



Excess mortality associated with the COVID-19 pandemic during the 2020 and 2021 waves in Antananarivo, Madagascar

Joelinotahiana Hasina Rabarison, Jean Marius Rakotondramanga, Rila Ratovoson, Bruno Masquelier, Anjaraso Maharavo Rasoanomenjanahary, Anou Dreyfus, Andres Garchitorea, Fidisoa Rasambainarivo, Norosoa Harline Razanajatovo, Soa Fy Andriamandimby, et al.

► To cite this version:

Joelinotahiana Hasina Rabarison, Jean Marius Rakotondramanga, Rila Ratovoson, Bruno Masquelier, Anjaraso Maharavo Rasoanomenjanahary, et al.. Excess mortality associated with the COVID-19 pandemic during the 2020 and 2021 waves in Antananarivo, Madagascar. *BMJ Global Health*, 2023, 8 (7), pp.e011801. 10.1136/bmjgh-2023-011801. pasteur-04172088

HAL Id: pasteur-04172088

<https://riip.hal.science/pasteur-04172088>

Submitted on 27 Jul 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

Excess mortality associated with the COVID-19 pandemic during the 2020 and 2021 waves in Antananarivo, Madagascar

Joelinotahiana Hasina Rabarison,¹ Jean Marius Rakotondramanga ^{1,2}, Rila Ratovoson,¹ Bruno Masquelier,³ Anjaraso Maharavo Rasoanomenjanahary,⁴ Anou Dreyfus,¹ Andres Garchitorena ^{1,5}, Fidisoa Rasambainarivo,^{6,7} Norosoa Harline Razanajatovo,¹ Soa Fy Andriamandimby,¹ C Jessica Metcalf ⁶, Vincent Lacoste,¹ Jean-Michel Heraud ^{1,8}, Philippe Dussart¹

To cite: Rabarison JH, Rakotondramanga JM, Ratovoson R, *et al*. Excess mortality associated with the COVID-19 pandemic during the 2020 and 2021 waves in Antananarivo, Madagascar. *BMJ Glob Health* 2023;**8**:e011801. doi:10.1136/bmjgh-2023-011801

Handling editor Seye Abimbola

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjgh-2023-011801>).

JR and JMR contributed equally.

Received 18 January 2023
Accepted 17 June 2023



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Dr Jean-Michel Heraud;
jean-michel.heraud@pasteur.fr

ABSTRACT

Introduction COVID-19-associated mortality remains difficult to estimate in sub-Saharan Africa because of the lack of comprehensive systems of death registration. Based on death registers referring to the capital city of Madagascar, we sought to estimate the excess mortality during the COVID-19 pandemic and calculate the loss of life expectancy.

Methods Death records between 2016 and 2021 were used to estimate weekly excess mortality during the pandemic period. To infer its synchrony with circulation of SARS-CoV-2, a cross-wavelet analysis was performed. Life expectancy loss due to the COVID-19 pandemic was calculated by projecting mortality rates using the Lee and Carter model and extrapolating the prepandemic trends (1990–2019). Differences in life expectancy at birth were disaggregated by cause of death.

Results Peaks of excess mortality in 2020–21 were associated with waves of COVID-19. Estimates of all-cause excess mortality were 38.5 and 64.9 per 100 000 inhabitants in 2020 and 2021, respectively, with excess mortality reaching ≥50% over 6 weeks. In 2021, we quantified a drop of 0.8 and 1.0 years in the life expectancy for men and women, respectively attributable to increased risks of death beyond the age of 60 years.

Conclusion We observed high excess mortality during the pandemic period, in particular around the peaks of SARS-CoV-2 circulation in Antananarivo. Our study highlights the need to implement death registration systems in low-income countries to document true toll of a pandemic.

INTRODUCTION

Mortality has declined substantially in Madagascar over the past few decades, with life expectancy increasing by almost 15 years (from 52 to 66 years) between 1990 and 2022.¹ This progress was largely driven by a rapid decline in under-five mortality, which was reduced by two-thirds over the same

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Sub-Saharan countries lag behind the rest of the world in vital statistics leading to the difficulty of collecting information on annual deaths.

WHAT THIS STUDY ADDS

⇒ Our study is one of the firsts conducted in sub-Saharan Africa that made use of a local death notification system to assess the impact of COVID-19 pandemic on mortality and life expectancy in the general population.
⇒ The mortality burden during the COVID-19 pandemic in Antananarivo has been much higher than the official count of COVID-19-related deaths for the entire country.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study highlights the importance of local sources of death notification to better estimate mortality in the context of an outbreak or a pandemic.

period.² This gain is however fragile, in a country like Madagascar characterised by persistent high rates of poverty, political instability, a weak health system, rapid population growth and scarcity of resources.^{3,4} The recent epidemics of pneumonic plague in 2017 and measles in 2018–19 provide vivid examples of the precariousness of the health situation in the country.^{5,6} The COVID-19 pandemic might have jeopardised the life expectancy gains achieved over the last decades. In many low-income and middle-income countries (LMICs), in particular in sub-Saharan Africa, deaths associated with the COVID-19 remain difficult to estimate, however, mainly due to the absence of a comprehensive and efficient civil registration and vital statistics system.

According to estimates by WHO, when compared with the mortality expected in the absence of the pandemic, COVID-19 caused directly and indirectly, 25 582 additional deaths during the 2020–21 period in Madagascar.⁷ This would represent an increase of approximately 14% over the estimated annual number of deaths in the country.¹ However, as of 31 December 2021, the Malagasy Ministry of Health (MoH) notified 1067 deaths due to COVID-19 for the entire country.⁸ This discrepancy between WHO estimates and the Malagasy MoH deaths could be explained by the fact that the MoH only notified COVID-19 laboratory-confirmed deaths, and left indirect deaths unaccounted for. Moreover, a considerable proportion of deaths occurred outside the healthcare system and were never reported in the official statistics. Consequently, the total number of direct and indirect deaths due to the COVID-19 pandemic is unknown in Madagascar. Epidemiological models such as the WHO model are based on a number of covariates including the reported COVID-19 mortality rate and the COVID-19 positivity rate. But these official statistics can themselves be heavily biased due to limited testing capacity (max 1000 tests/day), insufficient staff to conduct contact tracing and changes in the testing policy during the course of the pandemic.⁹ There are also large uncertainties around prepandemic baseline mortality rates due to the incompleteness of death registration systems in LMICs. For example, in Guinea-Bissau, a seroprevalence study in the capital showed that the official number of PCR-confirmed COVID-19 cases greatly underestimated the prevalence of COVID-19 during the pandemic.¹⁰ In Zambia, most deaths due to COVID-19 were detected in the community outside of hospitals and were not tested before death.¹¹

Compared with other African countries, the situation of Madagascar is atypical since the capital city of Antananarivo has a relatively unique system of death notification in place, covering both hospital and community deaths, located at the Bureau Municipal d'Hygiène (BMH) of Antananarivo. An evaluation of this system before the pandemic concluded that high completeness of registration had been achieved over the last decades, with accurate data on the underlying diseases as established by physicians visiting relatives of the deceased or certifying deaths in healthcare facilities.¹² The available registers cover the period 1976–2021 and have previously been analysed to document a mortality crisis due to the resurgence of malaria and an urban famine in the mid-80s,¹³ the excess mortality during the H1N1 pandemic in 2009¹⁴ and the measles outbreak in 2018–19.¹⁵

The objectives of our study were to (i) leverage this death notification system to reconstruct recent mortality trends covering the years 2020 and 2021 in Antananarivo and (ii) assess the effects of the COVID-19 pandemic on mortality in the capital city of Madagascar.

METHODS

Study site and data sources

Since 2016, the National Influenza Centre located at the Institut Pasteur de Madagascar (IPM) has improved the death surveillance system at BMH. This office covers five of the six central districts of Antananarivo city, corresponding to the district of Antananarivo-Renivohitra with a total population of 1.14 million inhabitants according to the 2018 census (online supplemental method S1).¹⁶ The BMH is responsible for delivering and storing death certificates. To date, nine physicians are responsible for home-visits to establish a death certificate indicating the cause of death. The assignment of a cause of death is based on information provided by the family and available medical documentation. If the death occurred at the hospital, the family presents a death certificate signed by a clinician to the BMH. This hospital death certificate also indicates the presumed cause of death. For each death, the register includes the name of the deceased, date of birth, date of death, gender, address, place of death (hospital or home) and cause of death coded according to the International Classification of Diseases (ICD) (currently using the ICD 10th revision). In 2020 and 2021, COVID-19 deaths were coded as 'B97.2' or 'U07', following regulations set by WHO. For deaths that occurred in 2020 and 2021 within hospitals, the certificate also indicates the result of the COVID-19 test. Deaths at home were not tested but diagnosed according to clinical assessment by physicians and according to the epidemiological context. For the study period, we considered all death certificates stored at the BMH between 2016 and 2021. We also resorted to tabulations of deaths by age and sex from 1990 to 2015 to reconstruct trends in mortality over the period prepandemic.¹² Using the address of the deceased in the city of Antananarivo from registers of the BMH, we could restrict the analysis to residents of five of the six districts. The sixth district, Ambohimananarina, does not fall in the area covered by the BMH for historical reasons (online supplemental method S1).

Calculation of weekly excess deaths

To calculate weekly excess deaths, we considered calendar weeks (1–52nd) and assessed excess mortality in 2020 and 2021 as the percentage difference between the reported and the average expected number of deaths of the same week, using the relative change measure based on Farrington surveillance algorithm.¹⁷ First, the expected deaths were derived from the period 2016 to 2019, and the corresponding relative change was computed as the difference between the reported count and the upper bound of the 95% CI:

$$\text{Relative change (\%)} = \frac{\{\text{Reported deaths}\} - \{\text{Upper bound of expected deaths}\}}{\{\text{Upper bound of expected deaths}\}} * 100$$

A relative change of 100%, in a given week in 2020 (or 2021), would mean that the death count for that week was double from the expected death count. Based on

the upper bound of the baseline average weekly deaths during 2016–19, excess deaths were then assessed by considering weeks where relative change values were associated with significant positive excess of deaths. In order to classify these relative changes of excess deaths, their estimated values were split in <50% and ≥50% changes.

Second, two sensitivity analyses were performed: (1) to assess the appropriateness of using the relative change in deaths based on Farrington surveillance algorithm instead of the simpler method of relative change (P-scores), which may alter the estimate of excess mortality (online supplemental method S2)¹⁸ and (2) to remove the effects of the 2018–19 measles outbreak, which could have induced large excess mortality in the capital, especially among children and youth.⁶ To do so, for the second sensitivity analysis, weekly deaths were estimated to be the same as historical averages for the same week: using 2016–17 historical data for the October–December 2018 outbreak, and 2016–18 historical data for the January–March 2019 outbreak. Then, the relative changes—as described above—were recalculated considering these adjustments for the baseline years, 2016–19.

