PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Estimating the prevalence of chronic conditions in children who die in England, Scotland and Wales: a data linkage cohort study
AUTHORS	Hardelid, Pia; Dattani, Nirupa; Gilbert, Ruth

VERSION 1 - REVIEW

REVIEWER	Dr Lorna Fraser University of York, UK
REVIEW RETURNED	25-Apr-2014

GENERAL COMMENTS	This is an interesting paper which highlights the benefits the linkage of routine datasets to improve ascertainment of chronic health conditions in children. Minor comments: Page 5 line 16: the sentence ending address child deaths needs to be reworded and clearer. Page 5 Line 21 did you use the longitudinal hospital data and death certificate data to create your definition of chronic disease, it is confusing. Page 5 line 51. non-exclusive. Does this mean that one diagnosis may be in more than 1 group? If so why was this necessary? Figure 1 is too small in its current format Page 12 line 29 Were there non significant trends in Wales and Scotland that did not reach statistical significance due to small numbers? If not why would England be different, ? 20 diagnosis fields compared to 6? This needs to be discussed in the discussion section. Page 13 Line 13. What differing admission thresholds for age, wouldn't this be more likely to result in increased admissions in younger children? It is not that more complications are likely in children who have had a chronic disease for many years?

REVIEWER	Eyal Cohen Hospital for Sick Children
REVIEW RETURNED	07-May-2014

GENERAL COMMENTS	Nice study that replicates other findings that chronic conditions, particularly neurodevelopmental conditions and those that are multi system are accounting for an increasing proportion of childhood death. The manuscript is very clear and well written. My one major concern is the use of a de novo system of identifying chronic conditions in

	childhood. The authors mention that other definitions 'focus on comorbidities to healthcare costs or to death' and cite papers using Feudtner's complex chronic conditions. There are other systems (E.g. AHRQ's chronic condition index) that do not use this conceptual framework. In order to facilitate comparisons with existing (and future) literature, I would encourage the authors to use (at least in supplement) these or other existing algorithms.

REVIEWER	Chris Feudtner The Children's Hospital of Philadelphia, United States
REVIEW RETURNED	13-May-2014

GENERAL COMMENTS	The 3 "no" answers listed above can all be readily addressed. 1) The authors, as detailed below, need to clarify the purpose they envision for monitoring the population of children for chronic conditions associated with death, and how their operational definition of chronic conditions serves this purpose. 2) The authors need to not overstate their conclusion about their method obviating the need for primary data collection (this may be true, but this study does not demonstrate this point). The prevalence of chronic conditions in children who die in England, Scotland and Wales SYNOPSIS: The authors conducted a retrospective population based cohort study of all child (<19 years old) deaths in England, Scotland, and Wales from 2001 to 2010, focusing on deaths attributed to chronic conditions or occurring in children with chronic conditions. For this study, the authors devised their own classification scheme of ICD-10 codes found on death certificates as well as hospital discharge records. Using just the death certificate information, the study found that 65% of deaths were attributed to a chronic condition; if expanded to include diagnoses from the hospital discharge records during the year prior to death, the percentage of child deaths of children who had a chronic condition was 71%. Younger decedents were more likely to have a chronic condition. The most common chronic conditions were neurologic/sensory. The population-based rate of child deaths of children with chronic conditions has declined over the 10 year study period, while the proportion of deaths consisting of children who had chronic conditions has remained stable. From this, the authors conclude that their methodology provides a “sensitive, population-based method for examining chronic conditions in children who die without the need for primary data collection.” GENERAL COMMENTS: The authors are to be commended on performing a rigorous population-level assessment of child deaths. The comments below are meant to clarify the arguments made by the authors. 1. Deaths associated with chronic conditions — Opportunity for preventing death versus providing palliative care: The authors mention these 2 potential ways that the data might guide policy (Page 4, Line 33 forward). This 2 purpose are very important and will recur in the comments below. 2. Death attributed to a chronic condition versus coincidental

