

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The epidemiology of eating disorders in primary care in children and young people: A Clinical Practice Research Datalink study in England
AUTHORS	Wood, Sophie; Marchant, Amanda; Allsopp, Mark; Wilkinson, Kathleen; Bethel, Jackie; Jones, Hywel; John, Ann

VERSION 1 - REVIEW

REVIEWER	E. Thomaseo Burton University of Tennessee Health Science Center, USA
REVIEW RETURNED	03-Nov-2018

GENERAL COMMENTS	<p>This interesting and timely study is an epidemiological examination of eating disorder management trends of youth 11-24 years of age. Using a large electronic database of diagnostic, treatment, and referral information in UK primary care practices, the authors present estimated incidence of eating disorders as well as treatment (i.e., prescription, outpatient, and inpatient) patterns.</p> <p>Overall, this is a well-written and appropriately conducted manuscript. Furthermore, the implications are well thought out and helpful from research and clinical perspectives. However, there are a few issues that should be addressed to improve the manuscript.</p> <p>1. Please provide more detail about how deprivation is operationalized.</p> <p>For the following comments, this reviewer acknowledges that since data were collected between 2004 and 2014, these conventions may not have yet been applicable.</p> <p>1. Binge-eating disorder is more common in youth than anorexia nervosa and bulimia nervosa. Yet, binge-eating disorder (and subthreshold binge-eating behavior) is not mentioned in the manuscript. Please acknowledge binge eating and discuss how the symptoms are accounted for in this study (it seems that these behaviors are subsumed in EDNOS).</p> <p>2. EDNOS is now referred to in OSFED in DSM-5. While these data are based on ICD coding and largely before OSFED was formally introduced, it bears acknowledgement.</p>
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REVIEWER	Kenichi Asano Lecturer Mejiro University Japan
REVIEW RETURNED	07-Nov-2018

GENERAL COMMENTS	<p>This manuscript addresses an important issue about EDs and it was explored by analyzing valuable data. Please add some explorations to help reader's understanding of this datalink study.</p> <ol style="list-style-type: none"> 1. In introduction section; Please introduce the information about prevalence of EDs particularly in U.K.. It will help readers to understand the importance of this study. 2. In method section; Please state the reason why you defined the criteria from 11 to 24. Are there any reason you used 24 years old as an upper limit? 3. In method section, Age and sex; Please show the reason why you categorized age group 11 to15, 16 to 20, 21 to 24. Are there scientific or statistical reasons? 4. In result section, Age and sex patterns; Could you describe the reason why "crude annual incidence rates decreased significantly over the study period only for females? (in discussion section). 5. In result section, Age and sex patterns; Could you describe the reason why "crude incidence rates decreased significantly for 16 to 20 years old and 21 to 24 years old (in discussion section). 6. In result section, Deprivation; Please describe the discussion about "annual incidence rates significantly decreased across the study period for individuals from the most deprived areas, by half for the most deprived group. 7. In result section, Deprivation; Please describe the discussion about "the most significant decrease for BN. Rates for EDNOS fluctuated but overall there was a significant decrease. There was no significant change for AN". The differences among sub-types would help readers to understand the trends reported in this study (not only about overall EDs).
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REVIEWER	KariAnne Vrabel Research Institute of Modum Bad
REVIEW RETURNED	06-Mar-2019

