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Peer-reviewed author version

COX, Bianca; Gasparrini, Antonio; Catry, Boudewijn; Delcloo, Andy; BIJNENS, Esmee; VANGRONSVELD, Jaco & NAWROT, Tim (2016) Mortality related to cold and heat. What do we learn from dairy cattle?. In: ENVIRONMENTAL RESEARCH, 149, p. 231-238.

DOI: 10.1016/j.envres.2016.05.018
Handle: http://hdl.handle.net/1942/22570

Mortality related to cold and heat. What do we learn from dairy cattle?

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Abbreviations:

CI – confidence interval; Df – degrees of freedom; DLNM – distributed lag non-linear model; NO_2 – nitrogen dioxide; O_3 – ozone; MMT – minimum mortality temperature; PM_{10} – particulate matter with diameter less than 10 μm; RR – relative risk; SD – standard deviation

Highlights

- Epidemiologic studies in animals may be relatively free from confounding.
- High and low ambient temperatures increase the risk of mortality in dairy cattle.
- Heat effects are acute and cold effects are delayed and prolonged.
- Temperature effects go beyond short-term mortality displacement.
- The temperature-mortality association in dairy cattle corroborates human findings.

Abstract

Extreme temperatures are associated with increased mortality among humans. Because similar epidemiologic studies in animals may add to the existing evidence, we investigated the association between ambient temperature and the risk of mortality among dairy cattle. We used data on 87,108 dairy cow deaths in Belgium from 2006 to 2009, and we combined a case-crossover design with distributed lag non-linear models. Province-specific results were combined in a multivariate meta-analysis. Relative to the estimated minimum mortality temperature of 15.4°C (75th percentile), the pooled cumulative relative risks over lag 0–25 days were 1.26 (95% CI: 1.11, 1.42) for extreme cold (1st percentile, -3.5°C), 1.35 (95% CI: 1.19, 1.54) for moderate cold (5th percentile, -0.3°C), 1.09 (95% CI: 1.02, 1.17) for moderate heat (95th percentile, 19.7°C), and 1.26 (95% CI: 1.08; 1.48) for extreme heat (99th percentile, 22.6°C). The temporal pattern of the temperature-mortality association was similar to that observed in humans, i.e. acute effects of heat and delayed and prolonged effects of cold. Seasonal analyses suggested that most of the temperature-related mortality, including cold effects, occurred in the warm season. Our study reinforces the evidence on the plausibility of causal effects in humans.

Key words

cold; dairy cattle; DLNM; heat; mortality

Funding sources

This work was supported by EU Program "Ideas" (ERC-2012-StG 310898), Flemish Research Council (FWO G073315N), and BOF Hasselt University grant. Dr Gasparrini was supported by Medical Research Council UK (Grants ID: MR/M022625/1 and G1002296).

Conflict of interest

All authors declare no actual or potential competing financial interests.

1. Introduction

It is well recognized that in developed countries, the major health consequences of climate change will be due to extreme weather events (IPCC, 2012). Daily variations in ambient temperature are associated with daily variations in human morbidity and mortality, with increased health risks at both ends of the temperature distribution (Gasparrini et al., 2015b; Guo et al., 2014).

Also farm animals such as cattle are known to suffer from temperature extremes. Studies have mainly focused on heat-related reductions in feed intake, milk yield, growth rate and reproductive performance (Kadzere et al., 2002). Despite the major economic burden of livestock mortality, the effect of temperature on death rates has received less attention (Mader et al., 2001; Stull et al., 2008; Vitali et al., 2009; Crescio et al., 2010; Morignat et al., 2014; Morignat et al., 2015). On-farm death of dairy cows has increased in recent years and there is large uncertainty about the exact causes of death (Thomsen and Houe, 2006). As lactating dairy cows create a large quantity of metabolic heat, they tend to be much more tolerant for low than for high temperatures (Kadzere et al., 2002). Consequently, effects of cold have not been studied much. Nevertheless, few studies reported cold-related decreases in milk yield (Brouček et al., 1991) and increases in mortality (Morignat et al., 2015; Stull et al., 2008).

The investigation of dairy cow mortality in relation to environmental risk factors might add to the epidemiological evidence on human health risks. Despite the recognition that animals could be useful sentinels for human (van der Schalie et al., 1999), the full potential of linking animal and human health information has not been realized (Rabinowitz and Conti, 2013). Reasons appear to include the professional segregation of human and animal health communities, the separation of human and animal surveillance data, and evidence gaps in the linkages between human and animal responses to environmental health hazards (Rabinowitz and Conti, 2013).

Animal populations have the advantage that they are less subject to exposure misclassification than human populations (Reif, 2011). Also confounding factors such as occupational exposures, lifestyle factors, housing construction, and the use of air conditioning, are absent or limited in animal species such as dairy cows.

In this study, we investigated whether the short-term association between temperature and mortality in humans can be corroborated in an animal population, to further elaborate on the causality of this association. We applied a multivariate meta-analysis on province-specific associations in Belgium, allowing for non-linear as well as delayed temperature effects through the use of distributed lag non-linear models (DLNM) (Gasparrini et al., 2010). A DLNM has the advantage of providing cumulative effects of temperature by flexibly estimating contributions at different lag times, thus accounting for delayed effects and short-term mortality displacement (harvesting).

2. Materials and methods

2.1. Data

Data on cattle mortality were extracted from Sanitrace, a national-level computerized database for the registration and traceability of farm animals (Federal Agency for the Safety of the Food Chain, 2012). Our study population consisted of all adult dairy cows (≥2 years) that died (different from culling in slaughterhouse) in Belgium during the period 2006-2009.

Province-specific data on daily mean air temperature and average relative humidity were provided by the Belgian Royal Meteorological Institute. Belgium has 10 provinces with an average size (range) of 3035 (1093 to 4443) km^2 (Figure 1). We used data from 9 meteorological measuring stations as mortality data from Flemish and Walloon Brabant (and the Brussels Region) were aggregated because of low daily death counts.

As ambient air pollution levels might confound the association between temperature and mortality (Analitis et al., 2014; Cox et al., 2016), we obtained data on ozone (O_3, 8-hour maximum values), particulate matter with diameter less than 10 µm (PM_{10}, daily averages), and nitrogen dioxide (NO_2, daily averages) from the Belgian Interregional Environment Agency. In Belgium, air pollution is measured by a dense network of automatic monitoring sites (average distance between the nearest measuring stations is 25 km), collecting real-time data on a half-hourly basis. Daily air pollution concentrations at the level of the municipality are obtained by a spatial-temporal (Kriging) interpolation model that combines data from monitoring stations with land cover data obtained from satellite images (Janssen et al., 2008). Daily province-specific average air pollution concentrations were calculated by weighing the municipality-specific concentrations by the number of animals (herd size at the moment of data extraction) per municipality.