	association with chronic conditions: The authors make a point about their focus on just performing an association study (5, L9 forward). This does limit the inferences that can be gained from this study, since some proportion of the cases in this study the deaths occurred independent of the identified chronic condition, so that targeting that chronic conditions would neither prevent death nor enhance palliative care. The authors need to clarify early in the paper the advantages and disadvantages of this broad definition for the analysis they set out to perform. 3. The "sensitivity" of the definition of chronic conditions offered by the authors (P5, L23 forward): This definition is a broader, less restrictive definition than used in other studies, but the term "sensitivity" has a very specific meaning in epidemiology, and is being misused here. To use it appropriately, the authors would need to have some external gold standard definition of chronic conditions, or some verified set of cases with chronic conditions, and determine the test characteristics of their operationalized definition compared to other operationalized definitions of chronic conditions. 4. The broadness of the definition of chronic conditions used by the authors: Even classification definition is a tool that should serve a purpose. What is the purpose of grouping together diseases with high risks of mortality and major morbidity (such as E70-72 disorders of amino acid, which can lead to accidental death if mismanaged, or Q23.4 hypo plastic left heart, which requires extensive surgical and medical management) with skin disorders (which in the authors scheme includes L40 psoriasis, L90 lichen sclerosis, and many other examples in their list)? Going back to the 2 items that the authors outlined (item 2 in this list), the heterogeneity of these conditions makes policy decisions about either quality of care concerns or need for palliative care difficult. Again, greater clarity about the goal of using this classification system is essential. Similarly, in the discussion (P15, L51), how will the inclusion of patients with outpatient only diagnoses of asthma or depression help with thinking about palliative care? (Answer: probably not at all). Quality of care? Yes, if the patients died of asthma or suicide, i.e., causes directly related to the chronic condition. Bottom line: the authors need to clarify the value of having a very heterogenous set of diagnoses for health policy or epidemiological research. 5. Is the incremental increase (which seems to be about 5% absolute for the 1 year loopback) in the proportion of patients identified as having a chronic condition by including the hospital records important? Did the cases identified only this manner differ from the cases identified by only the death certificate data? In other words, is it worth the time and effort to do the linkage? The authors should comment on this, or examine the characteristics of the set of patients identified only via hospital records. 6. Cancer clearly is the diagnosis that does not get missed. This should be emphasized, in that it has relevance for policies based on data analyses that might not understand this ascertainment bias. The finding of the commonness of neurologic/sensory conditions maps to findings of other studies where neurologic conditions are often the leading diagnoses among patients who die or are frequently hospitalized. The authors note this in the discussion, but it

	is very important. 7. The finding about multiple chronic conditions increasing in the middle age ranges may be policy relevant, in that many studies are now focusing on the multiple-morbidities of hospitalized pediatric patients. 8. The authors conclusion to the abstract regarding the "sensitivity" of their method and the suitability of the method in lieu of primary data collection is not an outcome of the data or analysis presented in the paper. To make this claim based on data, they would need to have a comparable population-based study based on primary data collection, and they do not. They even contradict it on P16, L8, where they state that to identify expected deaths requires primary data collection. The authors should trim their sails and simply conclude that this method offers a feasible, relatively low cost means to monitor the child population for emerging trends in cause of mortality and the co-existence of chronic conditions, and conforms with findings from other studies.

VERSION 1 – AUTHOR RESPONSE

Reviewer Name Dr Lorna Fraser
Institution and Country University of York, UK
Please state any competing interests or state 'None declared': None Declared

This is an interesting paper which highlights the benefits the linkage of routine datasets to improve ascertainment of chronic health conditions in children.
Minor comments:
1.Page 5 line 16: the sentence ending address child deaths needs to be reworded and clearer.
We have now extended this paragraph to make the objectives of the paper clearer (please see responses to reviewer #3 below).

2.Page 5 Line 21 did you use the longitudinal hospital data and death certificate data to create your definition of chronic disease, it is confusing.
We agree that this sentence could be misleading, and have now amended it for clarification.

3.Page 5 line 51. non-exclusive. Does this mean that one diagnosis may be in more than 1 group? If so why was this necessary?
The non-exclusivity refers to the children, not the conditions e.g. a child can have conditions from more than one of the eight groups, for example neurological conditions and mental/behavioural conditions. We have now added another sentence in the methods section to clarify this.

4.Figure 1 is too small in its current format

We have contacted the BMJ Open Editorial Office who has let us know that the format of this Figure will be amended should the paper be accepted.

5.Page 12 line 29 Were there non-significant trends in Wales and Scotland that did not reach statistical significance due to small numbers? If not why would England be different, ? 20 diagnosis fields compared to 6? This needs to be discussed in the discussion section.