Cross-wavelet analyses

Cross-wavelet analyses were used to successively investigate associations between the time series of all-cause deaths over COVID-19 deaths (nationwide),⁸ and of SARS-CoV-2 positivity rate at the IPM laboratory⁹ over all-cause deaths (in Antananarivo). This method is useful for finding the frequency correlation between two non-stationary time series, combining time-frequency analyses and the statistical significance level of the relationships between lead and lag phases.¹⁹ It allows to characterise whether (i) changes in one time series follows or precedes similar changes in the other by a certain amount of time (ie, lead or lag), (ii) similar changes in both time series occur at the same time (ie, synchronous) or (iii) there is no association between the timing of changes in each of the time series. Here, the cross-wavelet analysis was performed twice for scaled time series according to each pair of comparisons of 2020–21 data: all-cause deaths in Antananarivo versus the registered COVID-19-related deaths in the whole country,⁸ and the SARS-CoV-2 positivity rate obtained from the virology unit of the IPM⁹ versus the all-cause deaths in Antananarivo. Using an appropriate combination of parameters, as detailed in the online supplemental method S3 (windows for time and period (scale) smoothing),¹⁹ these analyses can be used to infer the synchrony and association between two time series across time and period, providing wavelet coherence (the equivalent of the coefficient of determination in a statistical model) and phase-difference (angle).²⁰ Further details about the rescaled data and the wavelet analyses coherence and phase-difference can be found in the online supplemental method S3.

Calculation of trends in life expectancy

To construct annual life tables, the populations exposed to the risk of dying were reconstructed from the last three censuses of 1976, 1993 and 2018, assuming a constant rate of growth for each age segment, with growth rates estimated from the two intercensal periods and applied respectively to the periods 1975–1993 and 1993–2021. To calculate the life expectancy loss in 2020 and 2021 due to the COVID-19 pandemic, we projected mortality rates using the model by Lee and Carter and extrapolated the trends observed prepandemic, over the period 1990–2019.²¹ This model uses a singular value decomposition method to synthesise a matrix of logged age-specific mortality rates into three components: (1) an index k_t that reflects the level of mortality (all ages) and varies over time, (2) a general age schedule of mortality (a_x) and (3) a set of constants (b_x) that capture which rates change most rapidly in response to a change in k_t :

$$\log(m_{xt}) = a_x + b_x + k_t + e_{xt}, \text{ where } e_{xt} \sim N(0, \sigma_e^2)$$

This model is widely used for mortality projections. The k_t index is extrapolated using an autoregressive integrated moving average process, while the other two components (a_x and b_x) are held constant; and e_{xt} is the residual at age x and time t . The difference between the observed life expectancy in 2020 and 2021 and the predicted values for these 2 years provided the number of years of life expectancy lost due to the pandemic, and prediction intervals around the life expectancy allowed us to establish whether the trend was significantly deviating from the recent past.

Second, differences in life expectancy at birth between 2019 and 2020–21 are an algebraic function of the differences in the underlying age-specific and cause-specific mortality rates.²² To compute the contribution of each age group and categories of causes of death to the life expectancy difference, we used a decomposition method designed by Arriaga.²³ We first decomposed the difference by age. Then, assuming that the distribution of deaths by cause is constant within each age group, we further disaggregated the contribution within each age group by cause of death, isolating the COVID-19 deaths from all other causes.

All calculations were performed using R statistical software.²⁴ WaveletComp R package was used to perform cross-wavelet coherence analyses.²⁰

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Temporal trends of crude all-cause mortality in Antananarivo

A total of 45 959 death records, notified to the BMH, were included in our study from 2016 to 2021. Death records averaged 143 (range=118–174) deaths per week during the four prepandemic years (2016–19) considered as our

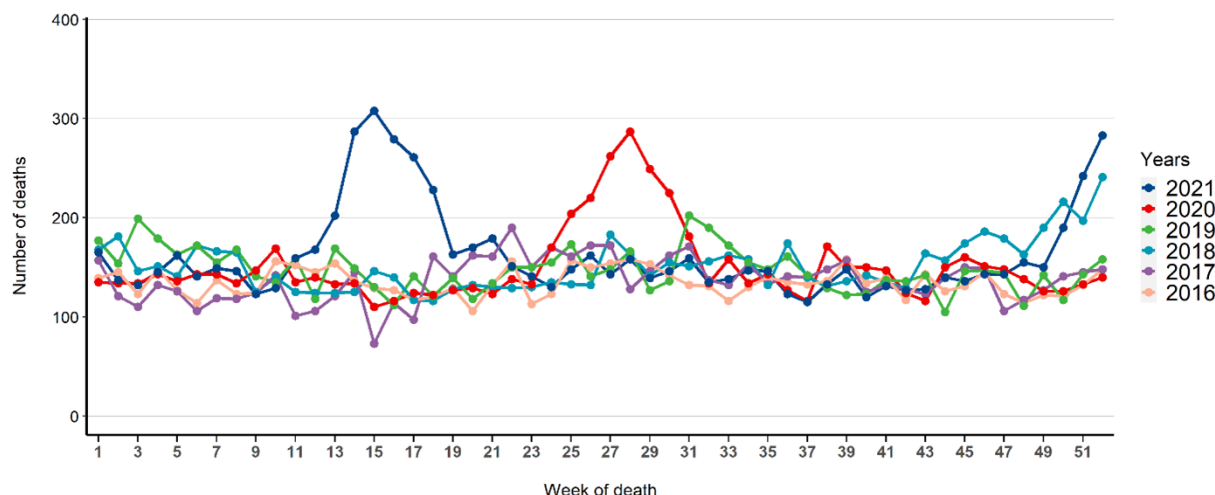


Figure 1 Temporal trends of all-cause crude mortality from 2016 to 2021 in the five central districts of Antananarivo (n=45 959).

baseline period. Before the COVID-19 pandemic period, waves with higher numbers of crude deaths were recorded at the end of 2018, reaching >200 weekly deaths during three consecutive weeks. The excess deaths observed in 2018 could be associated with the measles outbreak that affected the city during the last quarter of 2018.⁶ During the three successive waves of COVID-19, we observed higher peaks of deaths than in previous years, with >200 deaths in weeks 25–30 of 2020 and weeks 13–18 of 2021 as well as in the last weeks of 2021 (51 and 52) (figure 1 and online supplemental tables S1 and S2).

Excess mortality during the 2020–21 waves of COVID-19 infection in Antananarivo

A statistically significant increase in all-cause excess mortality was observed during 23 weeks in 2020 and 2021. During these weeks, we recorded 217 deaths per week on average, representing a 55.0% increase compared with 140 deaths per week over the same weeks during the baseline period (figure 2 and table 1). A total of 1179 all-cause excess deaths were assessed considering only significant relative change measures during the waves of COVID-19 in 2020 and 2021 in Antananarivo (table 1 and figure 2). Excess mortality of <50% was recorded during 9 and 8 weeks, corresponding to 244 and 222 excess deaths, respectively, in 2020 and 2021. In addition, excess deaths of 50% or greater, totalizing 195 and 518 deaths, were detected during 2 and 4 weeks in 2020 and 2021, respectively (table 1 and figure 2A). Normalised by the population size of the five districts of Antananarivo based on the general population census,¹⁶ the number of excess deaths were 38.51 and 64.91 per 100 000 inhabitants in 2020 and 2021, respectively. It is noteworthy that the positivity rate of SARS-CoV-2 virus was >25% during the same periods of the observed excess deaths with a peak reached 1 week before the peak of excess deaths in 2020 and 2021. Excess mortality was observed predominantly in adults aged 15–59 years and older adults aged 60 years and above. For these groups, the excess deaths

seemed to increase with age during the 2020 and 2021 waves of SARS-CoV-2 positivity (figure 2B and online supplemental figure S2). In children and adolescents <15 years, there were very few weeks with excess deaths.

Of note, by adjusting deaths during measles outbreaks (October 2018–March 2019)⁶ from our baseline years, a higher all-cause excess mortality was estimated during waves of COVID-19 in both 2020 and 2021 in Antananarivo: totalling 1500 deaths during 32 weeks (online supplemental figure S3 and online supplemental table S3). Furthermore, by avoiding thresholds in our calculation, all-cause excess mortality was observed during 51 weeks in 2020 (from 1% to 87%) and 2021 (from 2% to 158%)—totalling 2111 deaths and estimated at over 200% for the elderly (80+ years) for each wave (online supplemental figure S4).

Cross-wavelet coherence of SARS-CoV-2 positivity rate and death rate

SARS-CoV-2 test positivity rate by the IPM laboratory and all-cause death rate in Antananarivo, were in phase from June 2020 to September 2021 (online supplemental figure S1A, S1B, S1C, S1D); this was associated with a significant coherence level of ≥ 0.8 ($p < 0.05$), showing that changes in SARS-CoV-2 test positivity rate over time occurred at the same time as equivalent changes in all-cause deaths in Antananarivo during the first wave of COVID-19 (figure 2C). The death rate seemed to slightly precede the SARS-CoV-2 test positivity rate during the growth phase of the first wave of COVID-19, in June 2020.⁹ However, in the second wave of COVID-19, from February 2021 to May 2021, there was a significant lead in the SARS-CoV-2 positivity rate on the death rate (figure 3). In addition, in the first half of 2020, all-cause deaths in Antananarivo and national COVID-19 deaths were not in synchrony (ie, these two time series were out of phase); and the weekly national COVID-19 deaths preceded the Antananarivo deaths (online supplemental figure S3). However, from the second semester of 2020 to September