2.2. Statistical analysis

The association between ambient temperature and dairy cattle mortality was investigated by using a case-crossover design (Nawrot et al., 2011). Each subject serves as its own control so that known and unknown time-invariant confounders are inherently adjusted for by study design (Maclure, 1991). We used the bidirectional time-stratified design to avoid selection bias (Levy et al., 2001). Control days were taken from the same calendar month and year as the case day (i.e. day of death), both before and after the case, thus controlling for long-term trends and season by design. Cases and controls were additionally matched by day of the week to control for any weekly patterns in deaths.

In this study, we used conditional quasi-Poisson models that allow for overdispersion in daily deaths. When subjects have a common (province-level) exposure, the case-crossover using conditional logistic regression is a special case of time-series analysis (Lu and Zeger, 2007). Data can be aggregated into daily counts per province, and a Poisson model with stratum indicators gives identical estimates to those from conditional logistic regression. Although conditional Poisson models are computationally less intensive than conditional logistic models and they can allow for overdispersion or auto-correlation in the original counts, they are little used (Armstrong et al., 2014). We controlled for public holidays as an indicator variable and we adjusted for the moving average of humidity on the current day and the previous days (lag 0–1) using a natural cubic spline with 3 df.

In a first stage, we estimated province-specific associations between temperature and mortality by using DLNMs, which allow simultaneous estimation of the non-linear exposure-response association and the non-linear effects across lags (lag–response association) (Gasparrini et al., 2010). To adjust for potential harvesting and to completely capture cold effects which may be delayed by some weeks, we used a maximum lag of 25 days, similar to previous studies (Gasparrini et al., 2015b; Guo et al., 2011). We used a natural cubic spline with 4 degrees of freedom (df) to model the temperature–mortality association and a natural cubic spline with 5 df to model the lagged effect. Spline knots were placed at equally-spaced quantiles along the national-level average temperature range and knots in the lag space were set at equally-spaced values on the log scale of lags to allow more flexible lag effects at shorter delays (Gasparrini, 2011). For each province, the overall cumulative exposure-response association was used to derive the minimum mortality temperature (MMT) between the 5th and the 95th percentiles of the province-specific temperature distribution.

In a second stage, the estimated province-specific overall cumulative exposure-response associations were pooled using a multivariate meta-analytical model (Gasparrini and Armstrong, 2013; Gasparrini et al., 2012). We tested latitude, altitude, and average annual temperature of the measuring stations as potential meta-predictors by including them separately as well as simultaneously in the model. Residual heterogeneity was assessed by the multivariate extension of the Cochran Q test and I^2 statistic (Gasparrini et al., 2012). The national-level MMT was derived from the pooled cumulative exposure-response association and was used to calculate province-specific and national-level relative risks (RR) for extreme cold, moderate cold, moderate heat, and extreme heat, defined as the 1st, 5th, 95th, and 99th percentiles of the national-level average temperature distribution. Because the Cochran Q test suggested little heterogeneity across provinces after accounting for latitude, final results were obtained from a fixed-effects multivariate model. The modifying effect of latitude is presented by predicting the average temperature-mortality associations for the 25th and 75th percentiles of its distribution, using the national-level MMT as reference temperature.

In a secondary analysis we stratified by season because free-ranging cows are, apart from the daily milking moments, the majority of their time on pasture during the warm season (April-September), whereas they are mostly in the stable during the cold season (October-March). The robustness of results with respect to the specification of the DLNM cross-basis was tested by changing the maximum lag to 20 and 30 days, and by varying the df for the temperature-mortality function and for the lag-mortality function from 3 to 6. Secondly, we accounted for the potentially confounding effects of air pollution by adding a cross-basis for each air pollutant one at a time. The maximum lag of the air pollutant cross-basis was set at 25 days and we used a linear function for the exposure–response association and a natural cubic spline with 6 df for the lag-response association (Cox et al., 2016). Finally, the control for seasonality was tested by decreasing the stratum length to 14 days.

All analyses were performed with the statistical software R using the “dlnm” (Gasparrini, 2011) and “mvmeta” packages (Gasparrini et al., 2012).

3. Results

3.1. Data description

There were 87,108 dairy cow deaths in Belgium between 2006 and 2009, with the highest total number in West Flanders (14,120) and the lowest number in Brabant (4,620) (Table 1). The relation between latitude and temperature in Belgium is positive because there is a decrease in annual mean temperature from northwest (West Flanders) to southeast (Luxembourg and Liège) (Figure 1), which is related to distance from the sea and altitude. The distributions of the province-specific daily number of dairy cow deaths, meteorological and air pollution variables are presented in Supplementary Tables A.1 and A.2. Moderately low temperatures (5th percentile) ranged from -3.2°C in Liège to 1.7° in West Flanders, whereas summer temperatures (95^{th} percentile) were generally lowest in Liège (17.8°C) and highest in northeastern provinces Antwerp (20.6°C) and Limburg (20.8°C). Average relative humidity ranged from 76.0% in East Flanders to 87.1% in Namur. With the exception of Hainaut, daily average O_3 concentrations were generally higher in southern provinces (e.g. 70.9 $\mu g/m^3$ in Luxembourg) than in northern provinces (e.g. 61.5 $\mu g/m^3$ in Antwerp) and the other way around for PM_{10} (e.g. 20.4 $\mu g/m^3$ in Luxembourg and 29.6 $\mu g/m^3$ in East Flanders) and NO_2 (e.g. 10.9 $\mu g/m^3$ in Luxembourg and 21.6 $\mu g/m^3$ in Antwerp). Differences in air pollution between the north and south of Belgium are related to the higher urbanization levels in the northern part.

Table 1. Total dairy cow deaths and potential meta-predictors by province, Belgium, 2006-2009.

Province	Total deaths	Latitude, °N [a]	Altitude, m [a]	Mean temperature, °C [a]
West Flanders	14,120	51.3	9	11.3
East Flanders	10,382	51.0	15	11.1
Antwerp	12,617	51.2	21	11.0
Limburg	6,704	51.2	64	10.7
Brabant	4,620	50.9	46	10.9
Hainaut	10,693	50.6	63	10.9
Namur	6,566	50.1	233	10.0
Liège	13,826	50.5	673	7.3
Luxembourg	7,580	49.6	324	9.3

[a] Characteristics of the temperature measuring stations.

3.2. Main analysis

The province-specific overall cumulative exposure-response associations are presented in Figure 2. Most of the provinces showed an N-shaped curve: relative risks of mortality increased at high temperatures and at mildly to moderately low temperatures, but decreased again at moderately to extremely low temperatures. The MMT (identified within the 5-95th percentile range of the province-specific temperature distribution) ranged from 10.3 to 17.0°C, except for Luxembourg where the MMT was equal to the 95th percentile temperature (19.3°C). MMTs were generally lower in southern than in northern provinces (except for Luxembourg).