We agree with the reviewer that the lack of statistically significant trends for certain age groups in Scotland and Wales may be the result of the small number of deaths per year in these countries

resulting in large annual variation. For example, for 5-9 and 15-18 year olds in Scotland the parameter estimates from the logistic regression models indicated a decline of 4.1% and 3.6% respectively (p=0.31 and p=0.16 respectively). Similarly, for 1-4 and 10-14 year olds in Wales, the parameter estimates indicated increases of 8.8% and 10.3% respectively (p=0.20 & p=0.14 respectively). We found no evidence of trends in the other age groups.

We have now expanded the discussion section to discuss in more detail:
-small sample sizes in Scotland and Wales
-differences in the number of diagnosis codes which can be entered between England and Scotland, and
-different incentives for coding in England (through payment by results)

as possible explanations for the observed trends in the proportion of children who die with conditions from two or more chronic condition groups.

6.Page 13 Line 13. What differing admission thresholds for age, wouldn't this be more likely to result in increased admissions in younger children? It is not that more complications are likely in children who have had a chronic disease for many years?

We agree with the reviewer that this statement was not clear. We have now suggested in the discussion three reasons why the age pattern of admissions may be different among admitted children and among children who die: a) injury mortality is higher in older than in younger children b) attrition through deaths among younger children with chronic conditions and c) underascertainment of chronic conditions in older children who die. We have now also moved this paragraph to the second to last paragraph of the discussion section.

Reviewer Name Eyal Cohen
Institution and Country Hospital for Sick Children
Please state any competing interests or state ‘None declared’: None declared

Nice study that replicates other findings that chronic conditions, particularly neurodevelopmental conditions and those that are multi system are accounting for an increasing proportion of childhood death.

The manuscript is very clear and well written. My one major concern is the use of a de novo system of identifying chronic conditions in childhood. The authors mention that other definitions 'focus on comorbidities to healthcare costs or to death' and cite papers using Feudtner's complex chronic conditions. There are other systems (E.g. AHRQ's chronic condition index) that do not use this conceptual framework. In order to facilitate comparisons with existing (and future) literature, I would encourage the authors to use (at least in supplement) these or other existing algorithms.

We thank the reviewer for his positive comments. We are aware of the AHRQ classification of chronic conditions. We chose not to use this classification for two main reasons:

-it was developed for ICD-9, rather than ICD-10, and translation from one to the other is not straightforward
-the AHRQ classification of a condition as chronic does not necessitate contact with health services, whereas the main aim of our analyses was to identify children who would have had contact with health services. For example, AHRQ classifies minor congenital anomalies such as tongue tie, nail anomalies and hair anomalies as chronic (these in isolation are not likely to require follow-up). On the other hand, AHRQ classifies tuberculosis, organic anxiety syndrome or severe head injuries as not chronic, whereas according to our definition they should be.

We do agree with the reviewer that comparing our classification to that of AHRQ and also to Chris Feudtner's complex chronic conditions in children would be very informative, however we consider this should be the subject of a further paper. We have now added a sentence in the discussion pointing out the importance of this possible future work.

Reviewer Name Chris Feudtner
Institution and Country The Children's Hospital of Philadelphia, United States
Please state any competing interests or state 'None declared': None declared

A.1) The authors, as detailed below, need to clarify the purpose they envision for monitoring the population of children for chronic conditions associated with death, and how their operational definition of chronic conditions serves this purpose.

The objectives of this population-based study of chronic conditions in children who die were to:

-inform policy makers of the most prevalent chronic conditions in children who die, to indicate whether they are being seen in the health care system, and hence infer where improvements in health care might lead to improvements in life expectancy or improvements in quality of life, and
-establish a framework for identifying chronic conditions in children in routinely collected, linked health databases, based on the need for ongoing health care or follow-up.

We have now clarified these objectives in the beginning of the methods section (p5, para 2.)

A.2) The authors need to not overstate their conclusion about their method obviating the need for primary data collection (this may be true, but this study does not demonstrate this point).

We have now removed the sentence in the abstract regarding our study design obviating the need for primary data collection, since this sentence contradicts the points we make in the discussion regarding the need for case-note reviews to identify whether a death is likely to have been preventable or was expected.