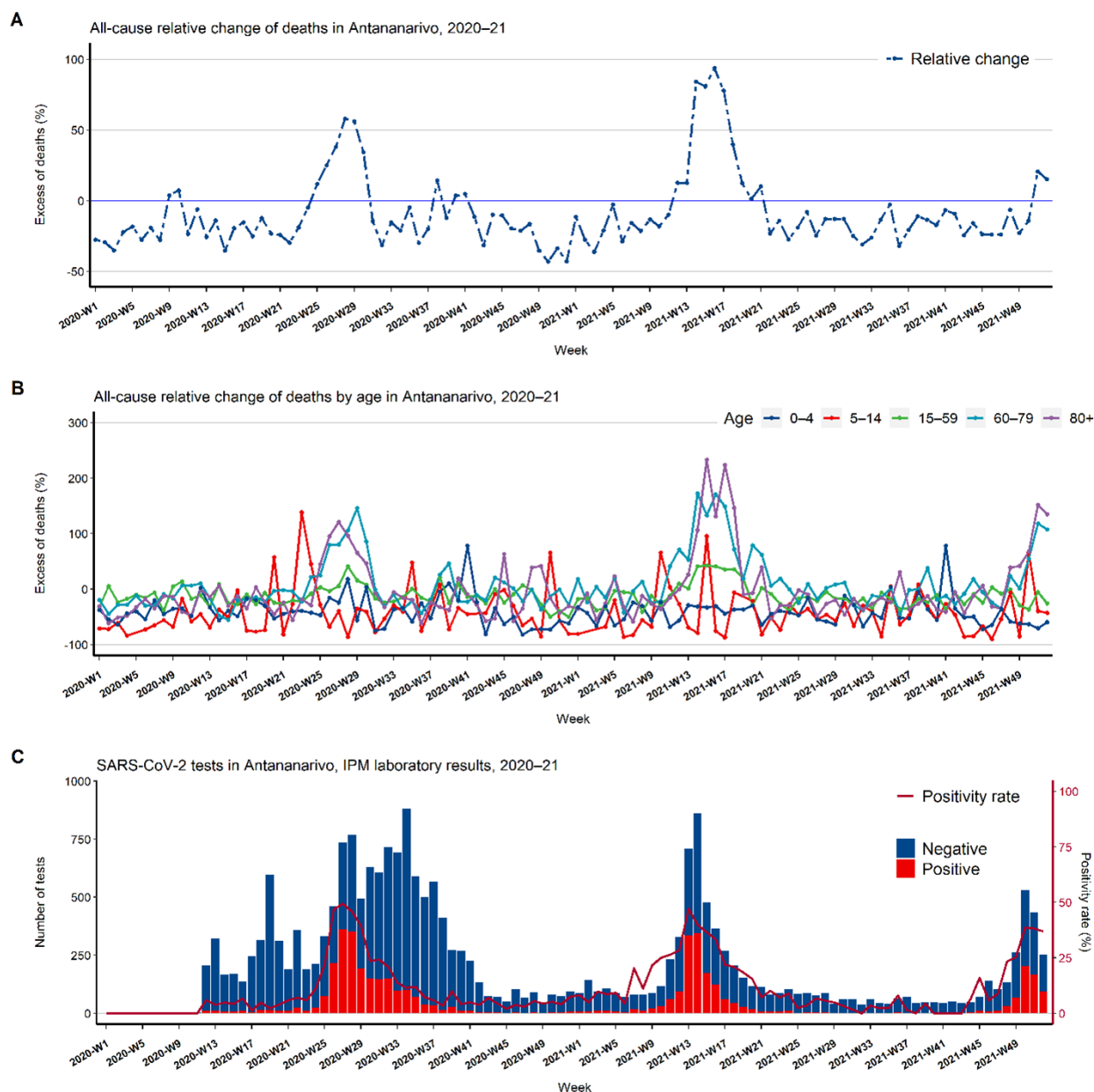


Figure 2 Weekly temporal trends, in five districts of Antananarivo from 2020 to 2021. (A) All-cause excess mortality using 2016–19 crude deaths as baseline years. (B) All-cause excess mortality by age group using 2016–19 crude deaths as baseline years (no death record was observed for age group 5–14 years during 1 week in 2020 and 2 weeks in 2021). (C) SARS-CoV-2 test results and positivity rates (data from the Institut Pasteur de Madagascar (IPM) for Antananarivo).⁹ Supplementary materials representing weekly all-cause deaths by age group (online supplemental table S1) and all-cause excess mortality by sex (online supplemental figure S2) support this figure.

2021, the all-cause deaths in Antananarivo were mainly in phase and preceded the national COVID-19 deaths, with a significant coherence level of ≥ 0.8 ($p < 0.05$), showing that changes in the weekly national COVID-19 deaths occurred at the same time as equivalent changes in all-cause deaths in Antananarivo from second semester of 2020 to September 2021. Additional result interpretations can be found in online supplemental method S3 and online supplemental figure S5.

Changes and differences in life expectancy

For both sexes, life expectancy at birth declined in 2021, compared with the recent past, but the year 2020

was in line with earlier years (figure 4). Male life expectancy has shown very little progress in the capital since 2004, hovering around 63–64 years. Projections (without COVID-19) placed the estimates for 2020 and 2021 at 63.4 and 63.6 years, respectively, compared with the observed values of 63.3 and 62.8. The life expectancy has thus been reduced by 0.1 and 0.8 years for men in 2020 and 2021, respectively. For women, progress has also been very modest since the mid-2000s, with life expectancy appearing to plateau at around 68–69 years. Projections were 68.8 years in 2020 and 69.0 years in 2021, compared with 68.9 and 68.0 observed in the context of

Table 1 Estimated all-cause excess mortality in 2020–21 using relative change and based on 2016–19 baseline of crude deaths data

Year	Relative change level (%)	Nb. of weeks of excess	Expected deaths (2016–19)		Reported deaths (2020–21)		Sum excesses death
			Mean	Range (minimum-maximum)	Mean	Sum	
2020	<50	9	144	128–164	188	1695	244
2020	≥100	2	148	142–154	268	536	195
2021	<50	8	141	123–174	204	1635	222
2021	≥100	4	125	118–139	284	1135	518
Total		23	140	118–174	217	5001	1179

Nb, number.

the pandemic. The levels are therefore virtually the same in 2020, while there is a 1-year drop in life expectancy in 2021. However, for both sexes, the observed drop in 2021 remains within the CIs around the projections, so life expectancy reduction associated with the COVID-19 is not statistically significant. The impact represented by COVID-19 on life expectancy was much smaller than the decline in life expectancy observed in the mid-1980s due to a resurgence of malaria and malnutrition.¹³

Table 2 displays the contributions by age to the differences in life expectancy between the observed life tables and the counterfactual life tables (based on extrapolating prepandemic rates). The contributions by age sum up to the difference in life expectancy at birth. For both sexes, mortality above age 60 years was higher than expected in

2020, with negative contributions of >1 year for men, but this unfavourable development was offset by a faster-than-expected mortality decline below age 60 years. In 2021, the same phenomenon is observed, but the increase in mortality between 60 and 80 years of age is greater. The risk of dying between the ages of 60 and 80 years is 16% higher than expected for women (+20% for men) and the mortality rate above 80 years is 14% higher (+44% for men).

As a result, favourable trends in mortality below the age of 60 years are no longer sufficient to compensate the excess mortality above the age of 60 years and life expectancy is reduced by 0.8 years for men and 1.02 years for women compared with expected levels. In other words, the loss of life expectancy in 2021 is explained exclusively

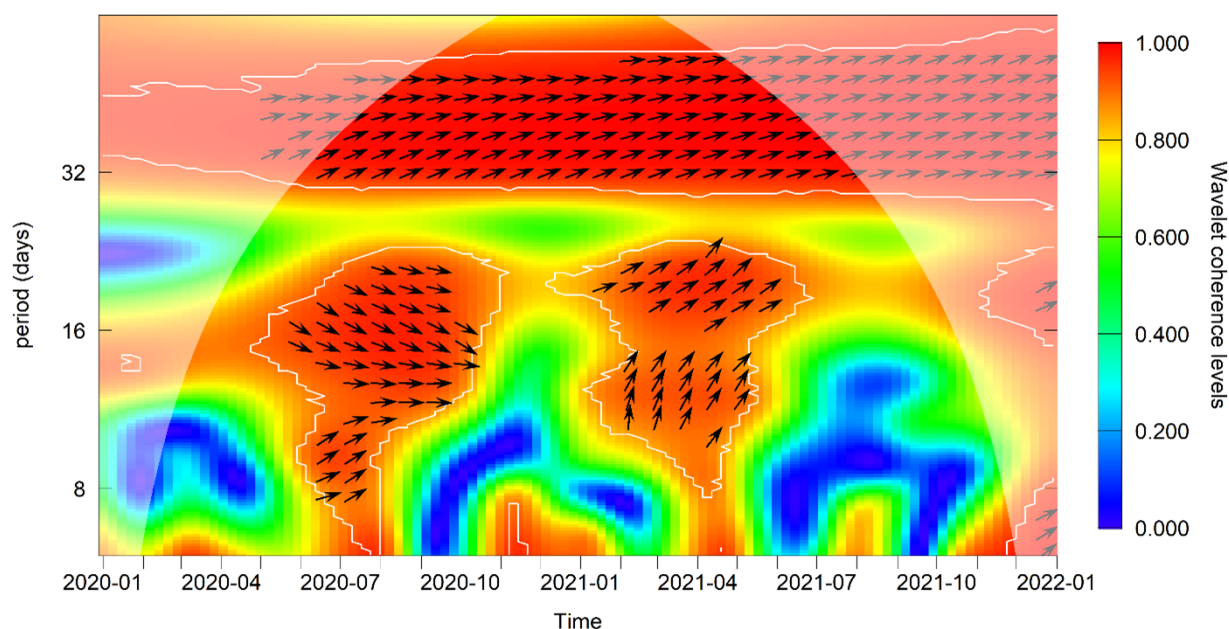


Figure 3 Cross-wavelet coherence and phase-difference of the SARS-CoV-2 positivity rate and all-cause death rate in Antananarivo. These two time series were in phase from June 2020 to September 2021 (phase-differences between 0 and $\frac{\pi}{2}$). During the first wave of COVID-19 (June 2020), the death rate seemed to lead the SARS-CoV-2 positivity rate (phase-differences $-\frac{\pi}{2}$ and 0). In the second wave (February 2021–May 2021), SARS-CoV-2 positivity rate significantly led the death rate (phase-differences between 0 and $\frac{\pi}{2}$). The significant coherence level is ranked from blue (0.0) to red (1.0) colour scale, and statistical significance is marked by the white contour plots, when $p < 0.05$. Supplementary materials representing all-causes deaths (online supplemental figure S1B) and SARS-CoV-2 tests positivity (online supplemental figure S1D), also online supplemental method S3 support the interpretation of this figure.

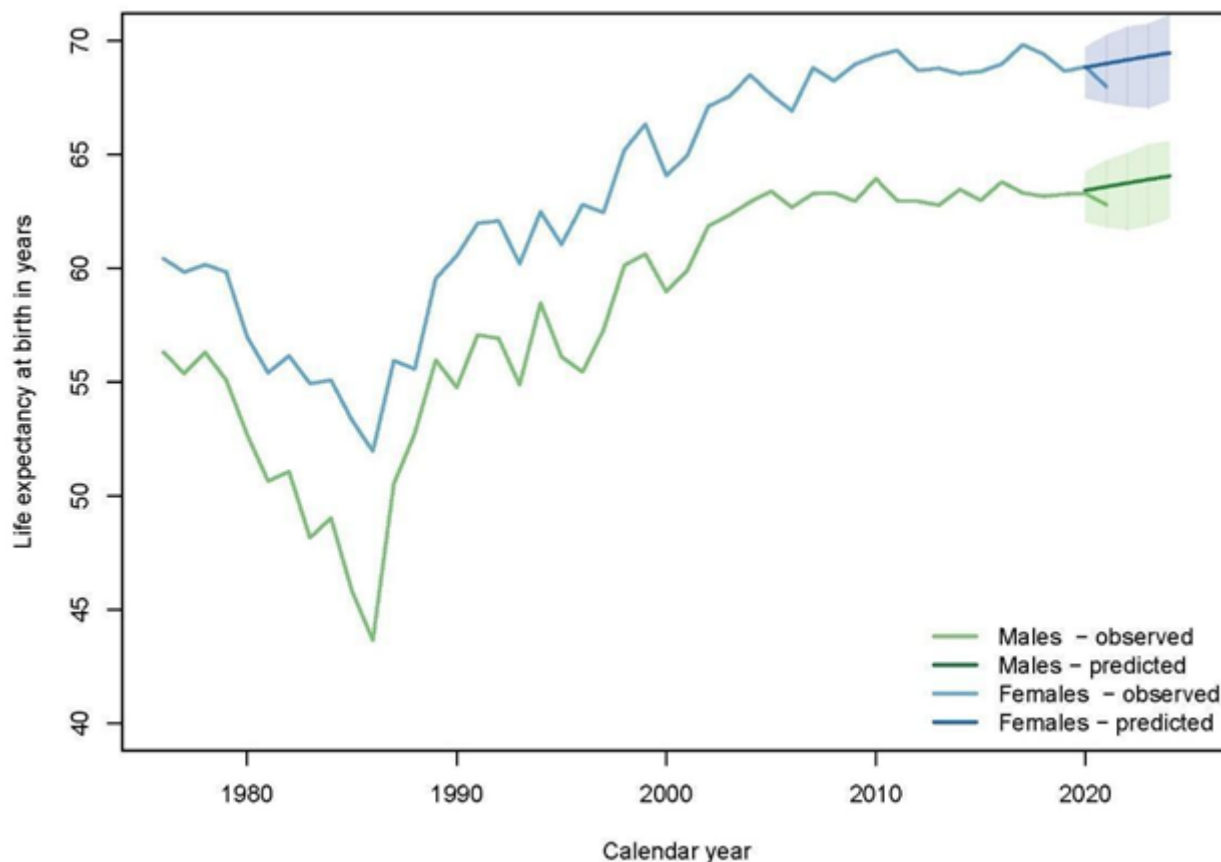


Figure 4 Observed and predicted life expectancy at birth in Antananarivo (1976–2021) for males (green) and females (blue). We projected to 2020–24, the observed life expectancy at birth and the predicted (bold) for both sexes based on the rates measured from 1990 to 2019.

by the sharp increase in a risk of dying above the age of 60 years. In children, youth or adults aged 15–59 years, the various direct or indirect effects of the pandemic (lockdowns, reductions in intervention coverage, etc) did not result in a loss in life expectancy.

