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Title

Seasonal variation in mortality secondary to acute myocardial infarction: a secondary data analysis

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Abstract

Background: Acute myocardial infarction (AMI) is a leading cause of death globally. Increase in AMI mortality during winter has also been identified in existing literature. This has been associated with low outdoor and indoor temperatures and increasing age. The relationship between AMI and other factors such as gender and socioeconomic factors varies from study to study. Influenza epidemics have also been identified as a contributory factor.

Objective: This paper aims to illustrate the seasonal trend in mortality due to AMI in England and Wales with emphasis on excess winter mortality.

Methods: Monthly mortality rates per 10,000 population were calculated from data provided by the U.K. Office for National Statistics (ONS) for 1997 to 2005. To quantify the seasonal variation in winter, the excess winter mortality estimates (Excess Winter Mortality (EWM), Excess Winter Mortality Ratio (EWMR), Excess Winter Mortality Index (EWMI) for each year were calculated. Negative binomial regression model was used to estimate the relationship between increasing age and excess winter mortality.

Results: The decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005. This decline was not seen with excess winter mortality. 17% excess deaths were observed during winter. This amounted to about 20,000 deaths over the 8 year period. Increasing winter mortality was seen with increasing age for AMI.

Conclusion: Seasonal variation in mortality secondary to AMI does occur in England and Wales. Excess winter deaths due to AMI have remained high despite decline in overall mortality. More research is needed to identify the relationship of sex, temperature, acclimatization and excess winter deaths due to AMI.

Strengths

- The data used involved a large sample size and this was able to capture relevant results in the data analysis and this data represents the population of interest.
- The paper gives further insight into the concept of excess winter mortality.

Limitations

- Although the data provided by the ONS was complete and considered accurate, the data characteristics however restricted the number of variables that could be controlled such as sex distribution.
- The population data which was used as denominator would reduce in accuracy as the year of study moved away from the recent census (29th April 2001). This is because the midyear populations after this date were extrapolated using birth and death data; these data are prone to their own type of error. However, it is anticipated that the brief period used in the research was unlikely to experience any dramatic changes in population.

Background

Studies over time have observed an increase in mortality rate during winter months[1-3]. This appears to be a global phenomenon with evidence of excess winter mortality occurring in a number of European countries, including the United Kingdom[4,5], Japan[6], Brazil[7], Canada[2], the United States[3] New Zealand [8] and likely any country where a winter season occurs.

The relationship between mortality and temperature observes a U shape[9]: an increase in mortality is seen with extremes in temperature. Excess winter mortality which is defined as "a significant increase in the number of deaths during winter compared with the average of the non-winter seasons" has been linked to the drop in temperature[10]. Low temperatures have been implicated in the increase in number of deaths during the winter months however, they are not due to hypothermia. There is evidence to suggest that low temperatures trigger pathological mechanisms that lead to increase in blood pressure and thrombus formation[2].

The consequence of this is the initiation of physiological stress that results in the development of a myocardial infarction or a stroke.

A study involving data from various countries in Europe found a similar association but also identified 18^{o}C as the threshold for this to occur[11]. Research carried out in Scotland[12] and in England[14] could quantify this relationship: a 1^{o}C drop in temperature resulted in a 1-2% increase in the number of deaths. This corresponds to increased odds of dying during the winter by 1.5%[10].

The effects of temperature are both direct and immediate. Time series analyses have shown that there is a minimum lag time of about 24 hours between drop in temperature and increase in mortality[12]. The impact of cold temperature could also extend over a period of 1 to 2 weeks. This lag time shows that there is a possible mechanism that is initiated by the low outdoor temperatures directly that leads to death supporting evidence from previous studies. It has also been shown that the effect of temperature is significantly potentiated by high relative humidity and strong winds[13].