In the meta-analytical model without meta-predictors, the estimated heterogeneity (I^2) in the cumulative exposure-response association between provinces was 26.8% (Cochran *Q* test *P*=0.08). Adding latitude to the model (Wald test *P*=0.01) decreased the heterogeneity to 10.2% (Cochran Q test *P*=0.31), motivating the use of a fixed-effects model to estimate RRs. Other meta-predictors were not significant, nor did they further reduce the I^2. The MMT of the pooled cumulative temperature-mortality association was 15.4°C, corresponding to the 75th percentile of the national-level average temperature distribution (Figure 3). The curve was N-shaped with highest heat effects at the end of the temperature distribution and highest cold effects around 0.6°C (7th percentile).

Figure 4 presents the pooled lag-response association for moderate cold and heat, estimated at the 5th (-0.3°C) and 95th (19.7°C) temperature percentiles and relative to the MMT of the pooled cumulative temperature-mortality association (15.4°C). The cold effect only appeared after a few days and lasted for more than 2 weeks (up to lag 17), whereas the heat effect was acute (lag 0) and was followed by negative RRs (although not significant) the few days after.

Cumulative cold and heat effects over lag 0–25 days, estimated relative to the MMT of the pooled cumulative association (15.4°C), are presented in Supplementary Table A.3. Although significance was only obtained for moderate cold in Antwerp, RRs were mostly considerably larger than one. RRs ranged from 0.50 (West-Flanders) to 1.59 (Antwerp) for extreme cold (1st percentile, -3.5°C), from 0.90 (West-Flanders) to 1.74 (Antwerp) for moderate cold (5th percentile, -0.3°C), from 0.93 (Luxembourg) to 1.30 (Brabant) for moderate heat (95th percentile, 19.7°C), and from 0.91 (Luxembourg) to 1.74 (Namur) for extreme heat (99th percentile, 22.6°C). The pooled cumulative RRs estimated by the meta-analytical model were 1.26 (95% Confidence Interval [CI]: 1.11, 1.42) for extreme cold, 1.35 (95% CI: 1.19, 1.54) for moderate cold, 1.09 (95% CI: 1.02, 1.17) for moderate heat, and 1.26 (95% CI: 1.08; 1.48) for extreme heat.

Figure 5A presents the effect modification by latitude. Cold-related increases in mortality risk appeared to be higher in the northern part of Belgium, consistent with the higher mean (winter) temperature in this part of the country. Although northern provinces also showed slightly higher heat-related RRs, evidence for effect modification by latitude was only observed for the cold effect (Wald test for latitude as meta-predictor: P=0.07 for moderate cold and P=0.79 for moderate heat). Overall cumulative associations obtained in the seasonal analysis are shown in

Figure 5B. Significantly increased RRs were only observed at temperatures above 23°C in the warm season. The warm season curve is U-shaped with RRs close to one between around 8 to 20°C, and sharp increases in mortality risk below and above these temperatures respectively. The estimated overall association for the cold season showed little evidence for temperature-related mortality. The curve is N-shaped with slightly increased RRs at moderately low temperatures.

3.3. Sensitivity analyses

Results of the sensitivity analyses are presented as the pooled cumulative (lag 0–25 days) RRs associated with extreme cold, moderate cold, moderate heat, and extreme heat, relative to the MMT estimated in the main analysis (Supplementary Table A.4). Estimates were fairly robust to changes in the maximum lag and df for the lag-response function. Decreasing the df for the exposure-response function decreased the estimated pooled MMT (14.6°C for 3 df), whereas increasing the df increased the MMT (17.3°C for 5 df and 18.2°C for 6 df). The latter resulted in a decrease in heat effect estimates when expressed relative to the MMT from the main analysis (15.4°C). For 5 df for instance, the estimated moderate heat effect was 1.03 (95% CI: 0.96, 1.10) relative to 15.4°C, but 1.05 (95% CI: 1.01, 1.09) relative to the analysis-specific MMT (17.3°C). Adding the cross-basis for PM_{10} and NO_2 to the model produced similar cold and heat estimates, but the inclusion of O_3 resulted in a decrease in the estimates for moderate (1.03, 95% CI: 0.94, 1.13) and extreme heat (1.12, 95% CI: 0.91, 1.37). Decreasing the stratum length to 14 days gave similar estimates for cold, but resulted in a considerable increase in heat estimates (moderate heat: 1.26, 95% CI: 1.10, 1.46).

4. Discussion

This study showed that low as well as high temperatures were associated with an increased risk of mortality among dairy cows in Belgium. The effect of heat was acute and was followed by a rather small deficit in mortality the days after, indicating that heat-related health effects go beyond short-term mortality displacement. The effect of cold was more delayed and persisted for more than two weeks. Mortality was found to be lowest at the 75th percentile of the observed temperature distribution (15.4°C). Relative risks of mortality associated with heat were largest at the most extreme temperatures, whereas the cold effect was highest around the 7th percentile (0.6°C) and decreased at lower temperatures. Overall, our study in cattle adds to the existing evidence in human populations. In addition, a quantification of temperature-related mortality in dairy cattle is important for animal welfare and health (Silanikove, 2000), as well as for economic reasons (St-Pierre et al., 2003).

Because of their high metabolic heat production, the thermal comfort zone for lactating dairy cows is cooler than the optimal temperature range for humans. However, we expect that biochemical and physiological changes in response to thermal stress are similar for both species. The temporal pattern of the temperature-mortality association, i.e. immediate effects of heat and more prolonged effects of cold, is consistent with findings for human mortality (Analitis et al., 2008; Anderson and Bell, 2009; Braga et al., 2002; Baccini et al., 2008; Guo et al., 2014). Using similar statistical methods as in our study, a recent multi-country analysis showed that the minimum mortality temperature among humans was around the 80–90th percentile in temperate regions (Gasparrini et al., 2015b). The somewhat lower minimum mortality temperature observed in our study (75th percentile) is in agreement with the lower thermal comfort zone for lactating dairy cows. Nevertheless, we observed significant increases in mortality at relatively mild low temperatures, with relative risks associated with moderate cold being considerably higher than those associated with moderate heat. Similarly, by translating the overall cumulative exposure-response association into attributable fractions (Gasparrini and Leone, 2014), we observed a much higher estimate for deaths attributable to cold (15.0%, 95% CI: 9.5, 18.9) than to heat (1.8%, 95% CI: 0.3, 2.9), which is consistent with findings from the above mentioned multi-country study (Gasparrini et al., 2015b). The decrease in mortality risk at very low temperatures observed in our study is probably due to the fact that cows are kept indoors during the coldest period of the year.

