Long-term trends in seasonality of mortality in Madagascar: the role of the epidemiological transition

Benjamin-Samuel Schlüter[*], Masquelier Bruno[†], Metcalf Jessica [‡]
Anjarasoa Rasoanomenjanahary[§]

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Abstract

Objectives Seasonal patterns of mortality have been identified in Sub-Saharan Africa but their changes over time are not well documented. Based on death notification data from Antananarivo, the capital city of Madagascar, this study assesses seasonal patterns of all-cause and cause-specific mortality by age groups and evaluates how these patterns changed over the period 1976-2015.

Methods Monthly numbers of deaths by cause were obtained from deaths registers maintained by the Municipal Hygiene Office in charge of delivering burial permits. Generalized Additive Mixed regression models (GAMM) were used to detect seasonal patterns, with months and years introduced as random intercepts and random slopes.

Results Among children, risks of dying were the highest during the hot and rainy season, but the seasonality in child mortality significantly reduced since the mid-1970s, due to declines in the burden of infectious diseases and nutritional deficiencies. In adults aged 60 and above, all-cause mortality rates are the highest in the dry and cold season, due to peaks in cardiovascular diseases, with little change over time. Changes in the seasonality within broad categories of causes of death have been modest.

Conclusion Shifts in disease patterns brought by the epidemiological transition, rather than changes in seasonal variations in cause-specific mortality, are the main drivers of trends in the seasonality of all-cause mortality.

[*]University of Louvain (UCLouvain), Belgium
[†]University of Louvain (UCLouvain), Belgium
[‡]Princeton University, USA
[§]Bureau Municipal d'Hygiène de la Commune Urbaine d'Antananarivo, Madagascar

1 Background

Deaths are not evenly distributed over the course of the year; in many parts of the world they exhibit strong seasonal variation, especially among children and the elderly. The underlying drivers are varied. Many aspects of human biology relevant to health status are seasonal. For example, vitamin D metabolism and sunlight have been suggested as important drivers of seasonality in immune function (Stevenson et al. 2015). Food intake can also vary substantially seasonally, from fluctuations in access to fruit and vegetables through to manifesting as a hungry season in the most severe cases, where poor rural families that are unable to maintain body weight and function throughout the year (Devereux et al. 2013). Both non-infectious and infectious causes of mortality will be modulated by such underlying biology. For non-infectious causes of mortality, seasonal fluctuations in temperature may modulate associated risk factors (such as the effects of temperature on blood pressure, and blood pressure on strokes); and seasonal fluctuations in behavior may alter psychological conditions (e.g. depression) or exposure to pollutants (Mackenbach et al. 1992). For infectious diseases, climatic variables may drive additional seasonality for a range of pathogens, via their effects on vector life-cycles, how infectious particles fall out of the air for directly transmitted pathogens, or by how flooding shapes transmission (Metcalf et al. 2017). Seasonal patterns of human behavior have also been shown to be a key driver of infections, with seasonal aggregation due to school terms (Bjørnstad et al. 2002) or seasonal migration (Ferrari et al. 2008) increasing the magnitude of measles transmission.

The drivers of seasonal variation in mortality are subject to change over time, as i) improvements in socioeconomic conditions, ii) epidemiological shifts, and iii) climate change can directly alter the dominant causes of death, or shift their distribution over the course of the year. Taking each in turn, first, in western countries, there is some evidence of a reduction in the seasonality of mortality in recent decades, partly because of the spread of central heating and improvements in housing (Gemmell et al. 2000, Carson et al. 2006, Lerchl 1998). Second, shifts in the hierarchy of causes of death (epidemiological shifts) can also drive trends in the seasonality in mortality, because seasonal variations are larger for some diseases than for others. Seasonal variation is characteristics of many infectious and parasitic diseases (including malaria), cardiovascular diseases, respiratory diseases, and acute gastroenteritis (Jaffar et al. 1997, Kynast-Wolf et al. 2006), but rare for neonatal disorders and neoplasms (Nakaji et al. 2004). (Currie and Schwandt 2013). Third, climate change is also affecting the seasonality of mortality, e.g., via increases in mortality in the summertime due to the increased frequency of heatwaves (Doyon et al. 2008).

With few exceptions (Jaffar et al. 1997, Delaunay et al. 2001, Kynast-Wolf et al. 2006), the literature on seasonal variation in mortality in Sub-Saharan Africa is particularly patchy, especially when it comes to analyzing cause-specific mortality, or long-term changes. This is because analysing seasonal patterns requires statistical series of deaths tabulated by months, for which death registers are the preferred source of data. However, very few countries in Sub-Saharan

Africa have a comprehensive system of civil registration and vital statistics in place. Often less than half of all deaths are registered at the national level, and causes of death are rarely established (Mikkelsen et al. 2015). As a result, few countries in Sub-Saharan Africa have high-quality data on causes of death, apart from geographically defined populations monitored in Health and Demographic Surveillance Sites (HDSS). Some studies based on HDSS data in Africa have highlighted profound associations between temperature or rainfall and all-cause mortality but they were somewhat limited by the relatively short length of the retrospective periods, the absence of disaggregation by causes of death and their concentration in rural areas (Mrema et al. 2012, Diboulo et al. 2012, Azongo et al. 2012).