There are suggestions that the influence of winters and low temperatures on the “spiked” increase in mortality rates is preventable. This is because there is ecological evidence that countries with colder winters do not have greater excess winter mortality when compared to countries with milder winters[4], for example the United Kingdom when compared to Scandinavian countries[14, 15]. This observation is referred to as the excess winter paradox.
Factors that are considered to play a role include socioeconomic status[15], influenza[16,17] and age[14]. Other factors considered include housing insulation and the concept of fuel poverty both of which affect the indoor temperature. Housing in Britain has lower insulation properties compared to houses in Germany, Russia or the Scandinavian countries[18]. Due to the low insulation properties of housing in England and Wales, it is more expensive to warm these homes when compared to houses in other European states. This introduces the concept of fuel poverty. Fuel poverty is defined as a situation *“when in order to heat its home to an adequate standard of warmth a household needs to spend more than 10% of its income on total fuel use[19].”* The World Health Organization’s (WHO) recommendation of adequate standard warmth is defined as 18^{o}C in occupied rooms and 21^{o}C in living room. The temperature level of 18^{o}C is remarkable because below this threshold has been identified as when significant mortality occurs. The ability to generate heat to a surrounding temperature

above this identified threshold might prove necessary. The UK Government has acknowledged that excess winter mortality is a problem and currently has put in place some policies to tackle this phenomenon[19]

There are few studies that have taken examined the phenomenon of excess winter mortality specifically due to AMI in England and Wales. Most studies treat the subject of excess winter mortality by assessing total mortality without isolating individual diagnosis. Assessing individual diseases might produce stronger evidence on the impact seasonal variation on a particular disease condition. Due to the overwhelming global impact of this condition, it is important to identify seasonal variation of mortality due to AMI and also points of possible preventive strategies that can help in reducing the incidence of the disease.

Methodology

This study was a secondary data analysis that assessed excess winter deaths due to AMI in England and Wales. The study used anonymised mortality data provided by the office of National Statistics (ONS), United Kingdom (UK) and mean monthly temperature data provided by the Meteorological Office, UK. The database provided by the ONS consisted of anonymised data of daily mortality in England and Wales for the period from 1997 to 2005. The International Classification of Disease (ICD) was used for coding the various cause of death. The ninth edition (ICD-9) was used from 1997 to 2000 while the tenth edition (ICD-10) was used between 2001 and 2005. The cause of death considered for the study was acute myocardial Infarction (ICD-9: 410; ICD-10: I21). This was presented in 3 age groups: 0 to 64 years, 65 to 74 years, and 75 years and above.

Age-specific mortality rates were also calculated for each age group. The daily, monthly, and yearly mortality rates were calculated and the age specific population served as denominator. The population data for each year and each age group was extracted from ONS yearly publications. The monthly rates were standardised to 30 day months.

Adjustments in mortality rates were also made to account for changes in ICD coding. This was done using this formula: MA (y, d) = MO (y, d). R. MA is the adjusted daily mortality (deaths) for a day, d, in year, y. MO is the observed mortality. R is the comparability ratio:

the ICD-10/ICD-9 comparability ratio for acute myocardial infarction 0.9889 was used to adjust ICD-9 code death counts[20].

Specifically the concept of excess winter deaths was explored in this study. The method used to analyse the excess winter deaths was first described by Curwen and it is similar to that used by the ONS[23]. The months of December to March defines the winter period. The non-winter period is defined as the months of August to November before this winter period, and the months of April to July following the winter period.

In order to quantify the seasonal variation in winter, the excess winter mortality (EWM), excess winter mortality ratio (EWMR), and the excess winter mortality index (EWMI) for each year was calculated. The EWM reflects the absolute difference in mortality between the winter season and non-winter season. Whereas the EWMR represents the relative risk of death during the winter months compared to the non-winter months. The EWMI represents a variant of relative risk reduction or "excess". The EWMR and EWMI are viable tools for comparisons between age, sex, regions or countries. These estimates were also calculated for each age group. These estimates were calculated using the following formulae:

- EWM= O –E
- EWMR = O/E
- EWMI = (O –E)/E or EWMR-1 (represented as a percentage)

Where, O is the observed death count. This is the total death counts during the winter months, a period of 4 months, (winter deaths). E is the expected death count which is the total death counts during the non-winter months, a period of 8 months, divided by 2.