We further decomposed the differences in life expectancy at birth between 2019 and 2020, and between 2020 and 2021, by the contribution of different age groups and two categories of causes of death: deaths identified as COVID-19 and all other deaths. From 2020 to 2021, the increase in mortality over age 60 years is attributable to deaths identified as COVID-19 and non-COVID-19 deaths (online supplemental figure S6). Between 2020 and 2021, more years are lost due to the increase in COVID-19-related mortality, for both sexes. The loss of years of life expectancy is concentrated in the 60–79 years age group, with little change in women in non-COVID-19 mortality. Among men, mortality in the age group 35–59 years from non-COVID-19 mortality seems to have improved when compared with 2020, but this could also reflect a more systematic coding of deaths as COVID-19 related (online supplemental table S4).

DISCUSSION

After over three and a half years since the beginning of the pandemic, the mortality burden due to COVID-19

across sub-Saharan Africa remains difficult to quantify. Taking advantage of a longstanding, rigorous death registration system from the city of Antananarivo, our study found several peaks of excess deaths in 2020–21, which were associated significantly with the waves of SARS-CoV-2 reported cases. By comparing trends during the prepandemic period (2016–19) and the pandemic one (2020–21), we estimated that all-cause excess mortality was 38.5 and 64.9 per 100 000 inhabitants in 2020 and 2021, respectively. Excess mortality reached over 50% during both the 2020 and 2021 waves. In sum, we estimated that there were 1179 excess deaths over the 2020–21 period, an estimate which is higher than the official 1069 COVID-19 deaths notified by the MoH for the entire country.⁸ The excess was even higher (1500) when excluding the excess deaths associated with the 2018–19 measles outbreaks, and twofold (2111) when no threshold was included in our calculation of relative change. This excess mortality resulted in a decline in life expectancy of 0.8 years in men and 1.0 years in women in 2021 but this decline is non-significant. The reduction in life expectancy was entirely attributable to increased risks of dying for both men and women above the age of 60 years and due to COVID-19 deaths rather than due to increases in other causes of death.

Table 2 Life expectancy at birth observed in 2019–21, predicted for 2020–21 based on past trends, in the absence of COVID-19, and decomposition of the differences in life expectancy at birth between the observed and predicted estimates

	Observed			Predicted based on 1990–2019		Difference in e0 and contribution in difference by age*	
	2019	2020	2021	2020	2021	2020	2021
Life expectancy at birth (years)							
Male	63.3	63.3	62.8	63.4	63.6	–0.14	–0.80
Female	68.7	68.9	68.0	68.8	69.0	0.03	–1.02
Under-five mortality (5q0—‰)							
Male	40	34	32	45	43	0.76	0.77
Female	38	30	29	39	37	0.58	0.59
Mortality in older children and adolescents (10q5—‰)							
Male	8	7	5	8	8	0.04	0.12
Female	8	4	5	6	6	0.10	0.03
Premature adult mortality ($_{45}q_{15}$ —‰)							
Male	314	314	306	316	316	0.15	0.42
Female	199	201	208	204	204	0.10	–0.04
Old-age mortality ($_{20}q_{60}$ —‰)							
Male	637	683	754	629	627	–0.94	–1.83
Female	517	543	592	513	509	–0.67	–1.38
Mortality rate above age 80 ($_{\infty}m_{80}$ —‰)							
Male	187	200	251	174	174	–0.16	–0.29
Female	170	182	199	174	174	–0.08	–0.22

*The last two columns display the difference in life expectancy at birth between the observed and expected values (in years), and these differences are decomposed into the contributions of the different age-specific rates, using the method by Arriaga.²³ Positive values in these last two columns refer to a decline in mortality, which was faster than expected based on trends in 1990–2019, while negative values refer to a slower progress than expected, or even an increase in mortality, possibly due to COVID-19 deaths.

Interestingly, the death rate mainly preceded the SARS-CoV-2 positivity rate during the first wave of SARS-CoV-2, which may indicate an ‘unsuitable’ screening strategy and the use of a case definition^{9 25} for suspected cases where MoH and WHO guidelines differed.²⁶ This may have led to a mismatch between waves because only few ‘true suspected cases’ were tested. In the second wave of COVID-19 (February–May 2021), the SARS-CoV-2 positivity rate preceded the waves of deaths. This may indicate an improvement in the screening strategy, enabling strong synchrony between laboratory data and virus circulation in Antananarivo, as previously found by Andriamandimby *et al.*²⁵ Indeed, the National Influenza Centre at IPM continued to receive specimens for influenza in 2020 and 2021 and laboratory tests showed no circulation of influenza viruses from March 2020 to mid-July 2021.²⁷ Our results also revealed that in the first half of 2020, the all-cause deaths in Antananarivo and national COVID-19 deaths were not synchronous. This may be explained by the fact that the first large SARS-CoV-2 outbreak occurred in the second highest populated city of Madagascar (Toamasina) in May 2020, followed a few weeks later by a major outbreak in Antananarivo (June 2020).^{9 25}

In the capital city of Antananarivo, we estimated an excess mortality of 38.51 and 64.91 per 100 000 inhabitants

in 2020 and 2021, respectively. These estimates are lower than estimates for Madagascar in a worldwide study using covariates pertaining both to the COVID-19 pandemic and to country-specific health-related metrics (125.4 per 100 000 inhabitants).²⁷ At the level of sub-Saharan African countries, this excess death is comparable to the excess death estimated for Eritrea, Burkina Faso and Ghana.²⁷ Compared with previous crises that have hit the capital city of Madagascar, the mortality shock observed in 2020–21 is less pronounced than other major crisis that have hit Antananarivo before, such as the urban famine and the resurgence of malaria in the mid-1980s. When comparing with the excess death in Antananarivo that occurred during the A(H1N1) pandemic in 2009, a similar impact on elderly people was observed.¹⁴

Our study is among the first to assess the impact of COVID-19 on the life expectancy of a sub-Saharan African population, based on local death registration systems. In contrast to many high-income countries, where reductions of more than an entire year of life expectancy at birth have been documented in 2020,²⁸ we found almost no change for that year (–0.14 for men and +0.03 for women). A faster decline in mortality before age 60 years than expected based on past trends could have offset the unfavourable evolution of mortality beyond age 60 years.

Countries where life expectancy at birth has decreased considerably include Russia, the USA, Italy and Spain²⁹; where populations are older and where baseline mortality rates are much lower in comparison with African populations. Mortality in Madagascar is still highly concentrated in the youngest age groups, and life expectancy remains dominated by variations in the chances of survival among children. Yet, the year 2021 was characterised by a 16% increase in the probability of dying between the ages of 60 and 80 years for women and a 20% increase for men in Antananarivo. The mortality rate over the age of 80 years increased by 14% for women and 44% for men. As observed elsewhere,³⁰ men appeared to have been more affected by the COVID-19 epidemic than women.

Compared with previous years, the excess mortality in Antananarivo was higher in 2021, reaching over 100% for 4 weeks. As a result, a substantial decrease in life expectancy at birth was observed, dropping by 0.8 and 1.0 years below the projected value for males and females, respectively. A similar situation was observed in Brazil where a decline in 2020 life expectancy at birth was estimated at 1.3 years in 2020 vs 1.8 years in the first 4 months of 2021.³¹ Several countries in Eastern Europe and the USA also witnessed sustained loss in life expectancy in 2021.³² Data on the impact of COVID-19 on life expectancy in other sub-Saharan African countries are needed to compare these estimates and shed light on the timing of the mortality shock in this region.

Our results highlight the granularity of Antananarivo's BMH death records as a powerful source to assess the burden of infectious diseases and the strengths and weaknesses of the Malagasy health system to face major threats such as the COVID-19 pandemic. Indeed, the estimated excess mortality in 2020 and 2021 could be due to the difficulty of finding intensive care unit beds for severe infections,³³ with mechanical ventilators and trained personnel, in addition to frequent disruptions in electricity supply observed regularly in LMICs.³⁴ The SARS-CoV-2 Beta variant (B.1.351) circulated in Madagascar from February 2021, preceding the beginning of the peak of mortality in 2021. Results from blood donors confirmed the contribution of this variant in the second COVID-19 wave that started in early 2021.³⁵ The Alpha, Beta and Delta variants of concern were known to be more transmissible and having caused more severe infections than the ancestral SARS-CoV-2.³⁶ In Qatar, patients infected with the Beta variant had an increased risk of progressing to severe disease and death compared with patients infected with the Alpha variant (B.1.1.7).³⁷ This could explain the higher excess of death observed in our study during the second wave when compared with the first one, combined with a vaccination strategy that was not effective at this time.³⁸ Optimal monitoring of variants and more studies on their severity and virulence in the general population are needed to better understand their burden.

Our study has some limitations. First, the Ambohidratrimo district—where the referral centre for severe

COVID-19 infections has been established at the Centre Hospitalier Universitaire Anosiala since 8 July 2020, totaling 442 244 inhabitants according to the 2018 census,¹⁶ does not fall in the six central districts of Antananarivo city nor the area covered by the BMH.³⁹ This may have led to an underestimation of excess mortality using BMH data; although all deaths that occurred among residents of the five central districts should be reported to the BMH, irrespective of the place of the occurrence of the death. Moreover, during the first waves of the pandemic, the virology unit at IPM was mainly focused on the diagnosis of SARS-CoV-2 due to logistic constraints and a lack of human resources, and this may have resulted in an underdiagnosis of other respiratory viral infections responsible for other causes of death. Similarly, a decrease in consultations was observed at health centres during the first and second waves of the pandemic,⁴⁰ which resulted in an under-reporting of other infectious diseases. Second, in our analysis, the estimation of excess mortality focused on the weeks when the excesses were most evident—using Farrington surveillance algorithm,¹⁷ which may induce an underestimation of mortality excess versus relative change method based on of P-scores.¹⁸ The comparison of our results with those of other countries may be biased because of this methodological choice. In other studies, negative binomial or Poisson regression modelling combined with Bayesian approaches or ensemble modelling techniques have been commonly used.^{1 7 27} In addition, between 2016 and 2020, Madagascar experienced other epidemics such as plague and measles that could have had an impact on the mortality of the population of Antananarivo.^{5 6} These epidemics raise our baseline mortality, although we also conducted a sensitivity analysis based on the average number of deaths per week during the pre-COVID-19 period without such peaks, revealing more excesses during the pandemic period.