Results of our seasonal analysis suggest that most of the temperature-related mortality occurred in the warm season, which may be explained by the difference in time spent outdoors between seasons. Despite the expected cold-tolerance of cows, we even observed cold effects in the warm season. This might indicate that, being outdoors, free-ranging cows mainly suffer from the indirect effects of cold, such as precipitation and wind speed. Heavy rain may penetrate the fur of an animal and decrease its insulation value, and a strong wind leads to additional excessive cooling. On the other hand, the importance of moderate, non-extreme low temperatures has recently been suggested by two multi-country studies on human mortality (Gasparrini et al., 2015a; Gasparrini et al., 2015b), with residual cold effects even observed in the four warmest months of the year (Gasparrini et al., 2015a).

Heat-related increases in dairy cattle mortality were also found in some previous studies. Some of them only focused on extreme heat episodes (Mader et al., 2001; Morignat et al., 2014), whereas others have investigated monthly (Stull et al., 2008) or daily (Vitali et al., 2009; Morignat et al., 2015; Crescio et al., 2010) variations in mortality associated with temperature. Estimated temperature-humidity heat thresholds for dairy cattle in an Italian study were 17°C for Cuneo, 21°C for Brescia, and 19°C for Rome (Crescio et al., 2010). The odds ratios of dying on a day with high exposure values (over the district-specific threshold) *versus* to a day with low exposure values (under the district-specific threshold) were 1.7 (95% CI: 1.4–2.1) for Cuneo, 1.6 (95% CI: 1.4–1.7) for Brescia, and 1.8 (95% CI: 1.4–2.3) for Rome. The impact of low temperatures on the performance and health of dairy cattle has received only limited research attention. A U-shaped association between temperature and dairy cow deaths has been reported by only two previous studies, one based on monthly averages (Stull et al., 2008) and the other based on the cumulative effect over 21 days (Morignat et al., 2015). Another study (Vitali et al., 2009) focused on same-day exposures and did not find an effect of cold on dairy cattle mortality. Together with findings from human studies, our current study suggests that the association between cold and mortality is likely to be underestimated or even missed when using short lags.

Human studies have shown evidence of adaptation to local climatic conditions (Baccini et al., 2008; Keatinge et al., 2000; Anderson and Bell, 2009; McMichael et al., 2008; Guo et al., 2014; Gasparrini et al., 2015b), with colder regions typically having lower minimum mortality temperatures or thresholds than warmer regions. Although no study has formally evaluated effect modification by local climate in dairy cattle, regional differences in thresholds between studies may indicate the existence of acclimatization. In our study, we observed a trend of lower minimum mortality temperatures in colder than in warmer provinces. Consistent with this, the heat threshold for the Italian district Cuneo (17°C) (Crescio et al., 2010) was lower than estimated heat thresholds in warmer regions of Italy (Crescio et al., 2010; Vitali et al., 2009) and in the warmer climate of California (Stull et al., 2008). A French study, however, showed considerable heterogeneity in estimated heat thresholds (ranging from 9 to 19°C) and cold thresholds (ranging from 4 to 11°C) between different areas, with no clear trend of higher thresholds for warmer areas (Morignat et al., 2015). Climate adaptation in cattle is supported by studies showing differences in hair coat characteristics between Holstein cows bred in temperate regions and cows bred in tropical and subtropical zones (Udo, 1978). Although acclimatization at smaller regional scales may exist, the observed differences in the temperature-mortality association between northern and southern provinces in our study are likely due to other factors than differences in local temperature, such as housing construction or other managerial features. This is suggested by the observation that, although latitude appeared to be an important meta-predictor, the inclusion of province-specific mean temperature in the model (with or without latitude) did not decrease heterogeneity between provinces.

A large part of temperature-related human deaths is caused by respiratory and cardiovascular conditions. Studies on human mortality in 15 European cities suggest that the effect of temperature on respiratory deaths is nearly twice as large as the effect on cardiovascular deaths, both for heat effects (Baccini et al., 2008) and for cold effects (Analitis et al., 2008). Although there is large uncertainty about exact causes of death in dairy cattle (Thomsen and Houe, 2006), cows are known to be susceptible for pulmonary diseases because of their small physiological gaseous exchange capacity, greater basal ventilatory activity, and greater anatomical compartmentalization of the lung as compared with other mammals (Veit and Farrell, 1978). Therefore, a considerable part of temperature-related mortality among cattle might be due to respiratory conditions.

Epidemiological observations in animal populations can add to findings from human studies, as demonstrated in this study. Confirming the temperature-mortality association in different populations and different species strengthens the evidence for causality. The restricted daily mobility and low frequency of migration in cattle populations contribute to the likelihood that exposure assessment can be conducted relatively accurately. Moreover, the majority of adult dairy cows are on pasture during summer, making outdoor exposure a good proxy for actual individual exposure, at least in summer. The use of DLNM models enabled the investigation of the net effect of temperature on cattle mortality, accounting for harvesting as well as delayed effects.

Our study also has some limitations. Meteorological variables were derived from outdoor measuring stations and we used data from only one station per province, which may have resulted in exposure misclassification, especially in indoor-kept cows and during the coldest period of the year. Provinces in Belgium have an average size of only 3000 km^2, so temperature variations within provinces is likely to be small, especially within rural areas (where most free-ranging cows are situated). Similarly, we used province-level estimates for air pollution concentrations, calculated from estimates modelled per municipality. As temporal variability in air pollution is much larger than spatial contrasts, exposure misclassification in studies on short-term effects is rather limited. The correlation between temperature and O_3 was high (Pearson correlation coefficient of 0.60), and results of the sensitivity analysis suggest that the association between heat and dairy cattle mortality might be confounded by O_3, which has also been observed in studies on human mortality (Baccini et al., 2008; Analitis et al., 2014). Another limitation of this study is that the primary effect of temperature on free-ranging animals might be strongly altered by wind, precipitation, humidity, and solar radiation. Moreover, observed results might be influenced by the effects that weather may exert on quantity and quality of pasture and water, or on survival and growth of infectious agents (Kadzere et al., 2002). Nevertheless, Stull et al. (2008) suggested that precipitation had little or no effect on dairy cattle mortality that was independent of temperature. We also did not have information on population sizes at risk for mortality, which may vary considerably due to seasonal variations in birth, death, or culling. However, sensitivity analyses showed that the seasonal control used in the main analysis is likely to be sufficient.

5. Conclusion

This study showed significant cold- and heat-related increases in dairy cattle mortality and a temporal pattern similar to that observed in human studies, suggesting that there are common pathophysiological patterns. As exposure misclassification is expected to be limited in dairy cattle, our study reinforces the evidence on the plausibility of causal effects in humans.