In Antananarivo, the capital city of Madagascar, a unique data source provides the opportunity to examine seasonality in mortality over a long period of time, including for specific causes of death taken separately. The registration of death was introduced in 1921 in the Municipal Hygiene Office (henceforth BMH for Bureau Municipal d'Hygine), in response to a major plague epidemic. Death certificates are needed for burial permits, and clandestine burials are rare as cemeteries are guarded. All records covering the period from 1976 to 2015 were transcribed from registers maintained by the BMH to build a database. Previous research has shown that this death notification system can be considered complete (Waltisperger et al. 1998, Masquelier et al. 2014). Cause-specific mortality fractions derived from these registers are consistent with epidemiological models (Masquelier et al. forthcoming).

In this study, we capture the seasonal patterns of mortality for infants, children aged 1-4, older children and adults aged 5-59 years, and the population aged 60 and above. We also evaluate whether these seasonal patterns have changed over time over the last 40 years. We hypothesize that the seasonality of deaths in childhood has attenuated because the share of communicable diseases has reduced, and the burden of neonatal disorders has increased. Based on the literature related to high-income countries, we anticipate a reduction in the seasonality of mortality among older adults. We also examine whether changes in seasonal variations can be ascribed to changes in the seasonality of cause-specific mortality, or shifts in the hierarchy of causes of death.

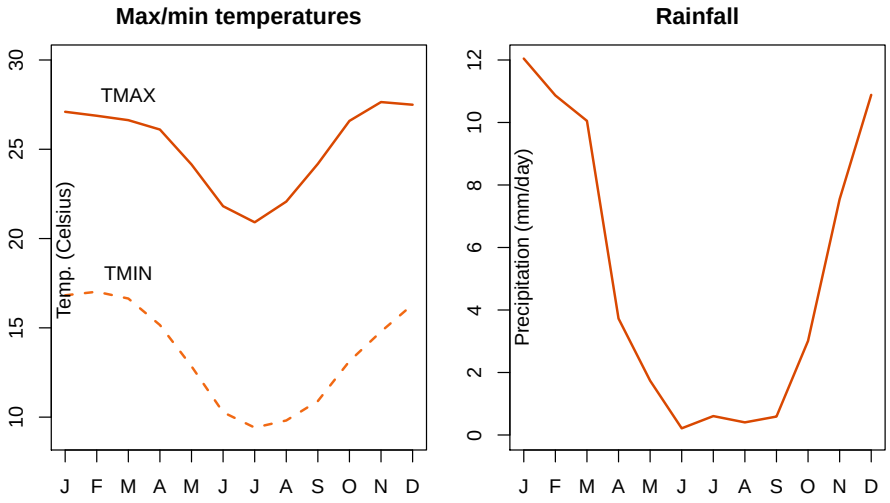
2 Methods

2.1 Setting

Antananarivo is located in the central plateau of Madagascar and culminates at an altitude of 1280m. It has a subtropical climate with a cold and dry season from May to October (with average minimal temperature around 11^oC) and a hot and rainy season from November to April (with average maximal temperature around 27^oC). Meteorological data displayed in Figure 1 illustrate the sharp contrast in maximum/minimum temperatures and rainfall between

seasons. January-February is the lean season, with a spike in the prices of rice and a drop in overall food consumption (**?**).

Figure 1: *Monthly means of daily maximum/minimum temperatures and rainfall in Ivato station (over the period 1976-2015). Sc: DGHCN /daily.*



Since the 1950s, climate change has led to a rise in temperatures in Madagascar, with pronounced increases in daily maximum temperatures in the dry season (Tadross et al. 2008). Dry spells have lengthened and the rainy season has been delayed (DGM 2008). The frequency of extreme events such as cyclones, floods and droughts is also increasing. All these changes are likely to modify seasonal patterns of mortality.

2.2 Data sources

This study is based on data relative to 249 421 residents of Antananarivo-city who died between 1976 and 2015. This corresponds to the central administrative sector of Antananarivo-city, covering the district of Antananarivo-Renivohitra and an estimated 1.03 million inhabitants in 2009 (estimates from the 2018 census were not available at the time of the study).

All deaths that occur within this area should be reported in the Bureau Municipal de l'Hygiène (BMH). About 60% of deaths occur at home. In this case, relatives of the deceased contact the BMH, and a physician is sent to the house of the deceased to establish a cause, based on the information provided by the family on the symptoms and circumstances preceding the death, as well as the medical documents available. For deaths occurring in the hospitals or clinics, the reports are filled by the medical personnel and transmitted to the BMH by relatives. More than 80% of deaths are reported on the day of death

or the day after (Waltisperger et al. 1998). The completeness of death reporting among adults was higher than 90% in the intercensal period 1975-1993. In more years, it was not possible to estimate completeness due to the lack of a recent census, but under-five mortality rates inferred from the BMH were consistent with trends derived from Demographic and Health Surveys (Masquelier et al. forthcoming).

