Author’s response to reviews

Title: Estimating cause-specific mortality in Madagascar: an evaluation of death notification data from the capital city

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Author’s response to reviews:

Dear editor and reviewers,

We are grateful that you offered us an opportunity to revise and resubmit our paper entitled “Estimating cause-specific mortality in Madagascar: an evaluation of death notification data from the capital city” for possible publication in Population Health Metrics. We would like to express our sincere thanks to the three reviewers for their comments and suggestions. We revised areas needing clarification in the manuscript and improved our redistribution algorithm. Our main conclusions are unchanged, however. We provide below a point-by-point response to their comments and questions. Corresponding changes appear in the main text with tracked changes.

Reviewer #1:

[1. This is an interesting study based on routine subnational death notification data; data that are under-utilised as evidence of population health. The manuscript utilises a modified version of an existing framework to assess data quality and makes adjustments to the data produce cause-specific mortality in Antananarivo, Madagascar. There are however some areas where alternative methodological approaches should be used and more clarity provided. The major drawback of the paper is that the death distribution methods used to assess death notification completeness are out-of-date, being only for the period 1975-1993. This potentially results in biased life expectancy measures, should completeness have improved or declined in the decades since. Furthermore, these methods have been shown to have high levels of inaccuracy and not be]
suitable for subnational areas if there is high migration (see Murray et al, What Can We Conclude from Death Registration? Improved Methods for Evaluating Completeness, PLOS Medicine). The authors should instead use the recently developed empirical completeness method, which overcomes the drawbacks of death distribution methods. The method provides timely completeness estimates (i.e. for the latest year) using data that are available for Antananarivo and has relatively high accuracy (see Adair & Lopez, Estimating the completeness of death registration: An empirical method, PLOSOne).

Thank you for this suggestion. With the classical death distribution methods, we can only estimate completeness in the intercensal period 1975-1993. We agree that it could have improved or declined in recent years. When available, population counts from the 2018 census will make it possible to assess completeness for the recent period. However, based on discussions with colleagues at the National Statistical Office (INSTAT), the timing of the release of the 2018 census data is still uncertain. The disaggregated data for the capital city will probably not be available before 2020. In the absence of such data, to get a sense of the evolution over time of completeness, we compared our estimates of U5MR with DHS-based estimates. We found that they were consistent with one another, and there was no apparent change in the ratio of our estimates to DHS estimates in the most period, suggesting that completeness has not changed dramatically. Reviewer 1 also warned of the risk associated with using death distribution methods for sub-national analysis, but as we emphasize in the manuscript, rates of internal migration can be considered low in this case, and the selection of the age range to compute completeness reduces biases introduced by migration. We agree that the death distribution methods have high levels of inaccuracy, but we used both the Growth Balance and the Synthetic Extinct Generation methods to reduce the sensitivity of our results to some of the assumptions of the methods.

Tim Adair and Alan Lopez’s method was published after we first submitted our manuscript to Population Health Metrics, but we now have the opportunity to test their method with our database. Their model 1 includes the completeness of death reporting in children under the age of 5 among the covariates, while their model 2 does not. In our case, we cannot use coefficients from their model 1, because the true level of U5MR is unknown, and cannot be obtained from other sources. When using birth histories collected in the capital city in DHS surveys, we found that estimates from death notification fell above the DHS estimates (see Figure 3 in the manuscript). There could be several reasons for such difference in Antananarivo. First, DHS survey data could be affected by greater under-reporting of deaths. Second, the registers cover only the 6 central districts while in DHS it is only possible to locate the capital city as a whole, so the higher mortality in the death notification data could be a true reflection of higher mortality in the central districts. Fourth, estimates derived from the registers could be too high due to errors in the population at risk. Fifth, migration could introduce errors in mortality measurement from the surveys, because recent migrant mothers interviewed in the capital city could report on the experience of children born in rural areas. Given all these uncertainties, it is difficult to
estimate completeness in under-five mortality, and we decided to use Adair and Lopez’s second model. The Adair-Lopez method uses mixed-effect models to predict death registration completeness, based on the GBD estimates of mortality and completeness. The predictors of model 2 include the registered CDR, U5MR and the population age structure (share of the population aged 65 and above). Since Madagascar was excluded from their database, we use only the fixed-effects coefficients.

The completeness of death in females varies from 0.87 (in 2004) to 0.96 (in 1986). Among males, it varies from 0.88 (in 2008) to 0.96 (in 1987). The average completeness level estimated for the whole period (1976-2015) is 93% for males and 92% for females, which is remarkably close to our previous estimates based on death distribution methods with the 1975 and 1993 censuses (93% based on SEG, 92% based on GGB for both sexes).