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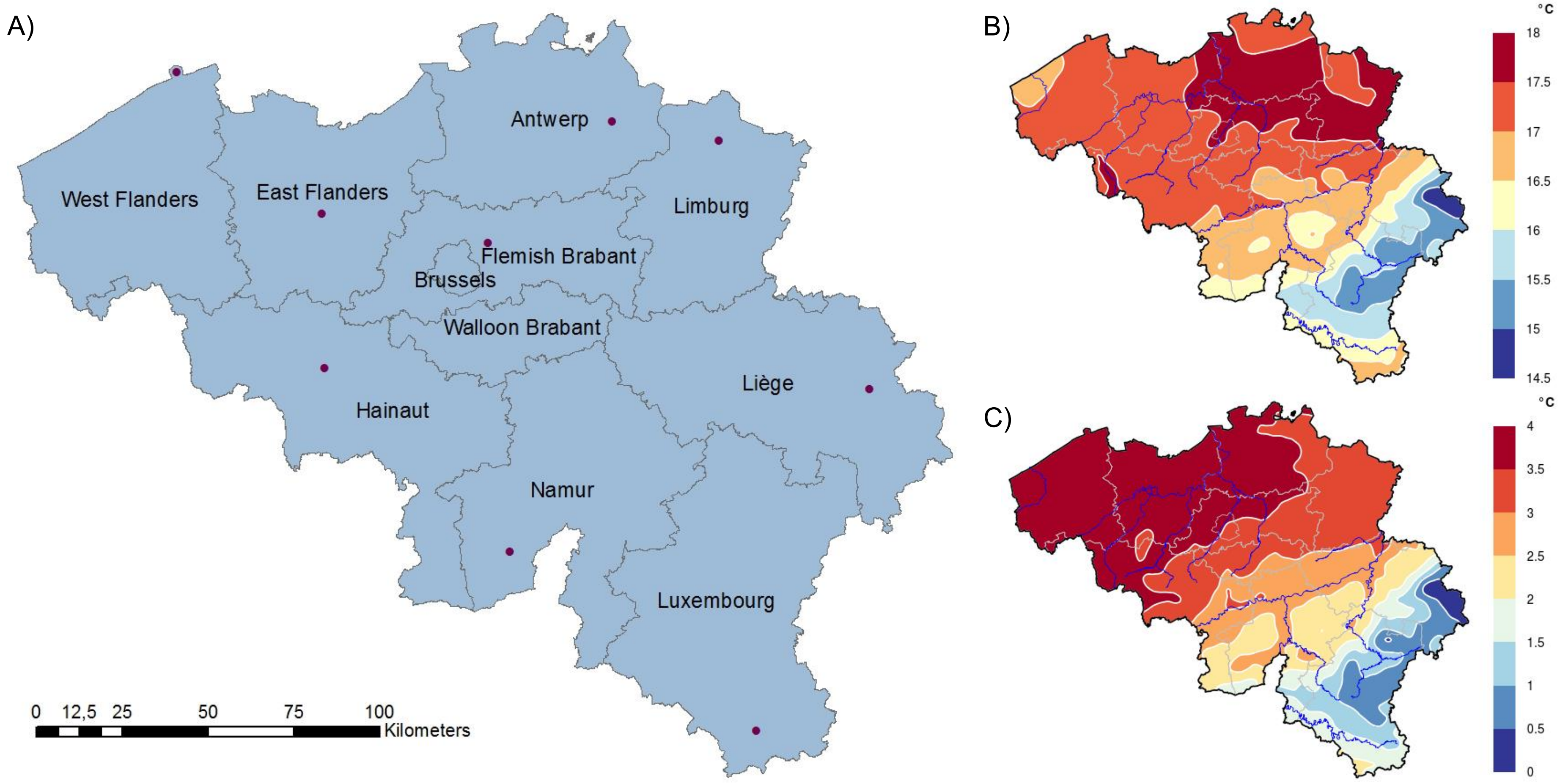

Figure 1. The location of provinces and measuring stations from which temperature data were used in this study (A), and mean temperatures gradients (1981-2010) for summer (B) and winter (C), Belgium. Source (B and C): Belgian Royal Meteorological Institute (http://www.meteo.be/meteo/view/fr/16788784-Atlas+Climatique.html)