Causes of death were first coded according to the 9th revision of the International Statistical Classification of Diseases (ICD-9). In order to group causes of deaths in broad categories, we used the hierarchical cause-of-death list established by the Global Burden of Disease (GBD) Study (Naghavi et al. 2017). This list has 4 levels. The first level distinguishes between (a) communicable, maternal, neonatal, and nutritional diseases, (b) non-communicable diseases, and (c) injuries. The second level refers to 21 broad categories, such as, for example, diarrhea, lower respiratory, and other common infectious diseases among one group of causes. The third and fourth levels refer to more detailed causes of death, such as, for example, intestinal infectious diseases (level 3) and typhoid fever (level 4). For this study, we considered the second level of the GBD hierarchy. All ICD 9 codes were mapped to a GBD cause of death. Some ICD codes were considered as "garbage codes". This refers not only to causes identified as "undefined" in the specific ICD chapters, but also deaths attributed to causes which should not be considered as initial causes, such as dehydration or septicemia. We used a simplified garbage code redistribution algorithm to map these codes to acceptable GBD causes. In total, 31.4% of deaths had to be redistributed. This redistribution is presented in the Appendix and described in detail elsewhere (Masquelier et al. forthcoming).

2.3 Statistical analyses

Mortality rate ratios associated with months are obtained from a Generalized Additive Mixed Model using a Negative Binomial distribution to account for overdispersion. The model includes a penalized regression spline (Wood 2006) to model long-term trend and avoid over-fitting, month as random effect to model seasonality and year as random slope to assess any change in seasonality, after stratifying by age groups. Age groups consisted in infants (less than 1 year old), young children (1 to 4 years old), older children and young adults (5 to 59 years olds) and people aged 60 or above. We used the Bayesian (BIC) Information Criteria to choose the best model among the model with penalized splines for the trend only (model 1), the model with random intercepts for months (model 2) and the model with random slopes and random intercepts (model 3). Retaining models that minimized the BIC with a difference of more than 10 (Kass and Raftery 1995) allowed us to characterize first, if seasonality was present and second, if it was changing over time. Because of the unequal number of days in a month, we multiplied each monthly death count by 30.4375 and divided by the number of days in each month. The full model (model 3) can be expressed as follows:

$$y_t \sim Poi(\ \alpha_{j[i]} + \beta_{j[i]} Year_i + s(t_i)\ )$$

$$\begin{pmatrix} \alpha_j \\ \beta_j \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_\alpha \\ \mu_\beta \end{pmatrix}, \begin{pmatrix} \sigma_\alpha^2 & \rho_{\sigma_\alpha \sigma_\beta} \\ \rho_{\sigma_\alpha \sigma_\beta} & \sigma_\beta^2 \end{pmatrix} \right)$$

where y_t are monthly counts of deaths, *s()* is a penalized spline, $j \in \{Jan., Feb.,.., Dec.\}, Year_i \in \{-20, -19, .., 0, 1, .., 19, 20\}$ where 0 represents 1996, the middle of the analysis period and t is a continuous variable $\in \{1, 2, .., 480\}$ reflecting the count of month.

We evaluated goodness-of-fit by visual inspection of the deviance residuals, considering that a good fit was obtained if 95% of the deviance residuals were between -2 and 2 standard deviations and no big outliers were present. All analyses were conducted using the R version 3.5.2 statistical software.

2.4 Ethical considerations

Ethical concerns regarding the free and informed consent of participants are not relevant here as the study participants are deceased persons. Ethical clearance was not sought because the dataset used for this study does not contain any identifiable information of study participants.

3 Results

Out of the 249,421 notified deaths over the 40 years studied, 37,775 (15%), 35,138 (14%), 101,111 (41%) and 75,266 (30%)[1] consisted of infants, children aged 1-4, older children and adults aged 5-59, and the population aged 60 or above, respectively.

Due to shifts in the age structure of the population and the decline in under-five mortality, the two younger age groups experienced a downward trend while the two older age groups showed an upward trend in their monthly mortality counts (Figure 2). In addition, the regular ups and downs in these time series suggest that seasonality was present. The amplitude of these monthly variations seems to have reduced over time for infants and young children.

