·6%)	26 (2·5%)	74 (1·8%)	0·9	1·39 (0·83–2·32)
Death (competing event)	36 (1·2%)	21 (2·1%)	57 (1·4%)	..	..
Bone fracture					
No event	2949 (96·0%)	959 (93·7%)	3908 (95·4%)	..	..
Event	88 (2·9%)	41 (4·0%)	129 (3·1%)	1·1	1·42 (0·97–2·09)
Death (competing event)	36 (1·2%)	23 (2·2%)	59 (1·4%)	..	..
Bowel obstruction					
No event	3017 (98·2%)	988 (96·6%)	4005 (97·8%)	..	..
Event	19 (0·6%)	12 (1·2%)	31 (0·8%)	0·6	1·65 (0·76–3·56)
Death (competing event)	37 (1·2%)	23 (2·2%)	60 (1·5%)	..	..
Acute kidney injury					
No event	3005 (97·8%)	966 (94·4%)	3971 (96·9%)	..	..
Event	35 (1·1%)	36 (3·5%)	71 (1·7%)	2·4	2·69 (1·62–4·46)
Death (competing event)	33 (1·1%)	21 (2·1%)	54 (1·3%)	..	..

Data are n (%) unless otherwise stated. HR=hazard ratio. *Proportional hazard assumption violation for any hospitalisation and cardiovascular disease outcomes, please refer to appendix (p 11) for time-dependent estimates.

Table 3: **Association between electrolyte abnormalities, death, and adverse health outcomes in people with an eating disorder younger than 25 years**

to account for treatment refusal, which might shape outcomes. Sixth, the estimates reported are conditional on patients having had an electrolyte test which reduces the generalisability of our findings to all individuals with an eating disorder that did not have an electrolyte measure. Seventh, although classification of electrolyte abnormality (*vs* no electrolyte abnormality) is a reasonable exposure, crossover could occur between groups. Eighth, given the differences observed between people with an eating disorder and an electrolyte test included in this cohort versus people with an eating disorder but not included due to no electrolyte test, some considerations on the generalisability of the findings should be mentioned. First, although several variables were statistically significantly different between the two groups, for several of them the standardised difference was less than 0·1, suggesting the difference was not substantial. Moreover, people with an electrolyte test were diagnosed in more recent years, which means they were probably more reflective of the present clinical population.

Nevertheless, compared with people excluded from this cohort, the participants included were older at the eating disorder diagnosis. Also, the people included more frequently had no previous hospitalisation, or greater than three hospitalisations, suggesting poor participation with indicated treatments or extreme forms of eating disorders. They also had more frequent physical health disorders. Hence, this study represents a group of patients with the most severe forms of eating disorders. It is also possible that people excluded from this study had no motivation for treatment, and so did not receive an electrolyte measure since they were not seeking help, despite extreme severity. Yet, the excluded sample had more frequent visits for mental health despite no substantial differences in specific mental health diagnoses, which does not align with poor help-seeking behaviour. Overall, although it is possible that some individuals had extreme forms of eating disorders in the excluded group, at the group level the lower rates of greater than three hospitalisations, the absence of electrolyte measures, and the lower rates of physical comorbidities make the excluded group less representative of severe or extreme clinical pictures than the included group. Finally, the distribution of specific eating disorder diagnoses did not substantially differ between the included and the excluded samples. We did not conduct analyses by specific eating disorder type, however we did assess the interaction between eating disorder type and electrolyte abnormality which was not statistically significant.

In conclusion, in this population-based cohort of individuals with an eating disorder, we found electrolyte abnormalities occurred in roughly one-third of participants within 1 year of diagnosis and this was associated with an elevated risk of all-cause mortality. Furthermore, multiple other physical health complications, such as all-cause hospitalisation, kidney disorders, fractures, and bowel obstructions, were more common with electrolyte abnormalities compared with people without electrolyte abnormalities. These findings support the importance of regularly monitoring electrolytes in people with eating disorders and promptly correcting any abnormalities found to reduce premature mortality and risk of medical complications. The severity criteria of eating disorders could be refined to include explicit mention of electrolyte abnormalities. Given that we focused on people with outpatient electrolyte abnormalities, our results might apply to the majority of patients with eating disorders (ie, people that do not need hospital admission), and are relevant for different provider stakeholders, including primary care providers and private practitioners, beyond hospital-based settings. Future research should aim to determine which specific electrolyte abnormalities are associated with various adverse health outcomes.

Contributors

AEC and MMS accessed and verified the data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

MS received honoraria or has been a consultant for AbbVie, Angelini, Lundbeck, and Otsuka. MMS has received consultancy fees from AstraZeneca, Bayer, Otsuka, and GlaxoSmithKline. All other authors declare no competing interests.

Data sharing

The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (eg, health-care organisations and government) prohibit the institute from making the dataset publicly accessible, access might be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca(das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs might rely on coding templates or macros unique to ICES and are therefore either inaccessible or might require modification.

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