CONCLUSION

Our findings indicate that the mortality burden of the COVID-19 pandemic in Antananarivo has been much higher than previously estimated, with excess deaths for the capital city being higher than the official count of COVID-19-related deaths for the entire country. The excess mortality was concentrated in older adults, with little impact on mortality among children and young adults. Our study also highlights the importance of local sources of death notification and the need to expand this system to other major cities in the country and use it for real-time surveillance to inform health policy makers. Strengthening local death registration systems in LMICs would allow more precise monitoring of changes in cause-specific mortality associated with COVID-19 and other potential future pandemics.

Author affiliations

¹Institut Pasteur de Madagascar, Antananarivo, Madagascar

²UMMISCO, Bondy, France

³Université Catholique de Louvain Centre de recherche en démographie et sociétés, Louvain la neuve, Belgium

⁴Bureau Municipal d'Hygiène, Commune Urbaine d'Antananarivo, Antananarivo, Madagascar

⁵UMR 224 MIVEGEC, IRD, Montpellier, France

⁶Department of Ecology and Evolutionary Biology, Princeton University, Princeton, New Jersey, USA

⁷Mahaliana Labs SARL, Antananarivo, Madagascar

⁸Institut Pasteur de Dakar, Dakar, Senegal

Twitter C Jessica Metcalf @CJEMetcalf and Jean-Michel Heraud @HeraudJeanMich

Acknowledgements The authors would like to acknowledge the BMH team in the Department of Water, Sanitation and Hygiene and the City of Antananarivo for their support and cooperation in data collection. We thank all involved team members from the Virology and Epidemiology and clinical research units (Mangahasimbola Reziky, Nasolo Frédéric Stanley, Randrianarivony Mamy Thomas desire) at IPM.

Contributors Conceptualisation: JHR, JMR, RR, BM, AD and J-MH. Data curation: JHR, JMR, RR and BM. Formal analysis: JMR and BM. Funding acquisition: RR, BM and J-MH. Methodology: JMR, RR, BM, AG and CJM. Project administration: JHR, AMR, VL, J-MH and PD. Resources: FR, NHR and SFA. Software and visualisation: JMR and BM. Supervision: RR, AG, VL, J-MH and PD. Writing—original draft: JMR, RR, BM, AD and JHR. Writing—review and editing: all authors contributed equally and accept final responsibility to submit for publication. JHR, JMR and BM had full access to the study data. Author acting as guarantor: PD.

Funding This work was supported by the Institut Pasteur de Madagascar (IPM), the Princeton Centre for Health and Wellbeing, the US Centers for Disease Control and Prevention (Cooperative Agreement Number: U51IP000812) and the US Agency for International Development, for Research, Innovation, Surveillance and Evaluation (RISE) Project Cooperative Agreement no. 72068719CA00001.

Disclaimer The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution 4.0 Unported (CC BY 4.0) license, which permits others to copy, redistribute, remix, transform and build upon this work for any purpose, provided the original work is properly cited, a link to the licence is given, and indication of whether changes were made. See: <https://creativecommons.org/licenses/by/4.0/>.

Author note J-MH and PD authors supervised this work equally.

ORCID iDs

Jean Marius Rakotondramanga <http://orcid.org/0000-0003-0490-7665>

Andres Garchitorena <http://orcid.org/0000-0001-6225-5226>

C Jessica Metcalf <http://orcid.org/0000-0003-3166-7521>

Jean-Michel Heraud <http://orcid.org/0000-0003-1107-0859>

REFERENCES

- Scortichini M, Schneider Dos Santos R, De' Donato F, *et al*. Excess mortality during the COVID-19 outbreak in Italy: a two-stage interrupted time-series analysis. *Int J Epidemiol* 2021;49:1909–17.
- Sharrow D, Hug L, You D, *et al*. Global, regional, and national trends in Under-5 mortality between 1990 and 2019 with scenario-based projections until 2030: a systematic analysis by the UN inter-agency group for child mortality estimation. *Lancet Glob Health* 2022;10:e195–206.
- Barmania S. Madagascar's health challenges. *Lancet* 2015;386:729–30.
- Lang E, Saint-Firmin P, Olivett M, *et al*. Analyse Du Système de Financement de la Santé À Madagascar pour Guider de futures Réformes, Notamment La CSU. Washington, DC. 2018.
- Randremanana R, Andrianavaoimanana V, Nikolay B, *et al*. Epidemiological characteristics of an urban plague epidemic in Madagascar, August–November, 2017: an outbreak report. *Lancet Infect Dis* 2019;19:537–45.
- Nimpa MM, Andrianirinarison JC, Sodjinou VD, *et al*. Measles outbreak in 2018–2019, Madagascar: epidemiology and public health implications. *Pan Afr Med J* 2020;35:84.
- Msemburi W, Karlinsky A, Knutson V, *et al*. The WHO estimates of excess mortality associated with the COVID-19 pandemic. *Nat* 2022;2022:1–8.
- Kiraeve SR, Mathieu E, Siemens F, *et al*. Lanthanide(III) complexes of Cyclen Triacetates and Triamides bearing tertiary amide-linked antennae. *Molecules* 2020;25:5282.
- Randremanana RV, Andriamandimby S, Rakotondramanga JM, *et al*. The COVID-19 epidemic in Madagascar: clinical description and laboratory results of the first wave, March–September 2020. *Influenza Other Respi Viruses* 2021;15:457–68. 10.1111/irv.12845 Available: <https://onlinelibrary.wiley.com/toc/17502659/15/4>
- Benn CS, Salinha A, Mendes S, *et al*. SARS-Cov-2 Serosurvey among adults involved in Healthcare and health research in guinea-Bissau, West Africa. *Public Health* 2022;203:19–22.
- Mwananyanda L, Gill CJ, MacLeod W, *et al*. Covid-19 deaths in Africa: prospective systematic postmortem surveillance study. *BMJ* 2021;372:n334.
- Masquelier B, Pison G, Rakotonirina J, *et al*. Estimating cause-specific mortality in Madagascar: an evaluation of death notification data from the capital city. *Popul Health Metr* 2019;17:8.
- Waltisperger D, Mesle F, Mandelbaum J. Economic crisis and mortality: the case of Antananarivo, 1976–2000. *Population (English Edition, 2002-)* 2005;60:199.
- Rajatonirina S, Rakotosolofo B, Rakotomanana F, *et al*. Excess mortality associated with the 2009 A(H1N1)V influenza pandemic in Antananarivo, Madagascar. *Epidemiol Infect* 2013;141:745–50.
- Rasambainarivo F, Rasaoanomenjanahary A, Rabarison JH, *et al*. Monitoring for outbreak-associated excess mortality in an African city: detection limits in Antananarivo, Madagascar. *Int J Infect Dis* 2021;103:338–42.
- Institut National de la Statistique. Troisième Recensement général de la population et de l'Habitation (Rgph-3). 2021. Available: <https://www.instat.mg/p/resultats-definitifs-du-rgph-3-2018-troisieme-recensement-general-de-la-population-et-de-lhabitation>
- Noufaily A, Enki DG, Farrington P, *et al*. An improved algorithm for outbreak detection in multiple surveillance systems. *Stat Med* 2013;32:1206–22.
- Serfling RE. Methods for current statistical analysis of excess pneumonia-influenza deaths. *Public Health Rep (1896)* 1963;78:494:494–506:.
- Cazelles B, Chavez M, Berteaux D, *et al*. Wavelet analysis of ecological time series. *Oecologia* 2008;156:287–304.
- Roesch A, Schmidbauer H. *WaveletComp: computational wavelet analysis*. 2018.
- Lee RD, Carter LR. Modeling and forecasting U. S. mortality. *J Am Stat Assoc* 1992;87:659.
- Auger N, Feuillet P, Martel S, *et al*. Mortality inequality in populations with equal life expectancy: Arriaga's decomposition method in SAS, STATA, and excel. *Ann Epidemiol* 2014;24:575–80.
- Arriaga EE. Measuring and explaining the change in life Expectancies. *Demography* 1984;21:83–96.
- R Core Team. R: A language and environment for statistical computing. 2020. Available: <https://www.r-project.org/>
- Andriamandimby SF, Brook CE, Razanajatovo N, *et al*. Cross-sectional cycle threshold values reflect epidemic Dynamics of COVID-19 in Madagascar. *Epidemics* 2022;38:100533.
- WHO COVID- 19: case definitions. 2020. Available: https://apps.who.int/iris/bitstream/handle/10665/333912/WHO-2019-nCoV-Surveillance_Case_Definition-20201-eng.pdf?sequence=1&isAllowed=y
- Wang H, Paulson KR, Pease SA, *et al*. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21. *The Lancet* 2022;399:1513–36.

- 28 Aburto JM, Schöley J, Kashnitsky I, *et al.* Quantifying impacts of the COVID-19 pandemic through life-expectancy losses: a population-level study of 29 countries. *Int J Epidemiol* 2022;51:63–74.
- 29 Islam N, Shkolnikov VM, Acosta RJ, *et al.* Excess deaths associated with COVID-19 pandemic in 2020: age and sex Disaggregated time series analysis in 29 high income countries. *BMJ* 2021;373:n1137.
- 30 Gebhard C, Regitz-Zagrosek V, Neuhauser HK, *et al.* Impact of sex and gender on COVID-19 outcomes in Europe. *Biol Sex Differ* 2020;11:29:29..
- 31 Castro MC, Gurzenda S, Turra CM, *et al.* Reduction in life expectancy in Brazil after COVID-19. *Nat Med* 2021;27:1629–35.
- 32 Schöley J, Aburto JM, Kashnitsky I, *et al.* Life expectancy changes since COVID-19. *Nat Hum Behav* 2022;6:1649–59.
- 33 Madagascar Government. National health emergency. 2021. Available: <https://www.presidence.gov.mg/actualites/conseil-des-ministres/1201-tatitry-ny-filan-kevity-ny-minisitra-natao-tamin-ny-alalan-ny-visioconference-ny-31-martsa-2021.html>
- 34 Gallifant J, Sharell D, Hashmi M, *et al.* Mechanical ventilators for Low- and middle-income countries: informing a context-specific and sustainable design. *Br J Anaesth* 2022;128:e279–81.
- 35 Razafimahatratra SL, Ndiaye MDB, Rasoloharimanana LT, *et al.* Seroprevalence of ancestral and beta SARS-Cov-2 antibodies in Malagasy blood donors. *Lancet Glob Health* 2021;9:e1363–4.
- 36 Davies NG, Jarvis CI, Edmunds WJ, *et al.* Increased mortality in community-tested cases of SARS-Cov-2 lineage B.1.1.7. *Nature* 2021;593:270–4.
- 37 Abu-Raddad LJ, Chemaitelly H, Ayoub HH, *et al.* Severity, Criticality, and fatality of the severe acute respiratory syndrome Coronavirus 2 (SARS-Cov-2) beta variant. *Clin Infect Dis* 2022;75:e1188–91.
- 38 Rasambainarivo F, Ramiadantsoa T, Raheinandrasana A, *et al.* Prioritizing COVID-19 vaccination efforts and dose allocation within Madagascar. *BMC Public Health* 2022;22:1–9.
- 39 Madagascar Government. TATITRY NY FILANKEVITRY NY MINISITRA NATAO TAMIN'NY ALALAN'NY « VISIOCONFERENCE » NY 08 JOLAY 2020. Cons. des Minist. 2020. Available: <https://www.presidence.gov.mg/actualites/conseil-des-ministres/907-tatitry-ny-filankevity-ny-minisitra-natao-tamin-ny-alalan-ny-visioconference-ny-08-jolay-2020.html>
- 40 Rasoanaivo TF, Bourner J, Randriamparany RN, *et al.* The impact of COVID-19 on clinical research for neglected tropical diseases (Ntds): A case study of Bubonic plague. *PLoS Negl Trop Dis* 2021;15:e0010064.