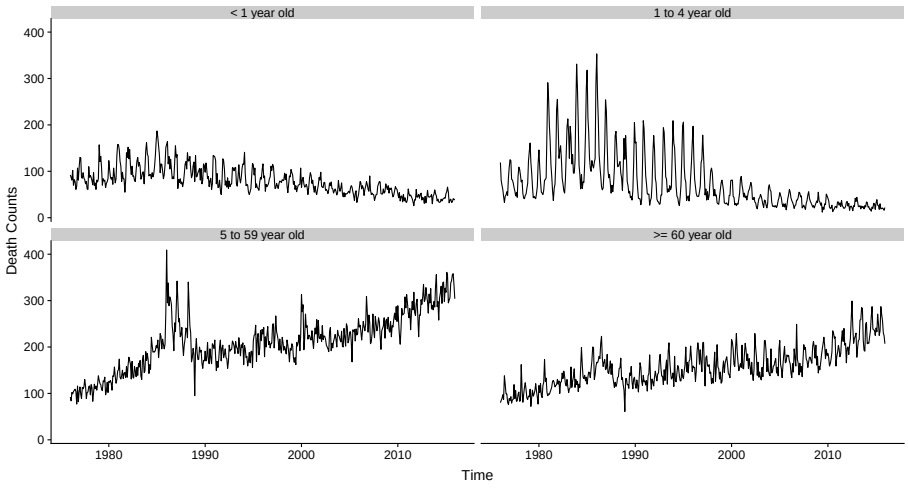
3.1 Seasonal patterns of all-cause mortality

In order to visually inspect if seasonality was present, we used seasonality plots (Figure 3). We divided the analysis period into three periods of equal length (13 to 14 years) to evaluate if seasonality was changing over time.

Figure 3a and 3b highlight that seasonality was present in the mortality of infants and children aged 1-4. This is easily spotted from the U-shape of

[1]The four age groups do not sum up to 249,421 as they were 131 death certificates that did not contain the date of birth or death.

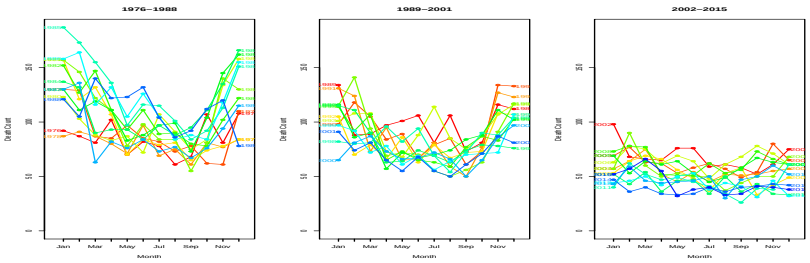
Figure 2: Monthly Mortality Counts by Age Group, over Time



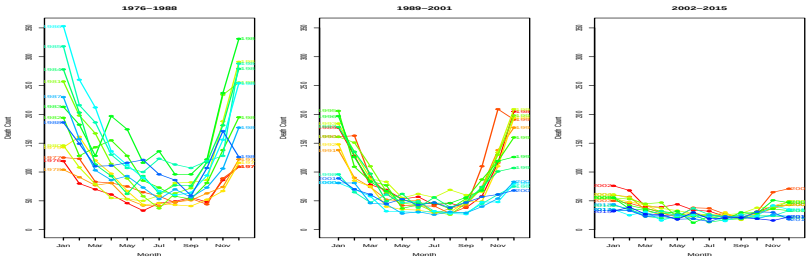
monthly mortality counts. Overall, 60% of all under-five deaths occurred in the hot and rainy season from November to April. However, seasonality seems to have reduced in recent years. Considering older children and adults aged 5-59, no regular pattern in mortality was observed on a yearly basis. Mortality of the population aged 60 and above exhibited seasonality with the dry season characterized by higher death counts.

Generalized Additive Mixed regression models (GAMM) allow us to test if seasonality was present and changed over time. Comparing our models according to the BIC (Appendix A.1), only the age group of children aged 1 to 5 experienced changes in the seasonality of mortality. That is, the full model (model 3) had a lower BIC than model 2 (with random intercepts only) and the difference was larger than 10. Among infants and people aged 60 and above, model 2 provided the best fit according to our criteria, suggesting that they experienced a constant seasonality over the analysis period. However, it should be highlighted that, when considering infants aged less than 1, the model allowing for changes in seasonality (model 3) was close to outperform the model reflecting constant seasonality. By contrast, mortality of adults aged 5-59 was better modelled by a simple penalized spline (model 1), suggesting that seasonality of mortality was not observed for this age group. We present in Figure 4 the random coefficients associated with the full model (model 3) allowing for changing seasonality in all age groups, despite the fact that it does not always provide the best fit. We do that in order to be able to compare random intercepts across age groups, and also because the fact that some random slopes are significant is informative. As we assumed a Negative Binomial distribution, the results are expressed in terms of rate ratios (RRs) and refer to the mid-period (1996).