SYNOPSIS: The authors conducted a retrospective population based cohort study of all child (<19 years old) deaths in England, Scotland, and Wales from 2001 to 2010, focusing on deaths attributed to chronic conditions or occurring in children with chronic conditions. For this study, the authors devised their own classification scheme of ICD-10 codes found on death certificates as well as hospital discharge records. Using just the death certificate information, the study found that 65% of deaths were attributed to a chronic condition; if expanded to include diagnoses from the hospital discharge records during the year prior to death, the percentage of child deaths of children who had a chronic condition was 71%. Younger decedents were more likely to have a chronic condition. The most common chronic conditions were neurologic/sensory. The population-based rate of child deaths of children with chronic conditions has declined over the 10 year study period, while the proportion of deaths consisting of children who had chronic conditions has remained stable. From this, the authors conclude that their methodology provides a "sensitive, population-based method for examining chronic conditions in children who die without the need for primary data collection."

GENERAL COMMENTS:
The authors are to be commended on performing a rigorous population-level assessment of child deaths. The comments below are meant to clarify the arguments made by the authors.

1. Deaths associated with chronic conditions — Opportunity for preventing death versus providing

palliative care: The authors mention these 2 potential ways that the data might guide policy (Page 4, Line 33 forward). This 2 purpose are very important and will recur in the comments below.

We deal with these two points in more detail in response to the reviewer's specific comments in points 2 and 4 below.

2. Death attributed to a chronic condition versus coincidental association with chronic conditions: The authors make a point about their focus on just performing an association study (5, L9 forward). This does limit the inferences that can be gained from this study, since some proportion of the cases in this study the deaths occurred independent of the identified chronic condition, so that targeting that chronic conditions would neither prevent death nor enhance palliative care. The authors need to clarify early in the paper the advantages and disadvantages of this broad definition for the analysis they set out to perform.

We accept the point on the need for clarity. We have now clarified the objectives of this study early in the methods section (see the answer to point A.1 above).

We argue that the cause of death may reflect the end event, not the potentially preventable factors that led to deterioration. Our approach aimed to determine the prevalence and types of underlying chronic conditions in children who died, thereby allowing inferences about which healthcare specialties are likely to be caring for these children.

We agree that analyses of administrative data do not allow differentiation between preventable or expected deaths. We have made clear in the discussion that this is an area for further research, using for example case note reviews.

We outline the advantages and disadvantages of our approach based on linked administrative health databases in the discussion where we raise the following points:

Advantages:
-population based coverage, less risk of selection bias
-we consider not just death certificates but also prior hospital admissions, which avoids underascertainment of non-cancer conditions (see answer to point 6 below).
-using standardised coding makes the study easy to replicate in other countries and means the algorithm can be used to monitor trends over time

Disadvantages:
-The linkage was limited to death certificates and hospital databases, and so we are undercounting conditions managed in primary care.
-Including many years of hospital data prior to death means that we may be overcounting some conditions which may have resolved (we have now added this as a further point in the discussion).

3. The "sensitivity" of the definition of chronic conditions offered by the authors (P5, L23 forward): This definition is a broader, less restrictive definition than used in other studies, but the term "sensitivity" has a very specific meaning in epidemiology, and is being misused here. To use it appropriately, the authors would need to have some external gold standard definition of chronic conditions, or some verified set of cases with chronic conditions, and determine the test characteristics of their operationalized definition compared to other operationalized definitions of chronic conditions.

We agree with the reviewer that the word 'sensitive' is usually referring to comparison with a gold standard. Here, we considered the standard to be data recorded on death certificates only, since these are most commonly used in national statistics and research studies. Since this could be

misinterpreted, we have now removed this word from the manuscript and reworded the relevant sentences. Instead, we emphasise that the linked data approach will overcome some of the under-recording of non-cancer conditions compared to using death certificates alone.

4. The broadness of the definition of chronic conditions used by the authors: Even classification definition is a tool that should serve a purpose. What is the purpose of grouping together diseases with high risks of mortality and major morbidity (such as E70-72 disorders of amino acid, which can lead to accidental death if mismanaged, or Q23.4 hypo plastic left heart, which requires extensive surgical and medical management) with skin disorders (which in the authors scheme includes L40 psoriasis, L90 lichen sclerosis, and many other examples in their list)? Going back to the 2 items that the authors outlined (item 2 in this list), the heterogeneity of these conditions makes policy decisions about either quality of care concerns or need for palliative care difficult. Again, greater clarity about the goal of using this classification system is essential.