1	Supplementary materials
2	Excess mortality associated with the COVID-19 pandemic during the 2020 and 2021 waves in
3	Antananarivo, Madagascar
4	J.H. Rabarison MD ^{1*} , J.M. Rakotondramanga MSc ^{2,3,4,5*} , R. Ratovoson PhD ^{2#} , B. Masquelier PhD ⁶ , A.M.
5	Rasoanomenjanahary MD ⁷ , A. Dreyfus PhD ² , A. Garchitorena PhD ^{2,5} , F. Rasambainarivo PhD ^{8,9} , N.H.
6	Razanajatovo PhD ¹ , S.F. Andriamandimby PhD ¹ , C.J.E. Metcalf PhD ^{8,10} , V. Lacoste PhD ¹ , J-M. Heraud PhD ^{1q\$#} ,
7	P. Dussart PhD ^{1\$}
8	Content
9	Supplementary Methods S1–S3
10	Supplementary Figures S1–S6
11	Supplementary Tables S1–S4
12	
13	

14 **Supplementary Methods**

15 **Method S1. The Bureau Municipal d'Hygiène (BMH) of Antananarivo**

16 This office was created in 1916 and covers five of the six central districts of Antananarivo-city, corresponding to
 17 the district of Antananarivo-Renivohitra. Its role has been to provide free consultations, conduct vaccination
 18 campaigns, manage malaria prophylaxis, and isolate patients with highly infectious diseases. Since 1921, the BMH
 19 has also been in charge of home verification of deaths. Historically, this system of death verification was motivated
 20 by recurrent plague epidemics but was maintained for the purpose of disease and outbreak surveillance. The 6th
 21 district (Ambohimananarina) does not fall in the area covered by the BMH for historical reasons; this locality was
 22 an autonomous urban commune under the 1st Republic, from 1958–72. Community and hospital deaths are
 23 recorded in a single register as they are reported to the BMH. These certificates are mandatory to obtain burial
 24 authorization. This system contributes to maintaining a high completeness of death registration, estimated at over
 25 90% since the 1970s.[1]

26

27

28 **Method S2: Relative change method based on P-scores**

29 The expected deaths were derived from the period 2016 to 2019, and the corresponding relative change was
 30 computed as follows:[2]

$$31 \quad \text{Relative change (\%)} = \frac{\{\text{Reported deaths}\} - \{\text{Average expected deaths}\}}{\{\text{Average expected deaths}\}} * 100.$$

32 A relative change of 100%, in a given week in 2020 (or 2021), would mean that the death count for that week
 33 was double from the expected death count.

34

35

36 **Method S3: Mathematical background to cross-wavelet analyses**

37 Cross-wavelet analyses were performed twice in order to detect and quantify the existing relationships between
 38 (1) the log-transformed of all-cause deaths in Antananarivo and national COVID-19 deaths (supplementary Figure
 39 S1A and S1C),[3] and (2) the transformed square root of SARS-CoV-2 test positivity rate by the IPM laboratory
 40 and all-cause death rate in Antananarivo, (Supplementary Figure S1B and S1D), as non-stationary time series. The
 41 concepts of cross-wavelet coherency and wavelet phase difference are natural generalizations of the basic wavelet
 42 analysis tools that enable us to appropriately deal and conclude with the time-frequency dependencies between
 43 two time series.[4]

44 Cross-Wavelet Transform (XWT) of two time series, $x(t)$ and $y(t)$ is defined as

$$45 \quad W_{xy} = W_x W_y^*,$$

46 Where W_x and W_y are the wavelet transforms of x and y , respectively. The cross-wavelet power (XWP) is

$$47 \quad (XWP)_{xy} = |W_{xy}|.$$

Here, we can interpret the wavelet power spectrum to depict the local variance of a time series; the cross-wavelet power of two time series depicts the local covariance between these time series at each time and frequency (the inverse form of scale/period). Furthermore, the cross-wavelet power informs us about a quantified indication of the similarity of power between two time series.

Then, given two time series $x(t)$ and $y(t)$, their complex wavelet coherency can be defined as ρ_{xy} by:

$$\rho_{xy} = \frac{S(w_{xy})}{[S(|w_x|^2)S(|w_y|^2)]^{1/2}},$$

where S denotes a smoothing operator in both time and scale (period). Without the smoothing, coherency would be identically one at all scales and times. That needs an appropriate choice of parameters combination. So, Bartlett window was used both for smoothing in time and scale (period) direction, without a detrending technique but with a default method of generating surrogate time series, white-noise.[5]

Then, the complex wavelet coherency can be written in polar form, as $\rho_{xy} = |\rho_{xy}|e^{i\Phi_{xy}}$:[6]

- The absolute value of the complex wavelet coherency is called the wavelet coherency and is defined as,

$$Coherency = R_{xy} = \frac{|S(w_{xy})|}{[S(|w_x|^2)S(|w_y|^2)]^{1/2}},$$

with $0 \leq R_{xy} \leq 1$ across time and scale direction.

Thus, the cross-wavelet coherence of a complex wavelet is,

$$Coherence = Coherency^2$$

- The angle of the complex coherency is called phase-difference (phase lead of x over y), i.e.

$$\Phi_{xy} = \left(\frac{\text{Im}(S(w_{xy}))}{\text{Re}(S(w_{xy}))} \right).$$

Thus, a phase-difference of zero indicates that the time series move together at the specified time-frequency; if $\Phi_{xy} \in (0, \frac{\pi}{2})$, then the series move in phase, but x leads y ; if $\Phi_{xy} \in (-\frac{\pi}{2}, 0)$, then it is y that is leading x . A phase-difference of π (or $-\pi$) indicates an anti-phase relation; if $\Phi_{xy} \in (\frac{\pi}{2}, \pi)$, then y is leading; x is leading if $\Phi_{xy} \in (-\pi, -\frac{\pi}{2})$. This is illustrated by arrows directions as in Figure 3.[6]

References

- Masquelier B, Pison G, Rakotonirina J, *et al.* Estimating cause-specific mortality in Madagascar: an evaluation of death notification data from the capital city. *Popul Health Metr* 2019;**17**:8.
- Serfling RE. Methods for Current Statistical Analysis of Excess Pneumonia-Influenza Deaths. *Public Heal Reports* 1963;**78**:494.
- Mathieu E, Ritchie H, Rod s-Guirao L, *et al.* Coronavirus Pandemic (COVID-19). *Our World Data* 2020.
- Aguiar-Conraria L, Soares MJ. The Continuous Wavelet Transform: A Primer. 2011. Available: <https://econpapers.repec.org/RePEc:nip:nipewp:16/2011>
- Cazelles B, Chavez M, Berteaux D, *et al.* Wavelet analysis of ecological time series. *Oecologia* 2008;**156**:287–304.
- Roesch A, Schmidbauer H. WaveletComp: Computational Wavelet Analysis. 2018. Available:

82

83

<https://cran.r-project.org/package=WaveletComp>

Supplementary Figures

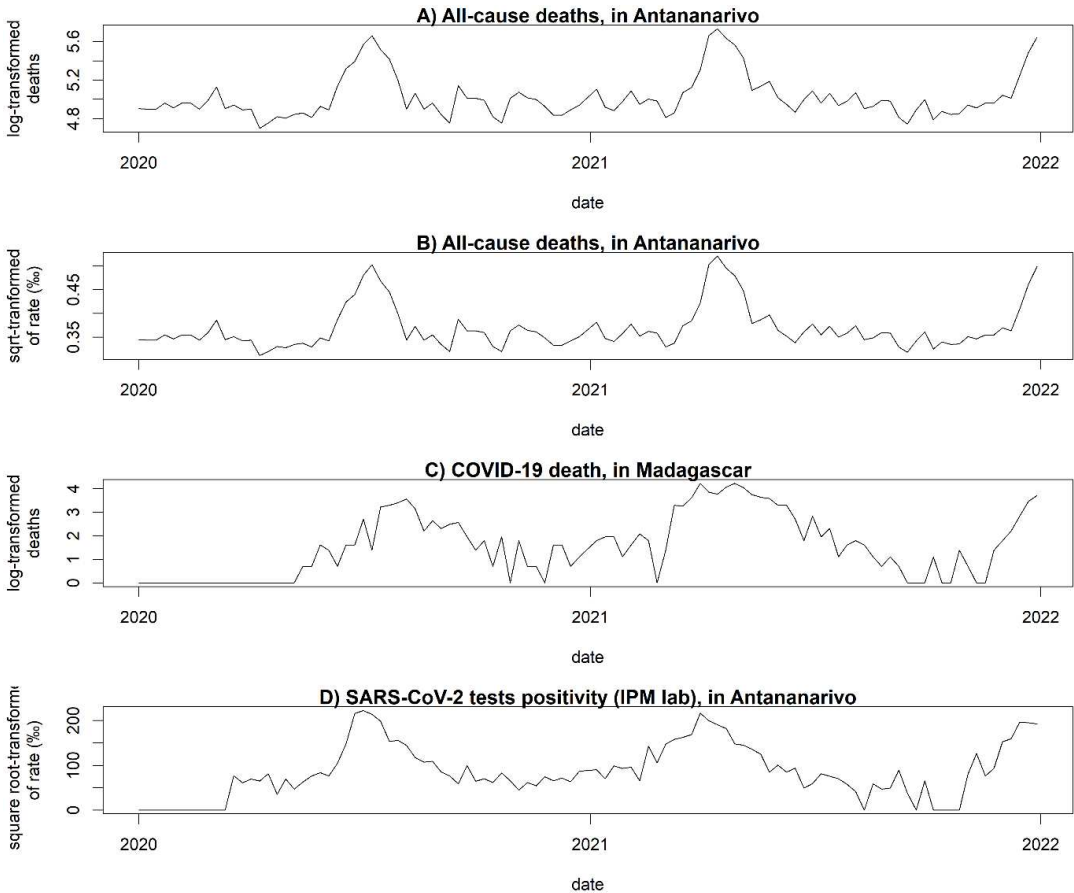


Figure S1. Temporal trends from 2020–21 of transformed data used for the wavelet analyses, cross-wavelet coherence and phase-difference: the log-transformed of all-cause deaths in Antananarivo and national COVID-19 deaths (panels A and C),[3] and the square root-transformed of SARS-CoV-2 test positivity rate by the IPM laboratory and all-cause death rate in Antananarivo (panels B and D).