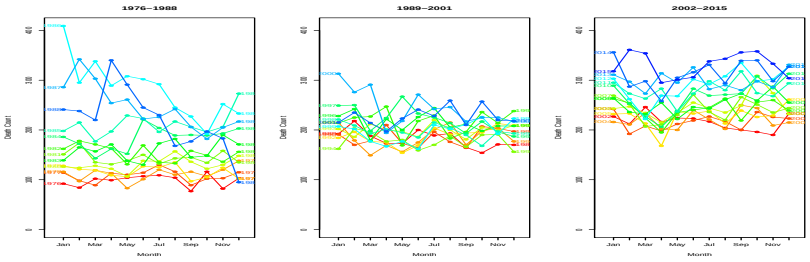
Figure 3: Seasonality plots, by age groups, Antananarivo (1976-2015)



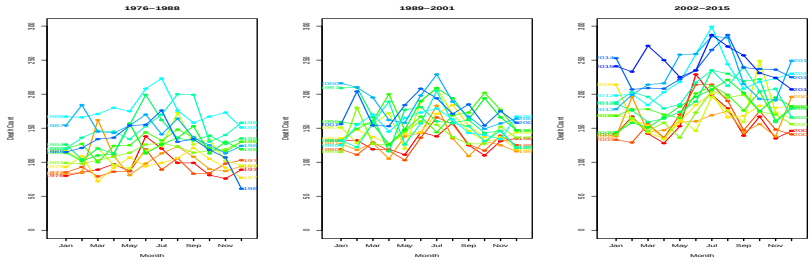
(a) Seasonal plots, < 1 year old



(b) Seasonality plot, 1 to 4 years old

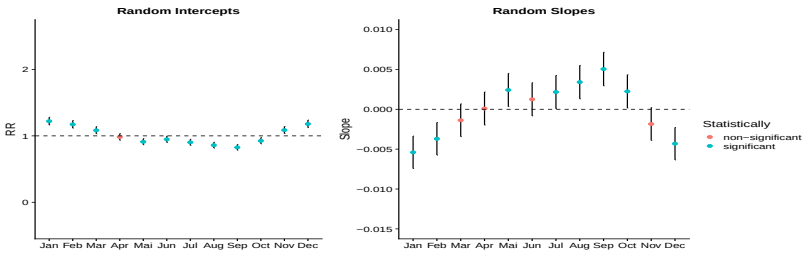


(c) Seasonality plot, 5 to 59 years old

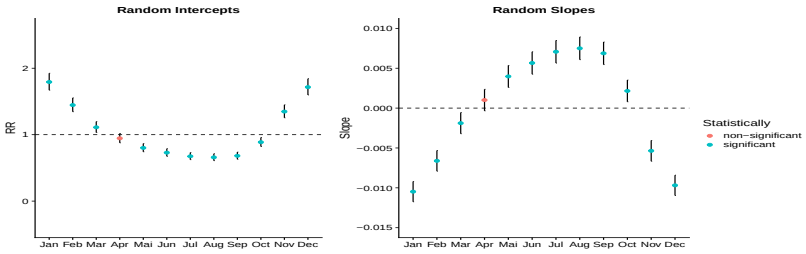


(d) Seasonality plot, >= 60 years old

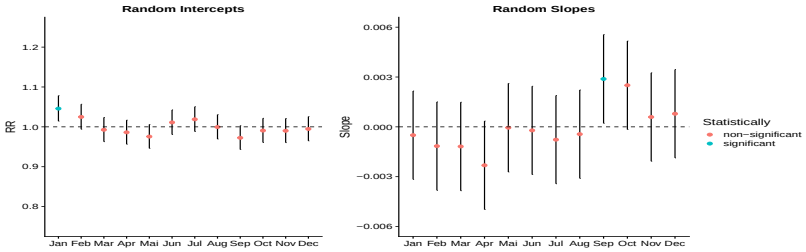
Figure 4: Mortality rate ratios from a NB GAM Model (model 3), stratified by age group



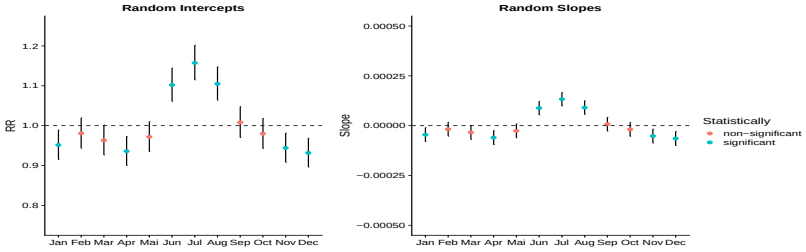
(a) < 1 year old



(b) 1 to 4 years old



(c) 5 to 59 years old



(d) >= 60 years old

Different scales are used for the y-axis. Scales for Figure 2a and 2b are the same. Scales for Figure 2c and 2d are the same for random intercepts but different for random slopes.

Month effects for infants reflect a slight U-shape pattern (Figure 4a) as was already highlighted in Figure 3a. Five months have RRs that are significantly higher than the average monthly rate, and six months have RRs that are significantly lower. In 1996, the higher mortality RRs were January and December, estimated at 1.22 (95% CI: 1.16-1.28) and 1.18 (95% CI: 1.12-1.24), respectively. The lower RR was estimated for September with 0.83 (95% CI: (0.78-0.87). We reiterate that the full model does not outperform model 2 (with random intercepts only), even though some random slopes are statistically different from 0.