A regression model was used in assessing the rates of death during the winter season and non-winter seasons. The log-linear model was derived with the mortality count during winter period as the estimated outcome while age was the explanatory variable. The hypothesis was to test if there was any difference between excess winter mortality ratios amongst the various age groups. Therefore, the log of the average non-winter deaths was used as offset to fit the model. The model was fitted using a negative binomial model with a log link function due to over dispersion in the initial analysis.

Results

Table: 1 Yearly mortality patterns of AMI from August 1997 to July 2005.

Year Period*	Mortality Rate per 10,000 (Number of deaths)			
	Age: 0 to 64 years	65 to 74 years	75 years and above	Total
97/98	1.96 (8184)	24.72 (14299)	83.59 (33678)	10.87 (56161)
98/99	1.81 (7581)	22.59 (13119)	79.84 (32283)	10.22 (52983)
99/00	1.64 (6924)	20.11 (11724)	74.70 (30330)	9.41 (48978)
00/01	1.52 (6435)	17.99 (10528)	67.98 (27716)	8.55 (44679)
01/02	1.40 (5964)	16.28 (9567)	65.00 (26610)	8.03 (42141)
02/03	1.35 (5784)	14.71 (8685)	64.45 (26495)	7.77 (40964)
03/04	1.21 (5189)	13.39 (7937)	60.84 (25125)	7.22 (38251)
04/05	1.16 (5005)	11.84 (7066)	55.79 (23180)	6.62 (35251)
Total	1.51 (51066)	17.70 (82925)	69.02 (225417)	8.59 (359408)

Between August 1997 and July 2005 there were 359,408 deaths due to acute myocardial infarction (AMI) with an average death count of 44,926 occurring yearly (Table 1). 62.7% of the total deaths were seen in the age group 75 years and above, 23.1% in age group 65 to 74 years and 14.2% in age group 0 to 64 years.

A steady decline in the absolute death counts as well as mortality rates were seen in all age groups across the years (Figure 1). Overall, the decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005.

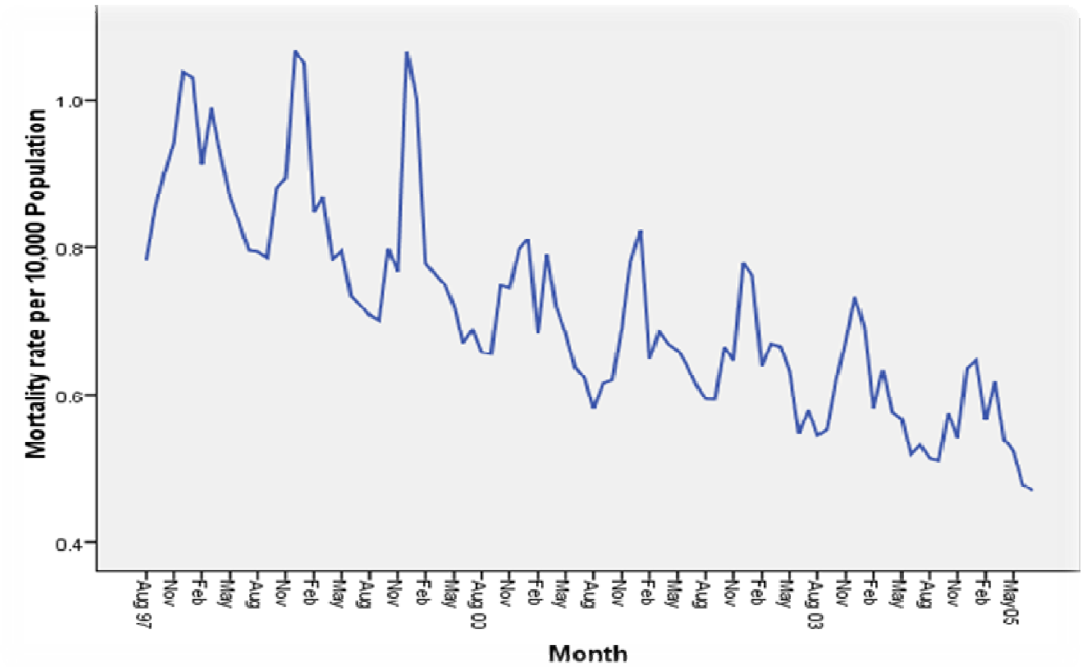

Figure 1: Mortality rate during the months of the year period

A sharp rise in mortality is noticed in early November and peaks between December and January (Figure 2). A second rise also occurs around the month of March but the mortality rate seen during this period is not as high as that observed during the December and January months. The lowest mortality rates occurred during July and August months.