Results obtained with Adair-Lopez method point to a slight decline in the completeness of death reporting over time (followed by an increase in recent years). However, this decline is largely driven by the sign of the coefficient linking calendar years with completeness in the Adair-Lopez model. In other words, it is inferred from information on time trends in completeness provided from countries in their sample, once the relationships with the age structure, the registered CDR and under-five mortality have been accounted for. If we multiply this coefficient by a constant (either 1976 or 2015) for all years for which we want predicted completeness, the decline is no longer apparent. If Antananarivo had in 2015 the registered CDR, age structure and U5MR observed in 1976, the model would produce an estimate of completeness which would be about 4% lower than with the 2015 values, holding all other things constant. We see no reason why completeness should decline over time in Madagascar, based on the observation that the sign of this coefficient is negative in the sample used to develop the Adair-Lopez method. The Adair-Lopez paper included an out-of-sample validation which showed that the model performs reasonably well at one point in time, but did not present validation results in terms of tracking changes in completeness over time. While awaiting the results of such evaluation, we decided not to mention this decline in the main manuscript, because we believe it is spurious.

We added the following sentence in the Methods section: “At the time of writing, the results from the 2018 census were not available. To assess completeness in more recent years, we used another method, developed by Adair and Lopez (2018), based on regression models to predict completeness of death registration from the crude death rate, the level of under-five mortality rate, and the population age structure, informed by estimates from the GBD Study [20].” We added the following sentence in the Results section: “The completeness estimate obtained from the Adair & Lopez method (model 2) is 93% for males and 92% for females for the whole period (1976-2015), which is remarkably consistent with results from the death distribution methods for the period 1975-1993.”
When discussing how CSMFs can vary subnationally, the different age structure of the population of a major city compared of the national population is important as well.

We agree that age structure is a confounder when comparing CSMFs, but we control for that since we use age-standardized CSMFs. We added the following sentence in the paper to make this clear: “CSMFs might also differ simply because the age structure of the population of the capital city could be different from the national age structure, but this can be accounted for through standardization.”

Yes. The individual-level dataset containing ICD-9 codes and GBD cause categories are available to any researcher upon request. The dataset for the period 1976-2015 will be available in the openicpsr repository (openicpsr.org) once the paper is published. The paper will be used for the data description.

Thanks for this suggestion. We edited the manuscript accordingly.

Many thanks for drawing attention to this. This helped us in revising our redistribution of garbage codes. Deaths believed to be from violent causes, or deaths that occurred in suspicious circumstances (potentially related to suicides or violence), are reported both to the police and to the BMH. In the capital city, the police will usually call the BMH when arriving on the scene if the BMH was not contacted by relatives of the deceased or witnesses of the event. Therefore, the differences in the share of violent deaths between death notification data and GBD estimates had to be found elsewhere. Following the reviewer’s comment, we tracked violent deaths to make sure that our redistribution algorithm for garbage codes had not resulted in lowering the percentage of external deaths. We realized that all deaths from chapter 17, codes 800-999 (Injury And Poisoning) are considered in GBD as Garbage code Level 2 because these codes refer to the nature of the injury, rather than the circumstances of the accident or violence which
produced the fatal injury. In our initial algorithm, all these deaths were redistributed pro rata by age, sex and year to acceptable Level 3 GBD causes in Step 7, which is incorrect. We revised this algorithm to include ICD-9 codes from Chapter XVII (injury and poisoning) in step 5 and redistributed them pro rata by age and sex to the GBD categories for intentional and unintentional injury. As a result, the discrepancies between death notification data and GBD estimates in terms of violent mortality have greatly reduced.