Random intercepts for young children exhibit a clear U-shape with mortality RRs reaching 1.79 (95% CI: 1.67-1.92), 1.44 (95% CI: 1.34-1.55), 1.35 (95% CI: 1.25-1.55) and 1.72 (95% CI: 1.60-1.84) for January, February, November and December 1996, respectively. In other words, mortality rates estimated in December are approximately twice those estimated in September, as compared with 1.78 in infants. The random slopes show the exact reverse trend than that observed for the random intercepts (comparing the right side and left side of Figure 4b). Months that are characterized by a high RR have a statistically significant negative slopes, and vice versa. In other words, the difference of RR between months reduces over time.

Mortality among children aged 5 years and above and young adults aged less than 60 does not reflect any seasonal pattern as all months but January show RRs that are not statistically significantly different from one (Figure 4c). This is in line with what has been observed in Figure 3c.

The seasonality of mortality for the oldest age group was characterized by a slight inverse U-shape. It is the reverse pattern of what was observed in Figures 4a and 4b (also note the change of scales). Despite being relatively close to one, the RR were statistically significantly different from one. The RRs for June, July and August 1996 were 1.10 (95% CI: 1.06-1.15), 1.16 (95% CI: 1.11-1.20) and 1.11 (95% CI: 1.06-1.17), respectively. Random slopes for June, July and August suggest that the peak associated with dry season has increased over time, although the full model with changing seasonality does not outperform the reduced one.

3.2 Seasonal patterns of major causes of deaths

We defined major cause of death as GDB causes consisting of more than 5 percent of death of a given age group experiencing seasonality in the previous section. We then ran the three different models, again using the BIC to select the best model (Table 1).

None of the major causes of death showed varying seasonality over time. Four others did not showed any seasonality. These were nutritional disorders and other non-communicable diseases for children aged less than one year and diarrhea, lower respiratory, and other common infectious diseases and neoplasms for people aged 60 or above. Six major causes exhibited constant seasonality. Figure 5 displays the monthly random effects (from model 2) associated with these causes of death.

Table 1: Seasonality of major causes of death, by age groups

Age group	Main GBD codes	Model 1	Model 2	Model 3
[0,1)	Diarrhea, lower respiratory, and other common infectious diseases	3663	3510	3503
	Neonatal disorders	3375	3373	3380
	Nutritional deficiencies	2354	2269	2277
	Other non-communicable diseases	2067	2075	2087
[1,5)	Diarrhea, lower respiratory, and other common infectious diseases	4047	3825	3827
	Nutritional deficiencies	3438	3187	3197
[60,Inf)	Cardiovascular diseases	3961	3852	3864
	Diabetes, urogenital, blood and endocrine diseases	2582	2566	2578
	Diarrhea, lower respiratory, and other common infectious diseases	3070	3063	3075
	Neoplasms	2707	2712	2724

No seasonality
Constant seasonality
Changing seasonality

Values inside the cells are BIC values associated to each major cause, age group and model.

For infants, diarrhea, lower respiratory, and other common infectious diseases show random intercepts reflecting a U-shape with higher and lower RRs during the rainy and dry season, respectively. The same is true for nutritional deficiencies in this age group. The maximum RRs are attained in January and December and equal 1.36 (95% CI: 1.23-1.50) and 1.33 (95% CI: 1.21-1.47) for the diarrhea, lower respiratory, and other common infectious diseases and 1.63 (95% CI: 1.37-1.95) and 1.54 (95% CI: 1.29-1.84) for nutritional deficiencies. The minimum RRs are attained in August and September 1996 and are estimated at 0.75 (95% CI: 0.67-0.83) and 0.74 (95% CI: 0.67-0.82) for diarrhea, lower respiratory, and other common infectious diseases. Months exhibiting the lowest RRs were July and September 1996 for nutritional deficiencies with 0.67 (95% CI: 0.57-0.83) and 0.65 (95% CI: 0.52-0.81).

Considering children aged 1 to 5, seasonality of mortality associated with these two broad causes of death also exhibit this pattern but with a larger amplitude. The difference between RRs of adjacent months is greater than for children less than 1 year old. RRs for nutritional deficiencies reach their higher values at 2.09 (95% CI: 1.77-2.46) and 1.84 (95% CI: 1.59-2.17) in January and December 1996, respectively.