Our remit for this study was broad, namely to examine the role of chronic conditions in children who died on a national, population basis. As we have now clarified in the methods section in response to point 2 made by the reviewer, we aimed to determine the most prevalent chronic conditions in children who die and also indicate whether these children are likely to be seen in the healthcare system, and this is reflected in the broad definition we used.

Our premise is that ongoing care may offer opportunities for healthcare to intervene to prevent events that lead to death. The reviewer appears to advocate clinical pathway analysis for specific conditions to identify mismanagement or safety issues. We agree this would be of interest but would not address the big policy picture of whether children are already being followed up by healthcare services.

Similarly, in the discussion (P15, L51), how will the inclusion of patients with outpatient only diagnoses of asthma or depression help with thinking about palliative care? (Answer: probably not at all). Quality of care? Yes, if the patients died of asthma or suicide, i.e., causes directly related to the chronic condition. Bottom line: the authors need to clarify the value of having a very heterogenous set of diagnoses for health policy or epidemiological research.

Our aims are now clarified in the methods section (see responses to point A.1). Our results make clear that 71% of children who die have a chronic condition that is likely to require ongoing monitoring by healthcare services. This finding shifts thinking about prevention from a focus mainly on injury prevention to improving health care for children with chronic conditions.

5. Is the incremental increase (which seems to be about 5% absolute for the 1 year loopback) in the proportion of patients identified as having a chronic condition by including the hospital records important? Did the cases identified only this manner differ from the cases identified by only the death certificate data? In other words, is it worth the time and effort to do the linkage? The authors should comment on this, or examine the characteristics of the set of patients identified only via hospital records.

We think this study clearly shows the importance and value of linkage, particularly to overcome underascertainment of non-cancer conditions on death certificates (see the point below). We now emphasise this point in the abstract, and in the ‘key points’ box.

The increase in the overall proportion of children who died with at least one condition is confounded by type of chronic condition. This is clear from Figure 1 and is also clarified in the text of the results section, para 2 and 3.

6. Cancer clearly is the diagnosis that does not get missed. This should be emphasized, in that it has

relevance for policies based on data analyses that might not understand this ascertainment bias. The finding of the commonness of neurologic/sensory conditions maps to findings of other studies where neurologic conditions are often the leading diagnoses among patients who die or are frequently hospitalized. The authors note this in the discussion, but it is very important.

We agree with the reviewer that a key finding in this paper is that using data from death certificates only appears to underestimate the prevalence of all types of conditions apart from cancer. We have now emphasised this in the abstract and in the key points box.

7. The finding about multiple chronic conditions increasing in the middle age ranges may be policy relevant, in that many studies are now focusing on the multiple-morbidities of hospitalized pediatric patients.

We agree that this is one of the key finding in this paper. We consider several reasons for this observation in the discussion, including a decrease in previously health children dying of accidental injury, and increased coding detail in hospital databases which means more conditions get picked up over time (see response to point 5 made by reviewer 1) .

8. The authors conclusion to the abstract regarding the “sensitivity” of their method and the suitability of the method in lieu of primary data collection is not an outcome of the data or analysis presented in the paper. To make this claim based on data, they would need to have a comparable population-based study based on primary data collection, and they do not. They even contradict it on P16, L8, where they state that to identify expected deaths requires primary data collection. The authors should trim their sails and simply conclude that this method offers a feasible, relatively low cost means to monitor the child population for emerging trends in cause of mortality and the co-existence of chronic conditions, and conforms with findings from other studies.

We thank the reviewer for this suggestion. We have now removed the term ‘sensitive’ from the abstract (see point 3 above), and taken out the reference to not requiring primary data collection. Instead, we say ‘Linkage between death certificate and hospital discharge data avoids some of the under-recording of non-cancer conditions on death certificates, and provides a low-cost, population-based method for monitoring chronic conditions in children who die’.

VERSION 2 – REVIEW

REVIEWER	Chris Feudtner The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States
REVIEW RETURNED	14-Jul-2014

GENERAL COMMENTS	The authors have responded fully to the comments and concerns I raised in my first review.