GENERAL COMMENTS	<p>The current paper describes the epidemiology in eating disorders in primary care in children and young people. The authors note that examination of current temporal trends and clinical management patterns of eating disorders in primary care is lacking. The authors' point is well taken that research is warranted to examine incidence of eating disorder diagnoses in primary care. Unfortunately the manuscript suffers from a number of limitations:</p> <ol style="list-style-type: none"> 1) The need for investigating how deprivation impact presentation could be better justified. Currently only one study is included, that explored this question, This study investigated the influence of school on whether girls develop eating disorders. Is there other research that could be drawn on here? The only place I can find a justification of this scope is in the end of the discussion part where the author state "Although it is well known clinically that EDs tend to manifest in young females from more wealthy backgrounds.....". I find this sentence rather speculative and if stated it should be accompanied by more references. Moreover, in the method, the authors describe that deprivation quintiles were derived from the English Index of Multiple Deprivation 2010, and in the result
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	<p>section the authors report on “least” and “most” deprived area. However, this information is too scarce for a reader that is not familiar with this register. What are the criteria’s for being from the “least” and “most” deprived area? It would be nice to have some information on this.</p> <p>In addition, a strong rationale is not provided for including associated psychotropic prescriptions, referrals to secondary care, outpatient attendances and inpatient admissions. As a result, the study reads as though many measures and reports were included just to see what happens without having a specific rationale for including them or a priori hypotheses. To name a few examples, what is hypothesized regarding psychotropic prescriptions, impact of referrals to secondary care, etc?</p> <p>2) In the method section the authors describe that the basis for their analysis was “CPRD’s list.... of patients with data of an acceptable standard”. What does an acceptable standard mean? It is frustrating not to know how much of the data material that is dropped-out due to a non-acceptable standard since this potentially could hamper the representativeness.</p> <p>3) The comprehensive nature of the information on clinical diagnoses recorded in the GPRD is as far as I understand that there are the GPs that set the diagnoses. I miss a discussion whether the diagnoses are valid. Given the nature of GPRD, it seems that it is impossible to systematically ensure that all diagnoses meet with the DSM-IV or ICD-10 criteria for ED. Are there none quality control of the information given in the records? E.g, could it be possible to evaluate some percent of the data material on weight and height and body mass index (BMI) at the time of diagnosis? This could increase the validity of the ED diagnosis.</p> <p>4) The discussion part needs extensive revision. A whole page is used to summarise the results. This is too much. The summary of the results need to be succinct and should be described in one paragraph. There is a need for a comprehensive discussion of why this study find that the incidence of ED diagnoses in primary care decreased between 2004 and 2014? And why for BN and for those aged 16 to 24 years? Is it a true decrease in the number of participants developing ED or are there any other reasons.</p> <p>6) In the discussion of limitations and strengths I miss a discussion of what the limitations means. It is e.g. stated as limitations that 1) “Deprivation data based on the patients LSOA was not available in Wales, Scotland or Northern Ireland”, 2) there were “poor recording of some data.....specialty code for referrals where 40.0% of the data was not entered”. In what way does this hamper this study and how have the authors accounted for this limitation?</p> <p>Additional minor points include:</p> <p>1) It is a bit confusing that the number of the lines end with 60 at page 3 and start again with 1 at page 4. It should be consecutively throughout the whole document.</p> <p>2) Do not start a sentence with a numeral. This accounts for several sentences in the manuscript: Include “A total of” in the start of line 30, 31, 37, 47, 8, 35</p>
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	<p>3) Spell out the GP first time, line 14</p> <p>4) In line 55, write up ED diagnoses not eating diagnoses</p> <p>5) In line 44 the authors “psychotropic prescriptions has increased between 2004 and 2013”. Should this be 2014? Seems strange that the time span has changed from 2004-2014 to 2004-2013.</p> <p>6) Remove the s after 18 in line 18.</p> <p>7) In Figure 1, Flow diagram the numbers do not add up. A total of 4775 are identified as a case with an ED. When adding up AN, BN and EDNOS below the total number is 5562.</p>
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REVIEWER	Catherine Welch University of Leicester
REVIEW RETURNED	22-Mar-2019

GENERAL COMMENTS	<p>This paper describes the change in incidence and prevalence of eating disorders in children. They extract English patients from the primary care database CPRD. Generally, this is a good paper, but the results are poorly presented, which makes them difficult to read and understand.</p> <p>Major comments:</p> <ol style="list-style-type: none"> 1. You appear to have reported all of the findings in the results text, including CIs and n. I recommend that you put all this information into tables and figures and then discuss what you find in the text. For example, you can add the crude incidence to table 1 and crude prevalence in supplementary table 1. Also, there is no need to put n in the text. It is meaningless as it is, just report the percentage or rate because they are more meaningful. 2. PYAR is not a common abbreviation, and I think repeating PYAR in the results contributes to making it difficult to read. I suggest using “per 100,000 person years” to help your results section read better. 3. In the Methods section, I suggest you do not mention the different files which constitute CPRD, especially not the name of the file. It would be difficult for someone who doesn't analysis CPRD to understand what this means. I recommend discussing what data is available in CPRD. 4. The tables and figures should report enough information so the reader does not need to refer to the text to understand them. In the tables, please could you expand the titles to say you used Poisson regression to obtain the adjusted incident rate ratio? Also add total number of patients in the study (somewhere) and report n (%) in the second column. If you use any abbreviations, put a description in the footnote. E.g. ED: eating disorder <p>Minor comments:</p> <ol style="list-style-type: none"> 1. In the data source section, please explain you are using HES data linked with NCRAS and describe HES. 2. Please add a reference for the first sentence of the data source section. 3. In the Study population and settings, please explain what CRPD's quality standard is. Could you also add a reference? 4. In the case definition section, please describe what “atypical AN” and “atypical BN” are.
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	<p>5. When was age recorded (e.g. when eating disorder was diagnosed)?</p> <p>6. I suggest changing supplementary tables 2 and 3 to figures.</p> <p>7. Consider putting 95% CI on the figures so you do not have to report them all in the text.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

This interesting and timely study is an epidemiological examination of eating disorder management trends of youth 11-24 years of age. Using a large electronic database of diagnostic, treatment, and referral information in UK primary care practices, the authors present estimated incidence of eating disorders as well as treatment (i.e., prescription, outpatient, and inpatient) patterns.