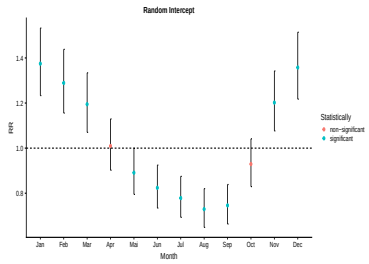
For people aged 60 or above, cardiovascular diseases have coefficients for June, July, August and September that are 1.11 (95% CI: 1.06-1.17), 1.19 (95% CI: 1.13-1.25), 1.14 (95% CI: 1.08-1.20) and 1.05 (95% CI: 1.01-1.11), respectively. Diabetes, urogenital, blood and endocrine diseases have a statistically significant RR in July reaching 1.22 (95% CI: 1.12-1.33)

4 Discussion

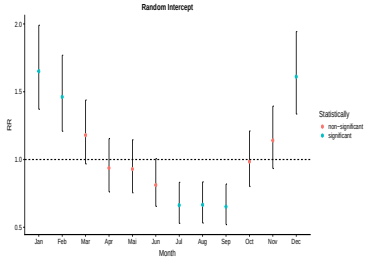
We observed a strong seasonality of mortality in Antananarivo, especially among children under age 5 and the elderly.

In infants, the seasonality of deaths is dominated by the association between

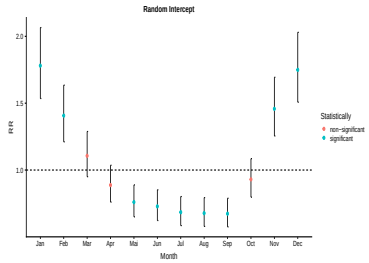
Figure 5: Mortality rate ratios from a NB GAM Model (model 2), stratified by major cause and age group



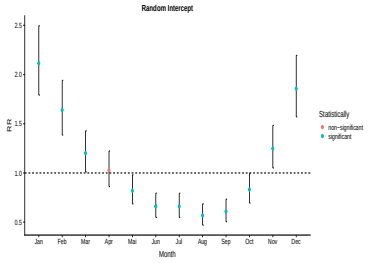
(a) Diarrhea, lower respiratory, and other common infectious diseases, < 1 year old



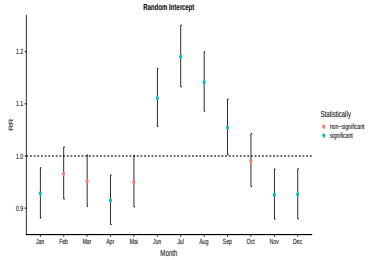
(b) Nutritional deficiencies, < 1 year old



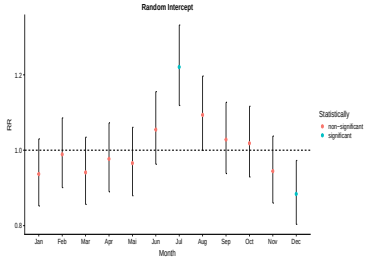
(c) Diarrhea, lower respiratory, and other common infectious diseases, 1 to 5 years old



(d) Nutritional deficiencies, 1 to 5 years old



(e) Cardiovascular diseases, >= 60 years old



(f) Diabetes, urogenital, blood, and endocrine diseases, >= 60 years old

Different scales are used for the y-axis.

hot temperatures and rainfall, and two groups of causes: (1) diarrhea, lower respiratory, and other common infectious diseases, and (2) nutritional deficiencies. Together, these two causes accounted for 48% of deaths below age 1 in 1976, but this percentage declined to 36% in 2015, as a result of the epidemiological transition. By contrast, the percentage of deaths due to neonatal disorders and other non-communicable diseases (mostly congenital birth defects) increased from 46% to 54% in the period 1976-2015. As mortality rates from these two last groups of cause do not exhibit a seasonality, the shift in disease patterns in infant mortality explains why there is some indication that seasonality tends to reduce in this age group. Random slopes associated with months in our all-cause mortality model were negatively correlated with random effects. However, the changes over time are modest, and overall, a model assuming a constant seasonality in infant mortality is the one to be preferred statistically.

Child mortality (1-4 years) has always been more sensitive to environmental factors than infant mortality, and we observe here particularly strong seasonal patterns at these ages. As in children, this seasonality of all-cause mortality is largely due to two groups of causes: (1) diarrhea, lower respiratory, and other common infectious diseases, and (2) nutritional deficiencies. Taken together, these two groups of causes accounted for 89% of child deaths in 1976 and 58% in 2015. As a result, monthly variations are more pronounced than in infants, and changes over time in the seasonality are also faster. Overall, there is strong evidence of attenuation in seasonality of all-cause child mortality, but this is driven by the reduction in the burden of these two causes, rather than changes in the seasonality of mortality attributable to these causes.

Finally, in adults aged 60 and above, seasonal patterns in all-cause mortality are in line with those of deaths from cardiovascular diseases and a group of causes made of diabetes, urogenital, blood and endocrine diseases. Most deaths from this second group were assigned to diabetes mellitus and chronic kidney disease. The percentage of deaths due to this group of causes has slightly augmented, from 9% to 11%. The percentage of deaths due to cardiovascular diseases has also increased over the period, from 46% in 1976 to 53% in 2015 among the elderly. This again reflects the normal path of the epidemiological transition, and is also associated with aging of the population. It explains why random slopes were positively correlated with random effects in this age group, suggesting that seasonality in all-cause mortality has accentuated in older adults. Yet changes over time have been modest and when comparing models with the BIC value, the model with constant seasonality is to be preferred, as is the case for infant mortality.