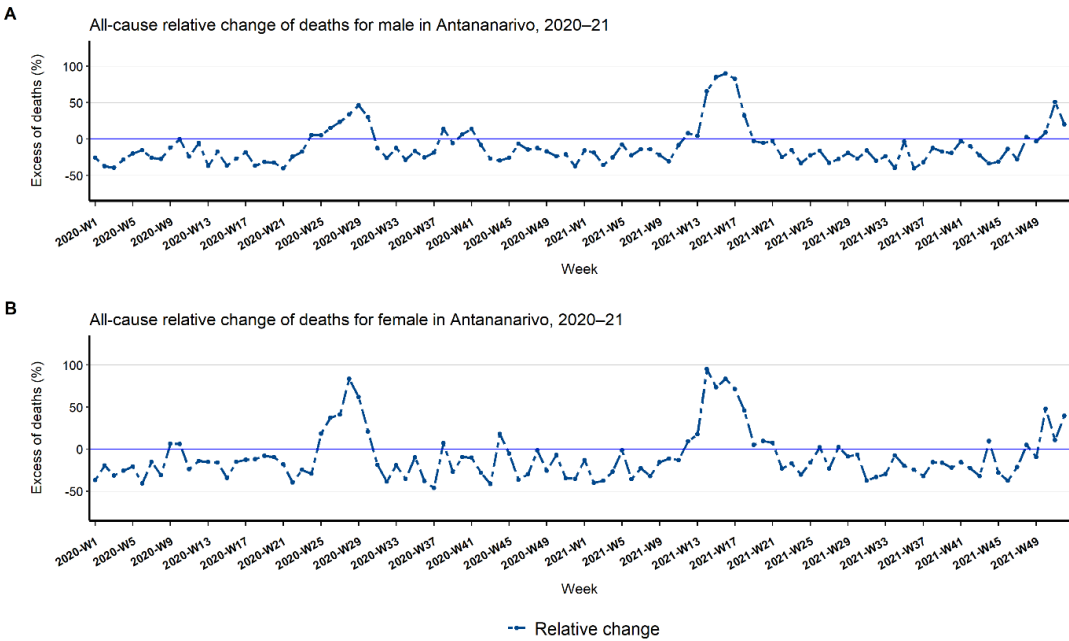


Figure S2: Weekly excess mortality by sex: for (A) Male and (B) Female deaths.

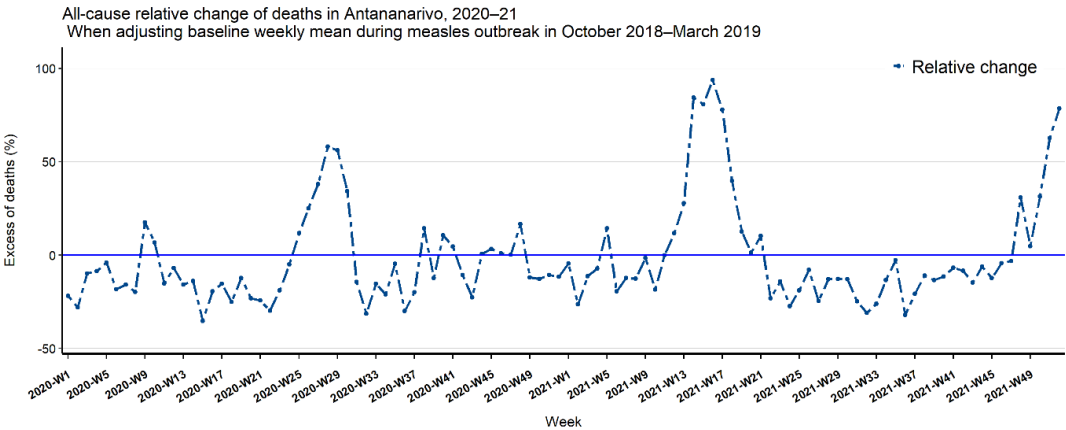


Figure S3. Weekly temporal trends, in five districts of Antananarivo from 2020–21. All-causes excess deaths were calculated using 2016–19 adjusted deaths as baseline (death from October 2018 to March 2019 was not considered due to measles outbreak affecting Antananarivo). Significant all-cause excess mortality was estimated during waves of COVID-19 in both 2020 and 2021 in Antananarivo: totalling 1,499 deaths for 32 weeks. (95 % CI is indicated in grey)

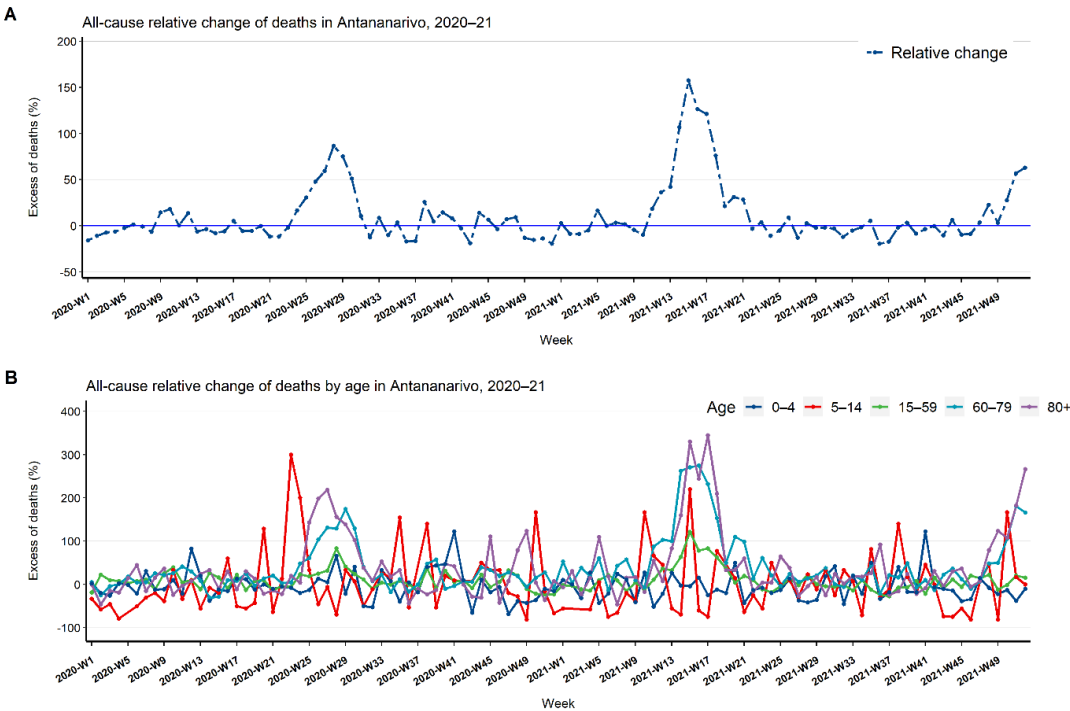
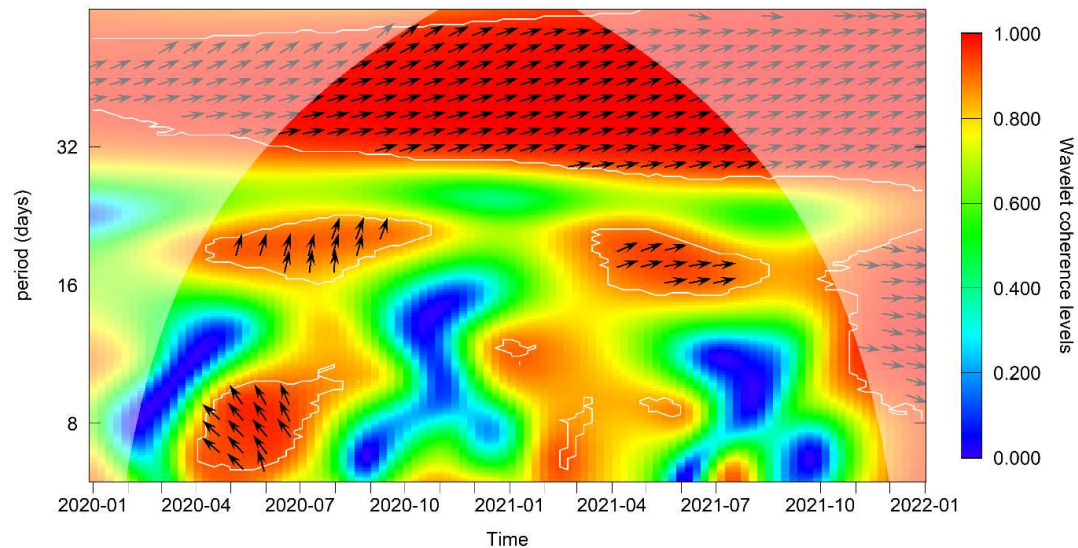


Figure S4. Weekly temporal trends using a relative change method based on P-scores, in five districts of Antananarivo from 2020–21. (a) All-cause excess mortality using 2016–19 crude deaths as baseline years, totalling 2,111 deaths for 51 weeks. (b) All-cause excess mortality by age group using 2016–19 crude deaths as baseline years; the excess mortality was estimated at over 200% for the elderly (80+) for each wave (no death record was observed for age group 5–14 age during one week in 2020 and two weeks in 2021). Supplementary Table S1 Supplementary materials representing weekly all-cause deaths by age group supports this figure.



128

129 **Figure S5: Cross-wavelet coherence and phase-difference of the all-cause deaths in Antananarivo and**
130 **national COVID-19 deaths.**[3] This figure shows that these two time series were out of phase, phase-differences
131 $\in (\frac{\pi}{2}, \pi)$; and the weekly national COVID-19 deaths led the Antananarivo deaths. However, from the 2nd half of
132 2020 to September 2021, the all-cause deaths in Antananarivo were mainly in phase and led the national COVID-
133 19 deaths, phase-differences $\in (0, \frac{\pi}{2})$. The significant coherence level is ranked from blue–red colour scale, and
134 statistically significant wavelet coherence is marked by the white contour plots when p-value < 0.05. This figure
135 is supported by the Method S3, Figure S1A and S1C.