[Reviewer 1 - comment 6. Line 602 (appendix): There is insufficient explanation about how the DHS estimates population. The relevant DHS publications are in French, which this reviewer does not read. Could further information on this methodology be provided?] We added the following paragraph in the appendix: “A new census has been conducted in 2018, but the disaggregated data was not available at the time of the analysis. The age structure of the population was derived by interpolating between the 1975 and 1993 censuses and four DHS surveys (1992, 1997, 2003-04 and 2008-09). Although DHS surveys do no provide population counts, they give a sense of the age and sex composition of the population in the absence of recent census data. All standard DHS conducted in Madagascar used a two-stage stratified sampling design. At the first stage, clusters were systematically selected from a list of enumeration areas obtained from a recent sampling frame. The sampling frame used for the 1992 DHS was obtained as part of the activities carried out in 1991 in preparation for the 1993 census. The 1997 and 2003/2004 surveys used the master sample constructed by the National Statistical Office (INSTAT) on the basis of the 1993 census. Maps and enumerations prepared for the 2008 census (postponed until 2018) provided another sampling frame for the 2008/2009 DHS survey. All samples were stratified by urban and rural status, and in the most recent surveys, they were also stratified by provinces or smaller administrative units. All households in these enumeration areas were listed and maps in the selected clusters were updated. At the second stage, households to be included in the surveys were selected, with the number of households selected per clusters being inversely proportional to the size of the clusters. Within each selected household, information was collected on the age and sex of household members. We identified clusters located in the capital city and extracted the population pyramids of members of households in these clusters. To break down by age and sex our estimates of the population at risk of dying, we used cubic spline functions to interpolate between the proportions of individuals by age and sex from censuses and surveys (Figure S2).”

[reviewer 1 - comment 7. Table A.2: The redistribution of Chapter XVI deaths results in a decline in Level 2 garage code deaths. Aren't these ill-defined deaths a Level 1 garbage code (i.e. highest severity)?]
In the GBD cause list, some Chapter XVI deaths are considered Garbage code level 1 (e.g. 780-782.2) while others are considered Garbage code level 2 (e.g. 782.4, 784.7-784.8), so it is expected that the percentage of garbage codes declines in both categories. However, we noted an error in our code, thanks to this question. We have revised our redistribution algorithm and percentages have changed. We also added the season of deaths in the redistribution algorithm, because there are strong weather variations in Antananarivo. The city is located in the central plateau of Madagascar and culminates at an altitude of 1250-1450 m. It is characterized by a subtropical highland climate with a cold and dry season from May to October (with minimum average temperature around 10°C) and a hot and rainy season from November to April (with maximum average temperature around 27°C). Among children, mortality rates from infectious diseases and nutritional deficiencies peak in the rainy season, while in adults, mortality rates from cardiovascular diseases and diseases of the respiratory system peak in the dry season. As a result of this revision of the algorithm, and the change mentioned above related to ICD codes from Chapter XVII, our cause-of-death estimates have been slightly modified.

[Reviewer 1 - comment 8. Table A.2: Can remaining codes in step 7 be redistributed to more specific causes (even broad causes) than just pro rata to Level 3 GBD causes?]

As a result of changes in the redistribution algorithm in previous steps, and particularly thanks to the redistribution of ICD 9 codes 800-999 (Injury And Poisoning) in the GBD categories for intentional and unintentional injury, the percentage of deaths redistributed in this final step has been greatly reduced (now 7.6% over the whole period). The leading ICD9 codes remaining after the first six steps are 586 (renal failure, unspecified, 13% of garbage codes left), 38.9 (Septicemia, NOS, 11%), 578.9 (Hemorrhage of gastrointestinal tract, unspecified, 10%), 276.5 (Volume depletion, 9%) and 401.9 (Unspecified essential hypertension, 5%). For all of these codes, it is difficult to establish plausible target causes. All other codes account for less than 5% of the remaining garbage codes and less than one thousand deaths in the database. We considered redistributing deaths assigned to unspecified hypertension or unspecified haemorrhage of gastrointestinal tract only within non-communicable diseases, and all others across all GBD cause categories, but we decided against adding an extra step specifically for those two causes, each representing less than 1% of all deaths. However, we improved the way these remaining codes are redistributed by taking into account the season of death (May – October vs November-April). For example, garbage codes assigned to deaths occurring in the rainy season among children are now more likely to be re-coded into causes associated with infectious diseases.

[Reviewer 1 - comment 9. Can a final VSPI be calculated? It would be relatively high by global measures. This could highlight how death notification systems can provide relatively good quality data for subnational areas, even if data are of poor quality elsewhere in the country. ]
Thanks for this suggestion. We added the following sentences in the conclusion: “Phillips and colleagues (2014) developed a procedure to combine the different dimensions detailed above in a composite vital statistics performance index (VSPI) [11]. Applied at the national level, this approach puts Madagascar among the countries with the weakest systems (VSPI below 0.25) [1]. However, our own assessment of death notification data from Antananarivo provides a much higher value of the composite index, estimated at 0.52 (Appendix A.3). This corresponds to levels attained at the national scale by countries such as Switzerland, Turkey, Iran and Peru in 2005-2012 [1]. Apart from South Africa and Egypt, no country in Africa had reached such high scores. Lowering the percentages of deaths assigned to ill-defined cardiovascular diseases, ICD-9 codes for symptoms, signs and ill-defined conditions or injuries undetermined whether accidentally or purposefully is the main way to improve the system in place in Antananarivo.” We also added a small section in the Appendix to detail how we estimated the composite VSP index.