Our study had some limitations. We did not include temperature and have no data on air pollution, which could be major confounders. Biases could also arise due to our redistribution of some deaths in GBD cause categories, but we accounted for the seasonality in our redistribution.

There are several ways to expand the study. According to (Dostie et al. 2002), the seasonal fluctuations in the price of rice are smaller in the capital city of Antananarivo than elsewhere in the country. Since fluctuations in the price of rice are highly correlated to fluctuations in specific causes of death,

it could be that seasonal variations for some specific causes of death are more pronounced in smaller cities and in the rural areas where variation in the price of rice are high. There are also large variations in climate, malaria endemicity and vaccination coverage across the country. This calls for an extension of the analysis to other cities, where the death notification systems are also in place. The database could also be used to study associations between temperatures and peaks in some cause-specific mortality, allowing for some lags. This could inform early warning systems.

A Appendices

A.1 BIC values

Table 2: Seasonality all causes of death, by age groups

	Age group			
	[0,1)	[1,5)	[5,59)	[60,Inf)
Model 1	4107	4548	4557	4440
Model 2	3928	4072	4556	4320
Model 3	3921	4048	4563	4333

No seasonality
Constant seasonality
Changing seasonality

Values inside the cells are BIC values associated to each age group and model.

A.2 Redistribution of garbage codes

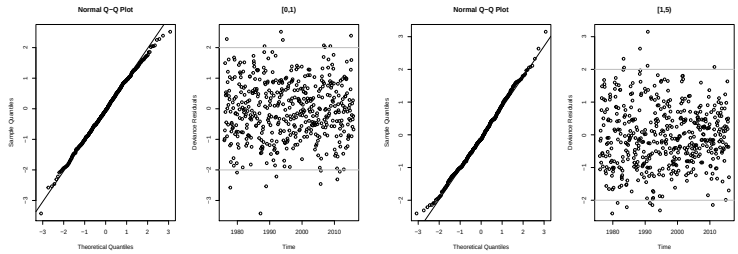
Table 3 lists the steps taken to redistribute garbage codes and shows how the percentage of deaths assigned to garbage codes declines progressively. The first column, refers to Level 1 garbage codes, which are ICD codes that should be redistributed across likely causes of deaths that span the three broad Levels 1 of the GBD cause list. For example, deaths coded "Cardiac arrest" (427.5 in ICD-9), could be redistributed across communicable, non-communicable diseases, and injuries. The second column refers to Level 2 Garbage codes, that is, cases for which an acceptable Level 1 cause can be assigned. For example, deaths coded 440.9 ("Generalized and unspecified atherosclerosis") should be redistributed within non-communicable diseases only.

	Level 1 garbage codes	Level 2 garbage codes
Before any redistribution	23.8%	7.6%
Step 1: Ill-defined cardiovascular diseases are redistributed to Ischemic heart disease and Other cardiovascular and circulatory diseases using the age-specific correction factors for "High ill-defined coding countries" available in WHO (2014). The corresponding ICD-9 codes are 427.1, 427.4, 427.5, 428, 429.0, 429.1, 429.2, 429.9, and 440.9.	15.6%	7.6%
Step 2: ICD-9 from Chapter XVI (symptoms, signs and ill-defined conditions) are redistributed pro rata across all GBD causes (excluding injuries) within each age group, sex, decade of death, and season of death.	5.2%	6.5%
Step 3: Injuries undetermined whether accidentally or purposefully inflicted (ICD-9 codes E980-989) or ICD-9 from Chapter XVII (injury and poisoning) are redistributed pro rata by age and sex to the GBD categories for intentional and unintentional injury.	5.0%	2.6%
Step 4: All remaining ICD-9 codes mapped to Level 1 or 2 garbage codes in the GBD 2016 are redistributed pro rata by age, sex, season and year of death to acceptable GBD causes.	0%	0%

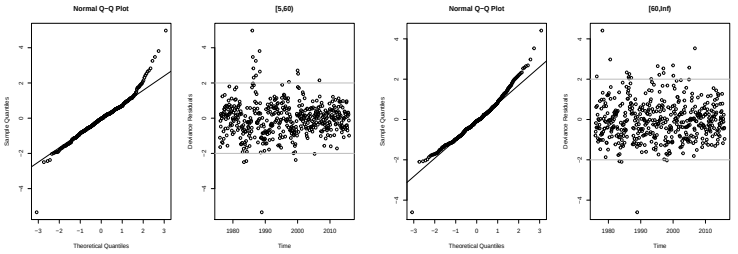
Table 3: Redistribution of garbage codes

A.3 Residual diagnostic

Figure 6: Deviance Residuals GAMM regressions, by age groups



(a) < 1 year old (b) 1 to 4 years old



(c) 5 to 59 years old (d) >= 60 years old

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