Overall, this is a well-written and appropriately conducted manuscript. Furthermore, the implications are well thought out and helpful from research and clinical perspectives. However, there are a few issues that should be addressed to improve the manuscript.

Thank you for taking the time to review our manuscript we very much appreciate it.

1. Please provide more detail about how deprivation is operationalized.

For the following comments, this reviewer acknowledges that since data were collected between 2004 and 2014, these conventions may not have yet been applicable.

Thank you, we have added the following to the manuscript on p5, para.3:

The index is based on seven key indicators of deprivation: income, employment, health and disability, education skills and training, barriers to housing and services, living environment, and crime. These are combined and weighted appropriately to produce an overall IMD score¹⁶. This score is divided into 5 equal groups to create the IMD quintiles 1 (least deprived) to 5 (most deprived).

2. Binge-eating disorder is more common in youth than anorexia nervosa and bulimia nervosa. Yet, binge-eating disorder (and subthreshold binge-eating behavior) is not mentioned in the manuscript. Please acknowledge binge eating and discuss how the symptoms are accounted for in this study (it seems that these behaviors are subsumed in EDNOS).

Thank you for the suggestion, we have altered the text to reflect this, please see p4, para.3:

We included atypical AN and atypical BN in the category EDNOS, in addition to other non-specified EDs, such as binge-eating disorder (BED)⁹..... BED is now a formally recognised eating disorder under the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) released in 2013 and

therefore after the remit of this analysis. Further, EDNOS is now referred to as Other Specified Feeding or Eating Disorder (OSFED) in DSM-5.

3. EDNOS is now referred to in OSFED in DSM-5. While these data are based on ICD coding and largely before OSFED was formally introduced, it bears acknowledgement.

Thank you, this has now been acknowledged on p4, para.3:

Further, EDNOS is now referred to as Other Specified Feeding or Eating Disorder (OSFED) in DSM-5.

Reviewer: 2

This manuscript addresses an important issue about EDs and it was explored by analyzing valuable data. Please add some explorations to help reader's understanding of this datalink study.

Thank you for taking the time to review our manuscript, we really appreciate it.

1. In introduction section; Please introduce the information about prevalence of EDs particularly in U.K.. It will help readers to understand the importance of this study.

Thank you for this suggestion. This has been added to the introduction on p3, para.1:

The Mental Health of Children and Young People in England Survey 2017, estimated that 0.4% of 5-19 year olds had an eating disorder⁵ with some sources quoting an overall population figure at 1.25 million people affected⁶.

2. In method section; Please state the reason why you defined the criteria from 11 to 24. Are there any reason you used 24 years old as an upper limit?

Thank you. The onset of eating disorders is most common in adolescence. There is a current discussion in the area of mental health based on life circumstances, neuroscience and service provision that young people should be defined up to the age of 25 years so we limited our cohort to those aged 24 years. Services are currently being developed that cover this age group. In the UK, individuals are now considered young people up to the age of 25.

I have amended the transcript, please see p4, para.1:

The onset of EDs is most common in adolescence⁹ and thus the basis of the age profile of the study population.

3. In method section, Age and sex; Please show the reason why you categorized age group 11 to15, 16 to 20, 21 to 24. Are there scientific or statistical reasons?

Thank you. The reason we categorized as categorized age group 11 to 15, 16 to 20, 21 to 24 was for clinical reasons. We have clarified this on p5, para.2:

Age was categorised by age groups 11 to 15 years, 16 to 20 years and 21 to 24 years or under 18 (11-17) vs over 18 (18-24) years for selected analyses. This was to reflect differences in ED service provision around the age of transition from child and adolescent services to adult services.

There were no statistical reasons behind this decision

4. In result section, Age and sex patterns; Could you describe the reason why “crude annual incidence rates decreased significantly over the study period only for females? (in discussion section).

Thank you for the suggestion, the following has been added to the discussion (p10, para, 4):

The numbers of males diagnosed with an ED were too small, particularly for BN which witnessed the greatest decrease for females, to demonstrate any significant change in rates over time.

5. In result section, Age and sex patterns; Could you describe the reason why “crude incidence rates decreased significantly for 16 to 20 years old and 21 to 24 years old (in discussion section).