[Reviewer 1 - comment 10. Line 290 - Why was the age pattern of deaths of the GBD used, when the population of Madagascar would have a different population age structure, age-specific mortality rates and therefore age pattern of deaths than Antananarivo? To what extent does the age pattern of deaths of GBD and these death notification records differ? If completeness of notification is in fact over 90%, it is likely that age patterns of death notification are only slightly affected by the level of incompleteness (unless there is significant age misreporting).]

As noted by Reviewer 1, we cannot cause-specific mortality fractions without standardizing, because the age pattern of deaths in the capital city differs from that in the GBD estimates. Differences in the age patterns of deaths are indeed related to completeness of death reporting, but we showed that completeness is higher than 90% overall. Differences are also due to differences in the age composition of the population at risk of dying. The capital city has an older population than the country as a whole. For example, in the 1993 census, the population aged 0-14 represented 35% of the capital city, against 45% in the country as a whole, due to lower fertility rates in Antananarivo. Trends in mortality will also affect the age pattern of deaths. In particular, under-five mortality has declined much faster in the capital city than in the national average (as captured in GBD). As a result, the fraction of deaths occurring in adult ages should be higher in the BMH data, and there should be fewer under-five deaths. While the age pattern is relatively similar in 1990 (although the percentage of deaths occurring in children under the age of 5 is lower in death notification data), there are substantial differences in 2015. We now present the age patterns of death in the appendix.

Reviewer 1 suggested using the age pattern of deaths in the death notification data as a reference for standardizing. Each of the two age structures could have been used. However, when using the age structure from the death notification data, the cause-specific mortality fractions from GBD will be modified, and the uncertainty intervals should be re-calculated. To respond to the
reviewer’s request, we know provide unstandardized cause-specific mortality fractions in the appendix, with treemaps for 1990 and 2015. In the main text, we continue to report on standardized CSMFs, using the GBD as our standard. We see three advantages related to the use of the GBD age pattern. First, readers will be able to compare with future revisions of the GBD Study, while this will not be possible if we report on standardized CSMFs using the death notification data as our reference for the age pattern. Second, it is only possible to provide uncertainty intervals around GBD estimates (in the main text and in Table 2) if we keep the GBD age pattern. Once we change the age structure, this is no longer possible, because the uncertainty intervals should be recalculated, and these are provided by IHME. Third, reporting on CSMFs after standardizing based on an age structure close to the national average will facilitate comparisons with other sources in the country.

[Reviewer 1 - comment 11. Can more detail be provided about efforts to strengthen the death notification/CRVS system. Is there a government strategic plan? Any there any plans to move to online system or to adopt ICD 10? ]

We added the following information in the conclusion: “In 2017, Madagascar undertook a comprehensive assessment of its CRVS system, supported by the Africa Programme for Accelerated Improvement of Civil Registration and Vital Statistics (APAI-CRVS). This assessment identified a series of priorities for strengthening the death registration system, such as introducing verbal autopsies with the WHO VA instrument, harmonizing the content of the death certificate used in health facilities and in municipal hygiene offices (see Appendix A.5), and reinforcing the interoperability between these offices and the Ministry of Health. With the support of the WHO and USAID, the Malagasy Ministry of Health is also piloting DHIS2, an open-source health management information system platform which will help in centralizing and standardizing the management of cause-of-death data, ideally through the adoption of a shortlist of ICD codes (such as the WHO Start-Up Mortality List).”

[Reviewer 2 - comment 1: This paper assesses the quality of the death notification system in Antananarivo. The paper is well presented and highlights that such systems could be used more widely in other cities in Madagascar and potentially cities in other African countries. The paper is topical as countries strive to attain better CRVS data and identify new techniques and systems to improve notification. The data provide interesting comparisons to GBD, not least the difference in the apparent rate of the epidemiological transition compared to GBD models for the country as a whole. The paper compares city register data to GBD 2016. The authors state that the GBD Study had access to death counts from the same registers, from 1984 to 1995 and that this is not therefore equivalent to validating independent data series. The understanding is that there were few other data sources available to the GBD Study in those years and GBD output
was modelled predominantly on the city registers. The sentence starting in line 141 states that the register data are more likely to be consistent with GBD in those earlier years than when they are compared to later GBD models for the whole country. This appears to understate the importance of GBD being modelled on the registers and how this influences the output, particularly in figure 4, and subsequent discussion of these interesting data. This should be clarified or emphasised and the lack of independent comparison data (which may indeed not be available) stated as a limitation of the study.