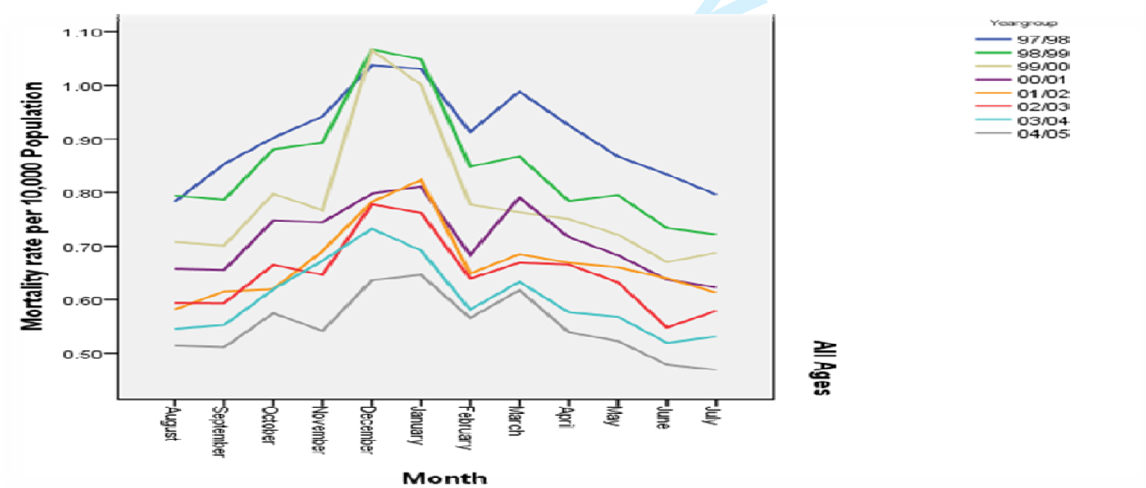

Figure 2: Relationship between Mean Monthly Temperature and Mortality

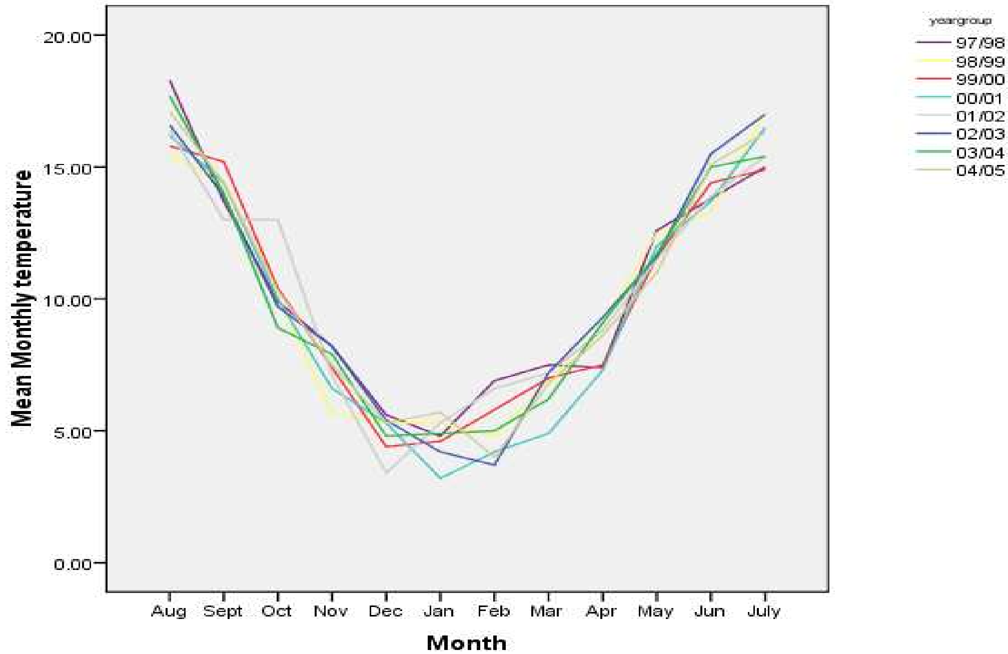

Figure 3: Mean Monthly Temperature

A plot of the mean temperatures (figure 3) showed a trough during the months of December to March and when compared to figure 2 this indicates that lower temperatures are observed during the peaks of mortality during the year. A plot of the mean monthly temperature with mortality rate showed a significant negative correlation between the two variables ($r = -0.479$; $P < 0.0001$).

Estimation of Excess Winter Mortality due to AMI

Excess winter mortality was seen in all the years observed. An average of about 2,463 excess winter deaths occurred yearly. In all year periods the highest absolute EWM occurred in those 75 years and above(Table 2). This age group also contribute an average of 70% to the excess winter deaths yearly. The excess winter mortality over the 8 year period resulted in 19,635 total deaths. This is equivalent to 5.5% of the overall yearly mortality due to AMI over the 8 year period.

The excess winter mortality ratio (winter: non-winter rate ratio) is greater than 1 in all year periods considered indicating that there is greater mortality in winter compared to the non-winter months. The excess winter mortality index which describes the risk in dying during winter compared to non-winter months. This shows that there is an average 17% excess death yearly.

Table 2: Excess Winter Mortality and index secondary to AMI between 1997-2005

Year Period	EWM (EWMI)			
	Age: 0 to 64 years	65 to 74 years	75 years +	Total
97/98	244.5(9%)	731.5(16%)	1716.0(16%)	2692.0(15%)
98/99	281.5(12%)	756.0(18%)	2280.0(23%)	3317.5(20%)
99/00	333.0(15%)	643.5(17%)	2715.0(29%)	3691.5(24%)