Thank you for the suggestion, we believe we already discuss why rates in diagnoses might have decreased and give various suggestions, such as shifts in Western culture, changes in coding behaviours, for instance on p11, para. 4, we state that:

Smink et al.⁷ suggest that BN is a Western world phenomena based on a pressure to be thin whereas AN is less culture bound existing across time, cultures and even species. Based on this theory, they suggest that the decrease in BN could be attributed to the normalisation of being overweight, thereby reducing the pressure to be thin and leading to a decrease in BN.

Further on p12, para.1, we state that:

Previous studies^{17 18} have attributed a decrease in diagnoses for common mental health disorders in primary care to a change in the coding behaviour of GPs to code for symptoms (in order to avoid labelling or strategically in relation to the Quality Outcomes Framework). ED symptom codes are less specific than symptom codes for conditions such as depression or anxiety and when explored further, the coding behaviour of GPs seen in studies for depression¹⁸ and anxiety¹⁷ was not observed for EDs. EDs can be problematic conditions for doctors to identify, refer and manage for several reasons. Currin et al.²¹ found that GPs diagnosed less than 70% of cases with clear ED presentation. House et al.²² found that GPs were less likely to diagnose if there were no specialist services in the area. A higher availability, and continued funding of child and adolescent mental health services (CAMHS) and lower thresholds for diagnosis in England, could explain why ED diagnosis rates for 11 to 15 year olds have remained stable over the study period, yet decreased for 16-24 year olds. NICE 2004 guidelines recommend that care is shared between primary and specialist care with a clear (preferably written) agreement of roles²³. It is argued that GPs are sometimes reluctant to diagnose EDs due to this associated burden of care and poor access to specialist services²⁴. If GPs are becoming more reluctant to diagnose EDs, then this could affect individuals from the most deprived areas the greatest since historically they suffer from an inequity of access to healthcare services²⁷. They may be less persistent in obtaining a diagnosis in order to access the services they need: a

phenomena named as the inverse care law²⁸. By diagnosing individuals later in the course of development of an ED, patients are put at greater risk of serious medical complications and increasing the likelihood of treatment resistance²⁵.

However we have added a suggestion for why rates have decreased for 16-24 year olds, but not 11-15 year olds. Please see p12, para.1:

Availability of child and adolescent mental health services (CAMHS) and lower thresholds for acceptance of referrals than in adult services for EDs, could explain why ED diagnosis rates for 11 to 15 year olds have remained stable over the study period, yet decreased for 16-24 year olds.

6. In result section, Deprivation; Please describe the discussion about “annual incidence rates significantly decreased across the study period for individuals from the most deprived areas, by half for the most deprived group.

Thank you for this helpful suggestion. We have added the following to the discussion on p12, para.1:

It is argued that GPs are sometimes reluctant to diagnose EDs due to this associated burden of care and poor access to specialist services²⁴. This type of impact on recording of diagnoses and labelling may impact on those from the most deprived areas disproportionately since historically they experience inequity of access to healthcare services²⁷. They may be less persistent in obtaining a diagnosis in order to access the services they need: a phenomena named ‘the inverse care law’²⁸.

7. In result section, Deprivation; Please describe the discussion about “the most significant decrease for BN. Rates for EDNOS fluctuated but overall there was a significant decrease. There was no significant change for AN”. The differences among sub-types would help readers to understand the trends reported in this study (not only about overall EDs).

Thank you for the suggestion, we have discussed the differences between subtypes in the discussion on p11, para.4:

Similar to previous studies, we found that rates of recorded AN have remained stable over time^{7 9} and EDNOS was the most commonly recorded ED⁹. We found that recorded rates of BN had decreased since 2009 in keeping with a Dutch study⁷. Micali et al.⁹ found that rates remained stable between 2000 and 2009. Smink et al.⁷ suggest that BN is a Western world phenomena based on a pressure to be thin whereas AN is less culture bound existing across time, cultures and even species. Based on this theory, they suggest that the decrease in BN could be attributed to the normalisation of being overweight, thereby reducing the pressure to be thin and leading to a decrease in BN. However this concept is contested with the rise in social media use suggested as increasing concerns about weight and body image leading to eating concerns and disordered eating^{19 20}.

However we have now added the following to account for EDNOS (p11, para.4):

The fluctuation of EDNOS rates found in this study could reflect the combination of the change in rates for BN and the stability of AN, since diagnoses in this category border both BN and AN.