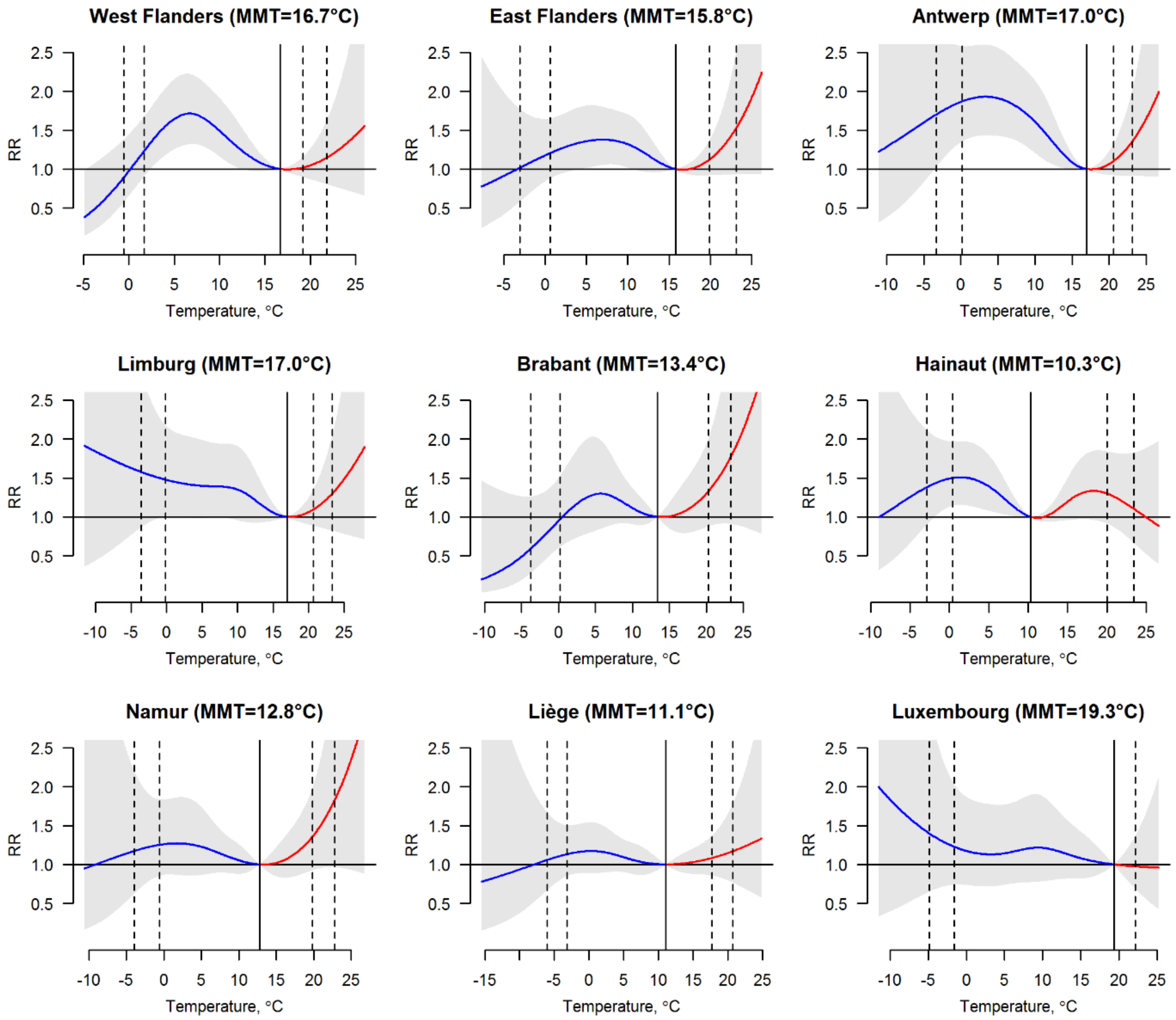

Figure 2. The estimated cumulative temperature-mortality association per province over lag 0–25 days. Solid lines represent relative risks (RR) and shaded areas are 95% CIs. The vertical solid line and the dashed lines represent the province-specific minimum mortality temperature and the 1st, 5th, 95th, and 99th temperature percentiles respectively.

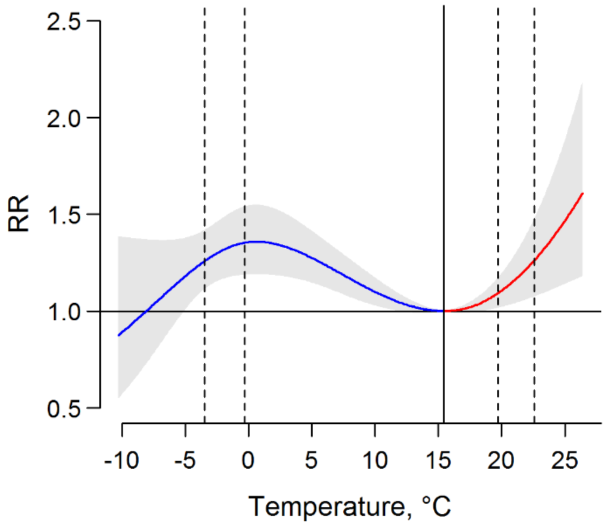

Figure 3. The pooled cumulative temperature-mortality association over lag 0–25 days estimated by the multivariate meta-analytical model. The solid line represents relative risks (RR) and the shaded area is the 95% CI. The vertical solid line and the dashed lines represent the minimum mortality temperature and the 1st (-3.5°C), 5th (-0.3°C), 95th (19.7°C), and 99th (22.6°C) percentiles of the national-level average temperature distribution respectively.

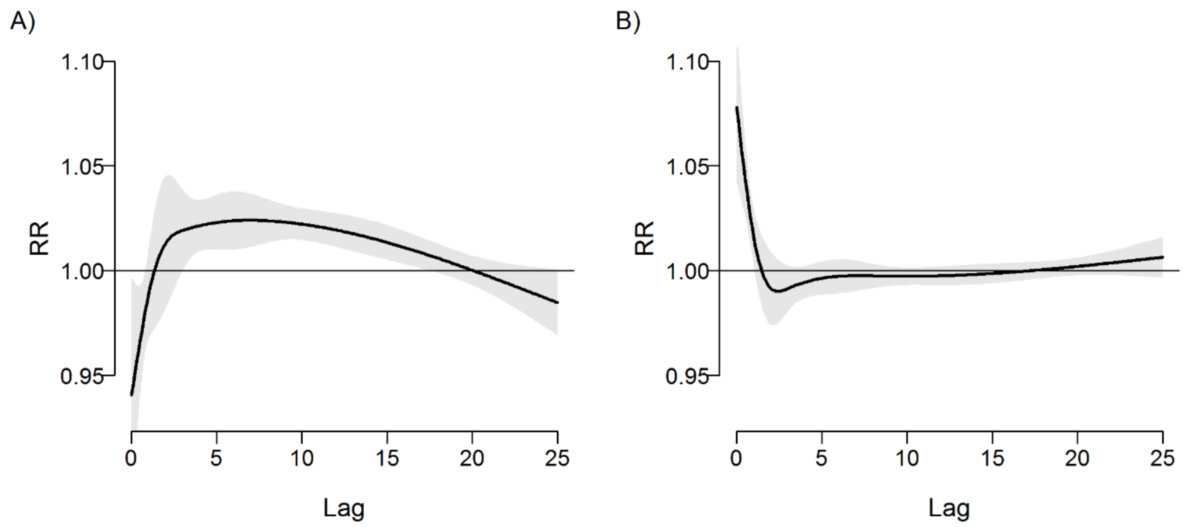

Figure 4. The pooled lag-response association for moderate cold (A) and moderate heat (B), estimated by the multivariate meta-analytical model at the 5th (-0.3°C) and the 95th percentile (19.7°C) of the national-level average temperature distribution respectively, relative to the minimum mortality temperature of the pooled cumulative association (15.4°C). Solid lines represent relative risks (RR) and shaded areas are 95% CIs.

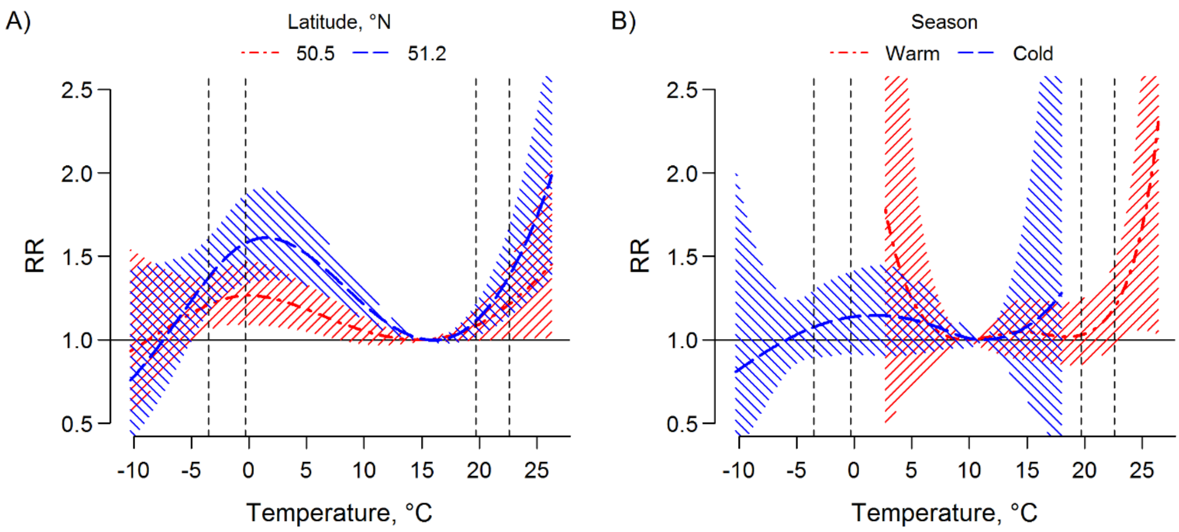

Figure 5. The pooled cumulative temperature-mortality association over lag 0–25 days by latitude (A) and by season (B). The dot-dashed lines (red) and the dashed lines (blue) represent the relative risks (RR) for the 25th and 75th percentiles of latitude respectively in A), and for the warm season and the cold season respectively in B). The shaded areas are 95% CIs. The vertical dashed lines represent the 1st (-3.5°C), 5th (-0.3°C), 95th (19.7°C), and 99th (22.6°C) percentiles of the national-level average temperature distribution respectively.