00/01	148.5(7%)	368.5(11%)	1332.5(15%)	1849.5(13%)
01/02	258.0(14%)	453.0(15%)	1372.5(16%)	2083.5(16%)
02/03	196.5(11%)	423.0(15%)	1430.0(17%)	2049.5(16%)
03/04	251.0(15%)	260.0(10%)	1339.5(17%)	1850.5(15%)
04/05	140.5(9%)	466.0(21%)	1494.5(21%)	2101.0(19%)
Total	1853.5	4101.5	13680.0	19635.0

EWM- Excess winter mortality EWMI- Excess winter mortality index

A regression analysis was carried using a negative binomial regression to estimate the excess winter mortality ratio and age (Table 3). The relative risk of excess mortality in age groups 65 to 74 years and 75 years and above was 1.36 and 2.45 respectively compared to the younger age group.

Table 3: Excess winter mortality ratio and age

Age	coefficient	SE	Odds ratio	P-value
0 to 64 years	reference			
65 to 74 years	0.308	0.0722	1.36 (1.18-1.57)	<0.0001
75 years +	0.894	0.0629	2.45 (2.16-2.77)	<0.0001

Discussion

The results from the data analysis showed there is a significant increase in mortality rates due to AMI during the winter period in England and Wales. In this study, the excess winter mortality ratio over the 8 year study period for all age groups was 1.17 with a resultant 17% excess winter deaths for acute myocardial infarction. This amounted to about 20,000 excess deaths due to this disease. From their analysis of 2266 deaths, Biedrzycki and Baithun[1] in their study of mortality from myocardial infarction found that December was the peak month of mortality. A decline was observed from February onwards with the lowest mortality rate observed during the month of August. This pattern is like what was elicited in this paper: the highest mortality rates peaked between December and January and lowest mortality rates were observed during the months of July and August.