Reviewer 3

The current paper describes the epidemiology in eating disorders in primary care in children and young people. The authors note that examination of current temporal trends and clinical management patterns of eating disorders in primary care is lacking. The authors' point is well taken that research is warranted to examine incidence of eating disorder diagnoses in primary care.

Thank you for your detailed comments, we really appreciate the time you have taken to review our manuscript.

Unfortunately the manuscript suffers from a number of limitations:

1) The need for investigating how deprivation impact presentation could be better justified. Currently only one study is included, that explored this question, This study investigated the influence of school on whether girls develop eating disorders. Is there other research that could be drawn on here? The only place I can find a justification of this scope is in the end of the discussion part where the author state "Although it is well known clinically that EDs tend to manifest in young females from more wealthy backgrounds....". I find this sentence rather speculative and if stated it should be accompanied by more references. Moreover, in the method, the authors describe that deprivation quintiles were derived from the English Index of Multiple Deprivation 2010, and in the result section the authors report on "least" and "most" deprived area. However, this information is to scarce for a reader that is not familiar with this register. What are the criteria's for being from the "least" and "most" deprived area? It would be nice to have some information on this. In addition, a strong rationale is not provided for including associated psychotropic prescriptions, referrals to secondary care, outpatient attendances and inpatient admissions. As a result, the study reads as though many measures and reports were included just to see what happens without having a specific rationale for including them or a priori hypotheses. To name a few examples, what is hypothesized regarding psychotropic prescriptions, impact of referrals to secondary care, etc?

Thank you for these suggestions. We have addressed your comments as follows:

We have now described our measure of deprivation better by adding the following to p5, para.3:

The index is based on seven key indicators of deprivation: income, employment, health and disability, education skills and training, barriers to housing and services, living environment, and crime. These are combined and weighted appropriately to produce an overall IMD score¹⁶. This score is divided into 5 equal groups to create the IMD quintiles 1 (least deprived) to 5 (most deprived).

We hope this better explains the comparison of least and most deprived quintiles. We present all quintiles in the tables 1 and 2

As we describe on p3, para. 1:

While Bould et al. found that females with higher educated parents had a higher risk of EDs⁶, few whole population level studies have explored how deprivation impacts presentation.

However we appreciate your thoughts in regards to the sentence “Although it is well known clinically that EDs tend to manifest in young females from more wealthy backgrounds....” So we have deleted this part of the sentence.

In regards to the rationale for including associated psychotropic prescriptions, referrals to secondary care, outpatient attendances and inpatient admissions; we did this in a large scale epidemiological perspective to explore trajectories of young people diagnosed with eating disorders in primary care. We say in p3, para.1

Most research on individuals diagnosed with EDs is based on psychiatric case registers, surveys or in secondary care data sets¹⁰. Few studies have explored the care received by ED patients in primary care, despite it often being the first point of contact and the gateway to secondary and/or specialist services¹¹. It is important that patients are triaged, referred, signposted and managed appropriately in primary care.

2) In the method section the authors describe that the basis for their analysis was “CPRD’s list.... of patients with data of an acceptable standard”. What does an acceptable standard mean? It is frustrated not to know how much of the data material that is dropped-out due to a non acceptable standard since this potentially could hamper the representativeness.

Thank you for highlighting this, we have added the following to the text to p4, para.2

The basis for the analysis was CPRD’s (anonymised) list of patients with data of an acceptable standard for research purposes aged 11 to 24 years at any point during the study period. Acceptable standard means that CPRD’s checks for data completeness and validity were satisfied, this includes poor data recording and non-continuous follow up¹².

This is standard practice for all CPRD based studies and published literature and recommended by CPRD when requesting data before receiving it (we therefore do not have the number dropped). Please see <https://academic.oup.com/ije/article/44/3/827/632531>.

In keeping with other studies this produces a representative sample. Please see Micali et al. <https://bmjopen.bmj.com/content/bmjopen/3/5/e002646.full.pdf> and Newlove-Delgado et al. <https://link.springer.com/content/pdf/10.1007%2Fs12402-019-00288-6.pdf>

3) The comprehensive nature of the information on clinical diagnoses recorded in the GPRD is as far as I understand that there are the GPs that set the diagnoses. I miss a discussion whether the diagnoses are valid. Given the nature of GPRD, it seems that it is impossible to systematically ensure that all diagnoses meet with the DSM-IV or ICD-10 criteria for ED. Are there none quality control of the information given in the records? E.g, could it be possible to evaluate some percent of the data material on weight and height and body mass index (BMI) at the time of diagnosis? This could increase the validity of the ED diagnosis.

Thank you for this suggestion.