Supplementary file

Mortality related to cold and heat. What do we learn from dairy cattle?

Bianca Cox, Antonio Gasparrini, Boudewijn Catry, Andy Delcloo, Esmée Bijnens, Jaco Vangronsveld, Tim S Nawrot

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Table A.1. Summary statistics of daily cow mortality and weather conditions by province in Belgium, 2006-2009.

				Percentiles								
Variable	Province	Mean	SD	Min	1th	5th	25th	50th	75th	95th	99th	Max
Death	West Flanders	9.7	5.0	0.0	1.0	3.0	6.0	9.0	13.0	19.0	24.0	43.0
	East Flanders	7.1	4.3	0.0	0.0	1.0	4.0	6.0	9.5	15.0	19.0	44.0
	Antwerp	8.6	4.9	0.0	1.0	2.0	5.0	8.0	11.0	16.0	21.0	81.0
	Limburg	4.6	2.8	0.0	0.0	1.0	3.0	4.0	6.0	9.0	12.0	35.0
	Brabant	3.2	2.3	0.0	0.0	0.0	1.0	3.0	4.0	7.0	10.0	14.0
	Hainaut	7.3	4.4	0.0	0.0	2.0	4.0	7.0	10.0	15.0	19.0	54.0
	Namur	4.5	3.3	0.0	0.0	0.0	2.0	4.0	6.0	11.0	15.0	25.0
	Liège	9.5	5.2	0.0	1.0	2.0	6.0	9.0	13.0	18.0	25.0	35.0
	Luxembourg	5.2	3.6	0.0	0.0	1.0	3.0	5.0	7.0	12.0	15.0	45.0
Mean temperature, °C	West Flanders	11.3	5.5	-4.9	-0.6	1.7	7.3	11.6	16.0	19.2	21.9	26.0
	East Flanders	11.1	6.1	-7.8	-3.1	0.6	6.7	11.4	16.0	19.9	23.2	26.2
	Antwerp	11.0	6.4	-11.2	-3.4	0.2	6.3	11.5	16.1	20.6	23.2	26.7
	Limburg	10.7	6.6	-11.7	-3.6	-0.2	5.9	11.0	15.9	20.8	23.4	27.9
	Brabant	10.9	6.3	-10.4	-3.8	0.2	6.4	11.3	15.8	20.3	23.4	27.5
	Hainaut	10.9	6.2	-9.0	-3.0	0.5	6.3	11.3	15.8	20.0	23.4	26.6
	Namur	10.0	6.4	-10.7	-4.0	-0.6	5.2	10.4	15.1	19.8	22.9	26.8
	Liège	7.3	6.5	-15.6	-6.0	-3.2	2.3	7.5	12.4	17.8	20.8	24.9
	Luxembourg	9.3	6.6	-11.5	-4.9	-1.6	4.3	9.6	14.6	19.3	22.1	25.2
Humidity, %	West Flanders	80.9	7.6	51.0	60.8	67.4	76.2	81.5	86.5	92.4	94.7	97.5
	East Flanders	76.0	8.6	36.3	51.0	60.8	71.0	76.9	82.1	88.4	91.7	98.2
	Antwerp	85.1	9.9	42.7	56.1	66.9	79.1	86.4	92.7	98.4	100.0	100.0
	Limburg	80.3	10.9	37.0	51.0	60.0	74.0	82.0	88.0	95.0	99.0	100.0
	Brabant	77.7	9.1	43.0	52.0	61.0	72.0	79.0	84.0	90.0	94.0	98.0
	Hainaut	80.5	9.4	37.0	55.0	64.0	75.0	81.0	87.1	94.0	98.0	100.0
	Namur	87.1	10.0	45.5	55.0	68.0	81.4	89.3	94.8	99.2	100.0	100.0
	Liège	84.0	12.9	23.2	40.1	56.1	78.8	88.7	93.6	95.4	96.3	97.1
	Luxembourg	79.3	10.3	28.4	47.4	59.0	73.8	81.1	87.2	91.8	93.8	98.7

Table A.2. Summary statistics of air pollution concentrations by province in Belgium, 2006-2009.

				Percentiles								
Variable	Province	Mean	SD	Min	1th	5th	25th	50th	75th	95th	99th	Max
O_3, µg/m^3	West Flanders	62.6	25.8	6.6	8.3	18.1	47.5	62.6	76.8	102.2	138.9	185.9
	East Flanders	61.9	28.0	8.7	10.0	17.8	43.6	60.8	77.2	109.7	147.8	191.1
	Antwerp	61.5	30.8	8.0	9.5	16.2	40.4	59.0	77.4	119.7	153.2	205.6
	Limburg	63.4	30.4	5.1	8.4	16.5	44.2	60.7	79.2	119.4	154.4	214.7
	Brabant	62.4	29.3	5.9	9.0	17.4	43.2	60.4	77.3	119.5	150.2	209.4
	Hainaut	61.3	27.3	6.8	9.9	19.0	43.6	59.9	76.1	111.7	140.7	198.2
	Namur	67.6	27.4	5.4	14.7	25.1	50.2	65.0	82.5	120.1	145.7	217.9
	Liège	66.6	27.3	4.9	16.4	25.5	49.0	64.0	81.7	118.1	143.7	204.9
	Luxembourg	70.9	25.8	8.9	24.1	33.2	54.0	67.9	85.2	120.6	145.1	195.2
PM_{10}, µg/m^3	West Flanders	28.2	14.2	7.4	11.5	13.9	18.7	24.2	33.5	56.3	87.6	112.4
	East Flanders	29.6	14.7	9.2	12.2	15.1	19.4	25.6	35.1	58.6	87.7	121.6
	Antwerp	26.3	13.1	7.6	10.7	13.1	17.6	22.8	31.3	50.0	76.0	111.6
	Limburg	25.1	13.3	4.9	7.8	10.9	16.1	21.5	30.2	49.8	76.3	99.0
	Brabant	26.6	14.8	5.8	8.3	11.2	16.5	22.3	32.5	54.2	85.9	111.0
	Hainaut	27.4	15.5	4.6	8.2	11.2	16.7	23.0	33.5	56.3	84.4	116.2
	Namur	24.0	14.8	2.9	5.3	8.4	13.5	19.9	30.3	53.3	78.3	106.5
	Liège	24.4	13.1	3.8	6.5	9.8	15.2	21.4	30.3	49.4	71.2	95.9
	Luxembourg	20.4	12.6	2.2	3.7	6.5	11.6	17.3	25.6	45.8	64.6	91.6
NO_2, µg/m^3	West Flanders	19.2	9.7	3.1	4.5	6.9	11.7	17.2	25.2	36.7	50.4	66.0
	East Flanders	21.0	10.2	3.3	5.3	7.8	13.3	19.0	27.2	39.3	51.5	71.1
	Antwerp	21.6	9.6	4.3	6.5	9.2	14.6	20.0	27.0	38.8	49.7	73.3
	Limburg	18.8	9.4	2.3	4.9	7.0	12.0	17.0	24.1	35.7	46.5	69.4
	Brabant	21.7	10.6	2.7	5.6	8.0	13.8	19.8	27.8	40.2	54.4	78.1
	Hainaut	19.3	9.5	3.0	5.1	7.5	12.3	17.7	24.9	35.7	49.5	68.5
	Namur	14.9	8.5	2.0	3.2	4.9	8.9	13.1	19.0	30.7	44.8	59.2
	Liège	15.4	8.1	2.6	4.0	5.7	9.4	13.9	19.7	30.4	42.0	69.5
	Luxembourg	10.9	7.0	1.8	2.4	3.4	6.0	9.3	13.8	24.3	37.8	57.7