136

137

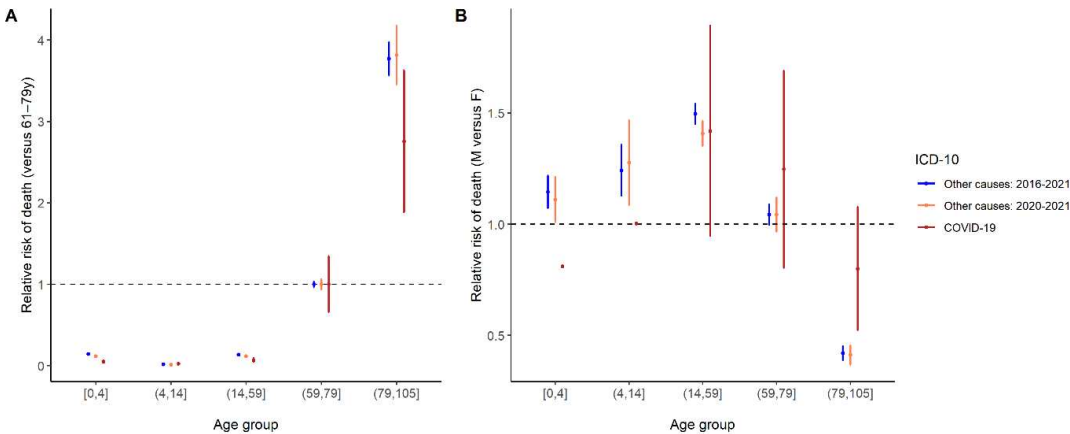


Figure S6. Relative risk ratios of COVID-19 and other causes of death, for each age group, (A) versus 60–79y, and (B) for Male (versus Female). The vertical bars represent confidence intervals. In 2020–2021, COVID-19 infection induced a significantly higher risk of death for the elderly aged 80+ compared to persons aged 60–79 years of age, with a risk ratio (RR) = 2.8 (IC95% 1.9–3.6) (panel A). A similar relative risk of dying from COVID-19 was observed for men and women in these two age groups, in comparison to other causes of deaths in the same period. That showed lesser risk for men 80+ years of age, RR = 0.4 (0.36–0.46) (panel B).

146 **Supplementary Tables**

147 **Table S1: Weekly mortality data in Antananarivo, 2016–2021.**

Year	Age	Mean	SD
2016	[0,4]	11.1	4.74
2016	(4,14]	3.02	1.63
2016	(14,59]	61.27	7.97
2016	(59,79]	33.17	5.87
2016	(79,105]	12.4	3.81
2017	[0,4]	11.73	3.75
2017	(4,14]	2.9	1.49
2017	(14,59]	62.31	12.15
2017	(59,79]	35.83	7.48
2017	(79,105]	12.25	4.41
2018	[0,4]	17	10.14
2018	(4,14]	3.92	2.51
2018	(14,59]	68.87	15.96
2018	(59,79]	37.69	8.43
2018	(79,105]	12.5	3.62
2019	[0,4]	16.12	5.9
2019	(4,14]	3.98	1.96
2019	(14,59]	69.23	11.44
2019	(59,79]	42.62	8.04
2019	(79,105]	15.19	4.29
2020	[0,4]	13.21	4.13
2020	(4,14]	3.18	1.82
2020	(14,59]	70.62	12.99
2020	(59,79]	46.96	19.25
2020	(79,105]	16.63	9.38
2021	[0,4]	12.75	3.92
2021	(4,14]	2.96	1.63
2021	(14,59]	71.21	15.09
2021	(59,79]	57.29	25.45
2021	(79,105]	19.1	9.49

148

149

150

151

152

153

154

155

Table S2: Weekly mortality data and excess deaths in Antananarivo, 2020-2021. Data shows estimated all-age excess mortality using positive lower bounds of relative change, the difference between weekly reported deaths in 2020–2021 and the upper bounds of 95%CI of the average expected deaths.

Week	Year	Reported deaths	Average expected deaths (2016–2019)			Death excesses by relative change
			Mean	CI Low	CI Up	
1	2020	135	160.25	134.22	186.28	-27.53
2	2020	134	150.25	110.81	189.69	-29.36
3	2020	134	144.50	82.02	206.98	-35.26
4	2020	143	152.50	121.41	183.59	-22.11
5	2020	136	139.25	111.80	166.70	-18.42
6	2020	143	141.00	83.80	198.20	-27.85
7	2020	143	144.25	111.40	177.10	-19.26
8	2020	134	143.50	101.07	185.93	-27.93
9	2020	147	128.50	115.22	141.78	3.68
10	2020	169	143.25	128.94	157.56	7.26
11	2020	135	134.25	91.96	176.54	-23.53
12	2020	140	123.25	97.29	149.21	-6.18
13	2020	133	142.00	104.82	179.18	-25.77
14	2020	134	138.75	121.79	155.71	-13.94
15	2020	110	119.50	68.64	170.36	-35.43
16	2020	116	123.25	102.57	143.93	-19.41
17	2020	124	118.00	89.36	146.64	-15.44
18	2020	122	129.50	95.91	163.09	-25.20
19	2020	127	134.25	123.59	144.91	-12.36
20	2020	129	129.50	91.10	167.90	-23.17
21	2020	123	139.25	116.03	162.47	-24.29
22	2020	138	156.25	115.99	196.51	-29.78
23	2020	133	135.75	107.33	164.17	-18.98
24	2020	170	145.75	112.54	178.96	-5.01
25	2020	204	156.00	129.31	182.69	11.66
26	2020	220	148.75	121.45	176.05	24.97
27	2020	262	164.25	138.58	189.92	37.95
28	2020	287	153.75	125.93	181.57	58.07
29	2020	249	142.00	124.52	159.48	56.13
30	2020	225	148.75	129.86	167.64	34.22
31	2020	181	164.00	116.39	211.61	-14.47
32	2020	134	153.50	111.23	195.77	-31.55
33	2020	158	145.50	104.14	186.86	-15.45
34	2020	134	149.25	128.65	169.85	-21.11
35	2020	143	138.25	126.46	150.04	-4.69
36	2020	127	152.75	124.10	181.40	-29.99
37	2020	116	138.75	132.47	145.03	-20.02
38	2020	171	136.00	122.44	149.56	14.33
39	2020	150	143.25	115.53	170.97	-12.27
40	2020	150	131.00	117.07	144.93	3.50
41	2020	147	135.75	131.00	140.50	4.63
42	2020	124	127.50	115.00	140.00	-11.43
43	2020	116	143.00	116.34	169.66	-31.63
44	2020	150	131.75	96.90	166.60	-9.96

45	2020	160	150.25	121.89	178.61	-10.42
46	2020	151	156.75	125.61	187.89	-19.63
47	2020	148	138.00	87.97	188.03	-21.29
48	2020	138	126.25	87.07	165.43	-16.58
49	2020	126	145.25	95.89	194.61	-35.26
50	2020	126	148.75	75.48	222.02	-43.25
51	2020	133	154.25	108.00	200.50	-33.67
52	2020	140	173.75	102.02	245.48	-42.97
1	2021	165	160.25	134.22	186.28	-11.42
2	2021	137	150.25	110.81	189.69	-27.78
3	2021	132	144.50	82.02	206.98	-36.23
4	2021	145	152.50	121.41	183.59	-21.02
5	2021	162	139.25	111.80	166.70	-2.82
6	2021	141	141.00	83.80	198.20	-28.86
7	2021	149	144.25	111.40	177.10	-15.87
8	2021	146	143.50	101.07	185.93	-21.48
9	2021	123	128.50	115.22	141.78	-13.25
10	2021	129	143.25	128.94	157.56	-18.13
11	2021	159	134.25	91.96	176.54	-9.93
12	2021	168	123.25	97.29	149.21	12.59
13	2021	202	142.00	104.82	179.18	12.73
14	2021	287	138.75	121.79	155.71	84.32
15	2021	308	119.50	68.64	170.36	80.79
16	2021	279	123.25	102.57	143.93	93.84
17	2021	261	118.00	89.36	146.64	77.98
18	2021	228	129.50	95.91	163.09	39.80
19	2021	163	134.25	123.59	144.91	12.48
20	2021	170	129.50	91.10	167.90	1.25
21	2021	179	139.25	116.03	162.47	10.18
22	2021	151	156.25	115.99	196.51	-23.16
23	2021	141	135.75	107.33	164.17	-14.11
24	2021	130	145.75	112.54	178.96	-27.36
25	2021	148	156.00	129.31	182.69	-18.99
26	2021	162	148.75	121.45	176.05	-7.98
27	2021	143	164.25	138.58	189.92	-24.71
28	2021	158	153.75	125.93	181.57	-12.98
29	2021	139	142.00	124.52	159.48	-12.84
30	2021	146	148.75	129.86	167.64	-12.91
31	2021	159	164.00	116.39	211.61	-24.86
32	2021	135	153.50	111.23	195.77	-31.04
33	2021	138	145.50	104.14	186.86	-26.15
34	2021	147	149.25	128.65	169.85	-13.45
35	2021	146	138.25	126.46	150.04	-2.69
36	2021	123	152.75	124.10	181.40	-32.20
37	2021	115	138.75	132.47	145.03	-20.71
38	2021	133	136.00	122.44	149.56	-11.08
39	2021	148	143.25	115.53	170.97	-13.44
40	2021	120	131.00	117.07	144.93	-17.20
41	2021	131	135.75	131.00	140.50	-6.76

42	2021	127	127.50	115.00	140.00	-9.28
43	2021	128	143.00	116.34	169.66	-24.55
44	2021	140	131.75	96.90	166.60	-15.96
45	2021	136	150.25	121.89	178.61	-23.86
46	2021	143	156.75	125.61	187.89	-23.89
47	2021	143	138.00	87.97	188.03	-23.95
48	2021	155	126.25	87.07	165.43	-6.30
49	2021	150	145.25	95.89	194.61	-22.92
50	2021	190	148.75	75.48	222.02	-14.42
51	2021	242	154.25	108.00	200.50	20.70
52	2021	283	173.75	102.02	245.48	15.28

156
157
158

Table S3. Estimated all-cause excess mortality in 2020–2021. Relative changes and expected deaths were calculated based on 2016–2019 baseline mortality adjusted by deaths during measles outbreaks (October 2018 to March 2019).

Year	Relative change level (%)	Nb. of weeks of excess	Adjusted expected deaths (2016–2019) ¹		Reported deaths (2020–2021)		Sum death excesses
			Mean	Range (min-max)	Mean	Sum	
2020	< 50	14	139	114-164	174	2,442	297
2020	≥ 100	2	148	142-154	268	536	195
2021	< 50	10	129	114-139	177	1,767	272
2021	≥ 100	6	132	118-150	277	1,66	736
Total		32	137	114-164	200	6,405	1,500

¹ Expected deaths were adjusted with deaths occurring during measles outbreak (October 2018-March 2019).
Nb=number

166 **Table S4: Contribution of deaths identified as COVID-19 and those associated with other causes of deaths to changes in life expectancy at birth between 2019 and**
167 **2020, and between 2020 and 2021.**

Age group	Males: e0(2020) – e0(2019)		Females: e0(2020) – e0(2019)		Males: e0(2021) – e0(2020)		Females: e0(2021) – e0(2020)	
	Covid-19 deaths	All other causes	Covid-19 deaths	All other causes	Covid-19 deaths	All other causes	Covid-19 deaths	All other causes
0–1	0.00	0.22	-0.01	0.07	0.00	0.01	0.00	0.06
1–4	0.00	0.19	0.00	0.44	0.00	0.12	0.00	0.03
5–14	0.00	0.08	0.00	0.21	0.00	0.05	0.00	-0.06
15–34	-0.02	0.04	-0.02	0.04	-0.04	0.08	-0.03	0.09
35–59	-0.13	0.27	-0.11	0.09	-0.31	0.62	-0.27	0.13
60–79	-0.17	-0.30	-0.19	-0.10	-0.48	-0.24	-0.55	-0.11
80+	-0.02	-0.04	-0.03	-0.09	-0.06	-0.09	-0.14	0.00
Total	-0.35	0.45	-0.36	0.66	-0.90	0.55	-0.99	0.13

168 The e_{xt} is the residual at age x and time t .