We base our codes on validated lists from a previous study that did use weight, height and BMI to validate 10% of the records. We have added some more information to p4, para.3 to explain this further:

Previously validated code lists⁹ that used weight, height and body mass index (BMI) to validate 10% of records, were updated to identify EDs.

4) The discussion part needs extensively revision. A whole page is used to summarise the results. This is too much. The summary of the results need to be succinct and should be described in one paragraph. There is a need for a comprehensive discussion of why this study find that the incidence of ED diagnoses in primary care decreased between 2004 and 2014? And why for BN and for those aged 16 to 24 years? Is it a true decrease in the number of participants developing ED or are there any other reasons.

Thank you for this suggestion. The results we present are novel and in a non specialist setting with implications for both types of care and so need to be understood by a wide audience, therefore we believe the length of our summary of the results is challenging to edit. We also provide as requested a lengthy explanation of changes in rates e.g. p11, para. 4, we state that:

Smink et al.⁷ suggest that BN is a Western world phenomena based on a pressure to be thin whereas AN is less culture bound existing across time, cultures and even species. Based on this theory, they suggest that the decrease in BN could be attributed to the normalisation of being overweight, thereby reducing the pressure to be thin and leading to a decrease in BN.

With further explanation on p12, para.1:

Previous studies^{17 18} have attributed a decrease in diagnoses for common mental health disorders in primary care to a change in the coding behaviour of GPs to code for symptoms (in order to avoid labelling or strategically in relation to the Quality Outcomes Framework). ED symptom codes are less specific than symptom codes for conditions such as depression or anxiety and when explored further, the coding behaviour of GPs seen in studies for depression¹⁸ and anxiety¹⁷ was not observed for EDs. EDs can be problematic conditions for doctors to identify, refer and manage for several reasons. Currin et al.²¹ found that GPs diagnosed less than 70% of cases with clear ED presentation. House et al.²² found that GPs were less likely to diagnose if there were no specialist services in the area. A higher availability, and continued funding of child and adolescent mental health services (CAMHS) and lower thresholds for diagnosis in England, could explain why ED diagnosis rates for 11 to 15 year olds have remained stable over the study period, yet decreased for 16-24 year olds. NICE 2004 guidelines recommend that care is shared between primary and specialist care with a clear (preferably written) agreement of roles²³. It is argued that GPs are sometimes reluctant to diagnose EDs due to this associated burden of care and poor access to specialist services²⁴. If GPs are becoming more reluctant to diagnose EDs, then this could affect individuals from the most deprived areas the greatest since historically they suffer from an inequity of access to healthcare services²⁷. They may be less persistent in obtaining a diagnosis in order to access the services they need: a phenomena named as the inverse care law²⁸. By diagnosing individuals later in the course of development of an ED, patients are put at greater risk of serious medical complications and increasing the likelihood of treatment resistance²⁵.

However we have added a suggestion for why rates have decreased for 16-24 year olds, but not 11-15 year olds. Please see p12, para.1:

Availability of child and adolescent mental health services (CAMHS) and lower thresholds for acceptance of referrals than in adult services for EDs, could explain why ED diagnosis rates for 11 to 15 year olds have remained stable over the study period, yet decreased for 16-24 year olds.

5) In the discussion of limitations and strengths I miss a discussion of what the limitations means. It is e.g. stated as limitations that 1) "Deprivation data based on the patients LSOA was not available in Wales, Scotland or Northern Ireland", 2) there were "poor recording of some data.....specialty code for referrals where 40.0% of the data was not entered". In what way does this hamper this study and how have the authors accounted for this limitation?

Thank you for the suggestions. We discuss the implications for the loss of deprivation data (i.e. cuts the sample by 22%), but we also explain why we do this and the benefits to the study (please see p12, para.4):

These data accounted for 22% of the total study population. This approach was different to Carr et al.¹¹ who used IMD data according to the postcode of the general practice, which had the benefit of availability across all nations. However we felt the accuracy of linking to the LSOA of the individual's home address was greater than using the general practice's address. Furthermore, since IMD is measured differently across nations, it is not considered comparable³⁰.

In regards to the poor recording on data, we have added the following to p13, para.1:

Another limitation was the poor recording of some data, particularly the specialty code for referrals where 40.0% of the data was not entered; this impedes the accuracy of the results reflecting the age appropriateness of GP referrals for EDs. Secondly, 97.3% of outpatient records had the diagnosis code 'Unknown and unspecified causes of morbidity'; this meant we could not infer whether outpatient attendances were for EDs.

Additional minor points include:

1) It is a bit confusing that the number of the lines end with 60 at page 3 and start again with 1 at page 4. It should be consecutively throughout the whole document.