Table A.3. The cumulative cold and heat effects of mean temperature on dairy cattle mortality over lag 0–25 days, per province and for Belgium, estimated by the province-specific and multivariate meta-analytical models respectively.

	Relative risk (95% CI) [a]							
Province	Extreme cold		Moderate cold		Moderate heat		Extreme heat	
West Flanders	0.50	(0.24, 1.03)	0.90	(0.61, 1.32)	1.00	(0.82, 1.22)	1.16	(0.74, 1.82)
East Flanders	0.98	(0.54, 1.77)	1.15	(0.82, 1.61)	1.10	(0.90, 1.34)	1.43	(0.92, 2.22)
Antwerp	1.59	(0.98, 2.58)	1.74	(1.28, 2.37)	0.99	(0.84, 1.17)	1.22	(0.84, 1.75)
Limburg	1.52	(0.87, 2.64)	1.43	(0.99, 2.05)	1.01	(0.83, 1.23)	1.19	(0.79, 1.79)
Brabant	0.60	(0.27, 1.36)	0.91	(0.54, 1.51)	1.25	(0.96, 1.64)	1.63	(0.92, 2.88)
Hainaut	1.10	(0.63, 1.90)	1.21	(0.87, 1.69)	1.07	(0.88, 1.30)	0.95	(0.62, 1.45)
Namur	1.15	(0.59, 2.25)	1.22	(0.80, 1.87)	1.30	(0.99, 1.72)	1.74	(0.94, 3.19)
Liège	1.09	(0.77, 1.54)	1.13	(0.84, 1.51)	1.10	(0.83, 1.45)	1.20	(0.68, 2.11)
Luxembourg	1.23	(0.69, 2.20)	1.11	(0.74, 1.64)	0.93	(0.69, 1.26)	0.91	(0.47, 1.75)
Belgium (pooled)	1.26	(1.11, 1.42)	1.35	(1.19, 1.54)	1.09	(1.02, 1.17)	1.26	(1.08, 1.48)

[a] Relative risk of mortality for extreme cold, moderate cold, moderate heat, and extreme heat, defined as the 1st (-3.5°C), 5th (-0.3°C), 95th (19.7°C), and 99th (22.6°C) percentiles of the national-level average temperature distribution respectively, and relative to the minimum mortality temperature of the pooled cumulative association (15.4°C).

Table A.4. The pooled cumulative cold and heat effects of mean temperature on dairy cattle mortality over lag 0–25 days, estimated by the multivariate meta-analytical model in sensitivity analyses.

	Relative risk (95% CI) [a]							
Change in main model	Extreme cold		Moderate cold		Moderate heat		Extreme heat	
/	1.26	(1.11, 1.42)	1.35	(1.19 1.54)	1.09	(1.02, 1.17)	1.26	(1.08, 1.48)
Maximum lag = 20	1.29	(1.15, 1.44)	1.24	(1.10, 1.40)	1.07	(1.00, 1.14)	1.22	(1.06, 1.40)
Maximum lag = 30	1.32	(1.16, 1.51)	1.39	(1.21, 1.60)	1.07	(0.99, 1.16)	1.21	(1.01, 1.46)
Lag df = 3	1.28	(1.13, 1.44)	1.39	(1.22, 1.58)	1.07	(1.00, 1.15)	1.22	(1.04, 1.43)
Lag df = 4	1.27	(1.12, 1.43)	1.37	(1.20, 1.55)	1.08	(1.01, 1.16)	1.24	(1.06, 1.45)
Lag df = 6	1.26	(1.12, 1.43)	1.35	(1.19, 1.54)	1.09	(1.01, 1.17)	1.26	(1.07, 1.47)
Temperature df = 3	1.15	(1.01, 1.31)	1.26	(1.13, 1.41)	1.10	(1.02, 1.19)	1.24	(1.07, 1.43)
Temperature df = 5	1.31	(1.15, 1.49)	1.38	(1.19, 1.59)	1.03	(0.96, 1.10)	1.23	(1.06, 1.43)
Temperature df = 6	1.31	(1.11, 1.55)	1.30	(1.14, 1.48)	0.98	(0.86, 1.11)	1.16	(1.01, 1.33)
Inclusion O_3 [b]	1.38	(1.18, 1.62)	1.45	(1.24, 1.70)	1.03	(0.94, 1.13)	1.12	(0.91, 1.37)
Inclusion PM_{10} [b]	1.25	(1.10, 1.41)	1.38	(1.21, 1.57)	1.09	(1.02, 1.17)	1.26	(1.07, 1.48)
Inclusion NO_2 [b]	1.30	(1.13, 1.50)	1.37	(1.20, 1.57)	1.09	(1.02, 1.17)	1.27	(1.08, 1.48)
Strata length = 14 days	1.25	(0.98, 1.59)	1.28	(1.01, 1.63)	1.26	(1.10, 1.46)	1.66	(1.20, 2.23)

[a] Relative risk of mortality for extreme cold, moderate cold, moderate heat, and extreme heat, defined as the 1st (-3.5°C), 5th (-0.3°C), 95th (19.7°C), and 99th (22.6°C) percentiles of the national-level average temperature distribution, relative to the minimum mortality temperature of the pooled cumulative association (15.4°C).

[b] DLNM cross-basis with a maximum lag of 25 days, a linear function for the exposure–response association and a natural cubic spline with 6 df for the lag-response association.