We entirely agree with the reviewer, and we thought that this point had been clearly made in the paper already. However, we insisted on this lack of independence again, in the discussion: “Hence, this high concordance is largely a result of GBD estimates being modelled on the basis of notification data during this period, although one would have expected larger differences, since data from the capital city should not be considered representative of the national level.” We also added the following sentence in the limitations: “Third, there is a lack of independent comparison data to assess the validity of the notified causes of death, since GBD estimates are in part informed by the registers from Antananarivo.”

[Reviewer 2 - comment 2. Typing correction in line 169 should read: medical personnel]

Thanks, this has been corrected.

[Reviewer 3 - comment 1: This is an important paper for all those interested in cause specific mortality in Africa. It demonstrates the application of a variety of useful methodological approaches for settings where the majority of deaths are notified to the health sector with a physician certified cause. Even in countries with highly sub-optimal national civil registration and vital statistics systems like Madagascar, such data sets are often available in large urban centers where there are large teaching hospitals and high physician access. This paper shows how much can be learned in such situations. A laudable feature of this paper is the effort that went into manually redistributing garbage codes according to principles modified from the GBD. Their garbage code algorithm logic is well explained, easy to understand and the result was still a highly plausible concordance with GBD CSMFs after redistribution of garbage codes, despite the urban and hospital bias of the source data. It would be good if the authors, given their wide experience in Africa, could add a few lines in discussion to comment on how this approach could be extended to other countries in the Region. In particular, what features in Antananarivo they would consider important to generalizing their approach elsewhere. I assume it includes the special case where the health sector issues burial permits only after there is a physician certified cause, even for home deaths, and that all hospitals, public, private, and teaching, participate. It is remarkable that 40 years of data were available for analysis. Much of this period would have been based on paper records (which don't last so long in Africa), so I assume that much of the
older data had already been "rescued" digitally for analysis in this series. There may be other features important to how well this worked in Antananarivo that could be listed in a table. e.g. the very prompt reporting of deaths to the health sector.]

Thank you for these comments. We added the following sentences in the conclusion: “This study is based on registers from one city only, and the system in Madagascar has some specific characteristics that may not be found in other countries. For example, the country has a very long tradition of civil registration dating back to the nineteenth century, encouraging the prompt reporting of deaths. Locally, village and neighbourhood chiefs (fokontany) are involved in the notification of deaths to the health sector. The repatriation of the deceased to the ancestral tomb plays a key role in the culture of Madagascar, and death certificates will be required to move the bodies of the deceased. In addition, for deaths occurring in cities, burial permits and death certificates are issued only after a physician has established a cause of death, and fines are imposed in case of unauthorized burial. All these factors contribute to good completeness of registration and make this system a relative exception in Africa. However, previous research conducted in other African cities (including Abidjan, Bamako and Libreville) has shown that functional death registration systems are in place elsewhere.”

The data was “rescued” as part of a research project, and in recent years, a collaboration has been initiated between the National Statistical Office (Instat Madagascar) and the BMH of Antananarivo. Another collaboration is ongoing with the Pasteur Institute.

[Reviewer 3 - comment 2. One point of interest to readers (that could be added to the annex) would be a copy or description of the typical medical certificate of cause of death form that has been used over the years. Did it conform to the general format of the WHO MCCoD certificate with immediate, intermediate, and underlying causes sequenced in the form?]

We provide a copy in the appendix and note in the main manuscript that the WHO MCCod is not used in the BMH, and not used in health facilities either.

[Reviewer 3 - comment 4. The authors refer to initiating cause as the underlying cause. It is interesting that the largest discrepancy from GBD is the relatively small proportion of Level 3 Injury / External causes seen in the data compared with the GBD estimates (Table 2). Could this be due to the fact that often in hospital deaths in Africa, the underlying cause of injury is not recorded on the MCCoD form?]

This discrepancy was due to our garbage code redistribution. This has been corrected now. As noted earlier, hospitals do not use the WHO MCCod in Madagascar.
[Reviewer 3 - comment 5. An important conclusion stated in this paper is the potential of verbal autopsy to augment such data sets where home deaths are a prevalent share of deaths. This is a rich paper, well and clearly written, that draws attention to an insufficiently considered source of mortality data in Africa and provides practical methodological approaches. I recommend acceptance for publication in Population Health Metrics. Minor revisions could be considered as above to add value.]

Thanks for this comment and thanks also to the two other reviewers for helping us in building a stronger paper.