Thank you. We are sorry, but it is BMJ open that provide the manuscript in that format for reviewers.

2) Do not start a sentence with a numeral. This accounts for several sentences in the manuscript: Include "A total of" in the start of line 30, 31, 37, 47, 8, 35

Thank you, we have amended as suggested.

3) Spell out the GP first time, line 14

Thank you, we have added general practitioner.

4) In line 55, write up ED diagnoses not eating diagnoses

Thank you for spotting this, we have amended.

5) In line 44 the authors "psychotropic prescriptions has increased between 2004 and 2013". Should this be 2014? Seems strange that the time span has changed from 2004-2014 to 2004-2013.

Thank you. There was only a significant increase between 2004 and 2013, the decrease was not significant for 2014.

6) Remove the s after 18 in line 18.

Thank you – removed.

7) In Figure 1, Flow diagram the numbers do not add up. A total of 4775 are identified as a case with an ED. When adding up AN, BN and EDNOS below the total number is 5562.

Thank you for highlighting this, we should explain further to make it clearer for the reader. An individual can have more than one incident subtype diagnosis (e.g. incident BN and AN over the study period). Eating disorder diagnoses can change over time and we wanted to capture this. When we report all eating disorders we do not double count, so the total number is reduced.

We have added an explanation to fig.1 study flow diagram:

*individuals can have more than one incident subtype diagnosis (e.g. incident BN and incident AN), therefore the total of incident AN, BN and EDNOS is different to the total for all ED diagnoses

Reviewer: 4

This paper describes the change in incidence and prevalence of eating disorders in children. They extract English patients from the primary care database CPRD. Generally, this is a good paper, but the results are poorly presented, which makes them difficult to read and understand.

We thank you for taking the time to review our manuscript, we really appreciate it.

Major comments:

1. You appear to have reported all of the findings in the results text, including CIs and n. I recommend that you put all this information into tables and figures and then discuss what you find in the text. For example, you can add the crude incidence to table 1 and crude prevalence in supplementary table 1. Also, there is no need to put n in the text. It is meaningless as it is, just report the percentage or rate because they are more meaningful.

Thank you for this suggestion. We agree it is often best to transfer to tables however we are limited here in the number of tables we can include by journal guidelines. In our discussions it was the crude rates that seemed most appropriate for the text. We are happy to be guided by the editor if they would like us to add more tables.

We included the numbers to give the reader an idea of scale since in previous publications this has been requested. We are happy to remove if that is preferred.

2. PYAR is not a common abbreviation, and I think repeating PYAR in the results contributes to making it difficult to read. I suggest using “per 100,000 person years” to help your results section read better.

Thank you for the suggestion, we have changed PYAR to person years throughout the paper.

3. In the Methods section, I suggest you do not mention the different files which constitute CPRD, especially not the name of the file. It would be difficult for someone who doesn't analysis CPRD to understand what this means. I recommend discussing what data is available in CPRD.

Thank you for your suggestion, we have removed references to specific files. Please see p4, line 39:

"CPRD includes a consultation and staff file where 'other' and 'admin' codes can be identified."
Changed to "CPRD categorises some events as 'other' and 'admin'."

AND

Please see p5, line 30:

"The CPRD referral file contains referral details to secondary care" changed to "CPRD contains referral details to secondary care"

We discuss what data is available in CPRD on p3, para.4:

Data includes anonymised patient demographic information, medical diagnoses, prescriptions, referrals to secondary care.

4. The tables and figures should report enough information so the reader does not need to refer to the text to understand them. In the tables, please could you expand the titles to say you used Poisson regression to obtain the adjusted incident rate ratio? Also add total number of patients in the study (somewhere) and report n (%) in the second column. If you use any abbreviations, put a description in the footnote. E.g. ED: eating disorder

Thank you for the suggestion. We have amended the main tables and the supplementary tables as you suggest. We have added n (%) to table 1 and supplementary table 1. The other tables are quite busy and it clutters them, however we would still be happy to change them if you think this is necessary.

Minor comments:

1. In the data source section, please explain you are using HES data linked with NCRAS and describe HES.

Thank you for the suggestion, the following has been added to p3, para.4:

A total of 75% of English practices in CPRD are linked to hospital episode statistics (HES) data¹² which includes both inpatient and outpatient records.

2. Please add a reference for the first sentence of the data source section.

Thank you- reference added

3. In the Study population and settings, please explain what CRPD's quality standard is. Could you also add a reference?

Thank you, the following has been added to p4, para.2:

Acceptable standard means that CPRD's checks for data completeness and validity were satisfied, this includes poor data recording and non-continuous follow up¹².

4. In the case definition section, please describe what "atypical AN" and "atypical BN" are.

Thank you, the following has been added to p4, para.3:

Atypical AN and atypical BN have commonalities with AN and BN, but they do not meet the threshold for diagnosis.

5. When was age recorded (e.g. when eating disorder was diagnosed)?

Thank you for highlighting this. We have added to p5, para 2:

Age was recorded at the time of diagnosis in primary care

6. I suggest changing supplementary tables 2 and 3 to figures.

Thank you for the suggestion, since these are supplementary we felt the tables gave more information but we are happy to add figures – please see supplementary figures 2 and 3

7. Consider putting 95% CI on the figures so you do not have to report them all in the text.

Thank you for this suggestion unfortunately the number of figures vs. tables would make this an inconsistent approach and it makes the limits of the CI difficult to see. We feel these limits allow for a more accurate interpretation and understanding by the reader, although we accept it allows visualisation of differences.

VERSION 2 – REVIEW

REVIEWER	Elvin Thomaseo Burton University of Tennessee Health Science Center
REVIEW RETURNED	29-Apr-2019

GENERAL COMMENTS	The authors have done a wonderful job of addressing reviewer comments and incorporating new language in a coherent fashion. The document is well written and the scientific contributions clear.
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REVIEWER	KariAnne Vrabel Research Institute of Modum Bad Norway
REVIEW RETURNED	08-May-2019

GENERAL COMMENTS	The before mentioned points has been taken into consideration regarding the revision of the manuscript, making this suitable for publication.
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REVIEWER	Catherine Welch University of Leicester UK
REVIEW RETURNED	10-May-2019

GENERAL COMMENTS	I am happy with the changes made to the paper. However, the results section is still difficult to understand because many findings are reported in the results instead of tables or figures. If you are limited by the number of tables in the manuscript you could either add them to existing tables (most of the crude incident rates can be added as an extra column in existing tables) or add new tables to supplementary material 2. I strongly recommend updating the manuscript in this way.
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

The authors have done a wonderful job of addressing reviewer comments and incorporating new language in a coherent fashion. The document is well written and the scientific contributions clear.

Thank you for the kind words, we are pleased you are happy with our changes.

Reviewer: 3

The before mentioned points has been taken into consideration regarding the revision of the manuscript, making this suitable for publication.

Thank you we are glad you are happy with our changes and you think the paper is suitable for publication.

Reviewer: 4

I am happy with the changes made to the paper. However, the results section is still difficult to understand because many findings are reported in the results instead of tables or figures. If you are limited by the number of tables in the manuscript you could either add them to existing tables (most of the crude incident rates can be added as an extra column in existing tables) or add new tables to supplementary material 2. I strongly recommend updating the manuscript in this way.

Thank you for re-reviewing our manuscript and for your helpful suggestions regarding the results section. We have amended the results section considerably to reflect this. Please see the following changes:

Table 1. p18 – crude incidence added. All numbers included in text that are now in the table have been removed. Text changed:

p6 para. 5 -The crude incidence rate decreased significantly between 2004 and 2014 (see Table 1).

p7 para. 1 - Females were nearly 11 times more likely to have an incident diagnosis for an ED than males (see Table 1).

P7 para. 2 - Crude incidence rates were significantly higher for 16 to 20 year olds across the study period than for 11 to 15 year olds and 21 to 24 year olds (see Table 1 for rates and [adjusted] IRR).

P7 para. 3- Crude incidence rates were significantly higher for individuals from the least deprived areas across the study period. Crude incidence rates and adjusted rate ratios are shown in Table 1.

Supplementary table 2 – new table with eating disorder symptom results added. All numbers included in text that are now in the table have been removed. Text changed:

P6 para. 6- There was similarly a significant decrease in recording of ED symptom codes between 2004 and 2014 (see Supplementary Material 2, Supplementary Table 2).

Table 3. p19 – new table added with psychotropic prescription results. All numbers included in text that are now in the table have been removed. Text changed to:

p7 para. 6 - Females and older age groups were more likely to be prescribed antidepressants. Older age groups were more likely to be prescribed anxiolytic/hypnotics, but there was no significant difference between sexes.

p7 para. 6- By medication type, there was an increase in antidepressant prescriptions and antipsychotic prescriptions. However, there was no significant change across the study period for anxiolytics/hypnotic prescriptions. See Table 3 for a breakdown of numbers and proportions.

p8 para. 1 - Individuals diagnosed with BN were the most likely to have an associated antidepressant prescription. There was no difference by ED sub-type for associated anxiolytics/hypnotic prescriptions, nor antipsychotic prescriptions (see Table 3).