Besides the demonstrable winter excess, the monthly mortality rate plot showed a double peak. A peak in mortality, which was clearly above the mean mortality rate, was observed around the month of March. This second peak in mortality was less than that seen in the months of December and January.

Since fluctuations in daily temperatures could not be appreciated from monthly mean temperature data, it is possible that absolute low outdoor temperatures may not be the only factor in causing mortality but rather daily changes in temperature may also be significant. It has already been established that in most countries in Europe a 1°C drop in temperature is associated in increasing in mortality[12,13]. Carson et al, in their study found that cardiovascular diseases were more sensitive to temperature changes than respiratory disease[21.] This relationship has also been recognized in other studies: Kysely et al[15] found that fluctuations in daily temperatures resulted in increase in mortality rates of cardiovascular diseases. They also noted that a second cold spell usually had a lower excess mortality and suggested that the reason for this might be that some form of acclimatization to the previous cold spell might be protective against the next. This might explain the double peaks that were observed in this study. Large variations in temperatures between winter and non-winter months as seen in countries with warm winters such as England and Wales may also explain the winter paradox observed in Europe. It is possible that the lack of acclimatization due to the non-persistent cold weather, unlike in Iceland and Russia, may lead to a greater impact when the winter season does arrive. However, this is not conclusive and would require more research to clearly define such an association.

The study has shown that AMI has undergone a steady decline in England and Wales over the years. This is remarkable. The decline of mortality rate from 10.87 deaths per 100,000 population to 6.62 deaths per 10,000 population was observed over the 8 years study period. The reasons for this may include such factors as better diagnostic and therapeutic procedures, healthier life styles of the population, and better awareness of the public. Despite this steady decrease in total yearly mortality rate, the risk of dying from AMI during winter has remained the same and relatively high over the years. This is suggestive that excess winter mortality is not a function of the overall mortality. This has important control and prevention implications: the measures used to control overall mortality may not necessary influence winter excess.

There was a gradient relationship between excess winter deaths and age: we found increasing winter deaths with increasing age. A regression model was used to estimate the relationship between age and winter mortality and we found a more than a two-fold increase in risk when the oldest age group was compared to the youngest. The older age groups seem to be more vulnerable to the effects of winter and should be an important risk targeted group for prevention policies and strategies.

The excess winter paradox observed across countries in Europe and the identified decline in winter deaths seen in some countries suggests that significant increases in death during winter are preventable. The decline observed in excess winter mortality in all age groups, as well as overall, observed during the 2000-2001 year is quite significant. This period had the lowest EWMR and also observed the highest percentage drop in EWMR. It also had the least absolute excess winter death counts among all the year periods studied. A few months earlier to this particular period, the UK government introduced innovative measures to tackle the burden of winter excess deaths. These measures were robust interventions incorporated in the fuel poverty strategy. This sharp drop in EWMR may suggest that these measures may have had an immediate impact. However, this study cannot conclusively confirm this. Nevertheless, if these strategies had had an immediate impact, it was definitely short-lived. This is because while unstable fluctuations in the yearly EWMR were seen in the younger age groups it seems to be threateningly increasing in age group 75+ and in total, with no signs of decreasing. In other words, the increased risk of dying during winter due to AMI has remained high in England and Wales despite the various strategies implemented by the government. It might be that it is too soon to evaluate the impact of these measures or they may not be effective.

Conclusion

This study has shown that seasonal variations in mortality due to acute myocardial infarction do exist. This is greater during the winter. The excess winter mortality has remained high for AMI for England and Wales over the years. The study also identified an association between increasing age and increasing excess winter mortality. There is a possibility that acclimatization may play a role in the mechanisms that initiate winter deaths.

A. Contributor ship Statement

Find below the contribution of each author

- **Osakpolor Ogbebor**: literature review, data analysis and interpretation of data. Drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Odugbemi Babatunde**: literature review, drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Maheswaran Ravi.**: Conception and design of study, acquisition of data, literature review, revising manuscript. Approval of the version of the manuscript to be published.
- **Patel Kavya**: drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published.

B. Competing interest: None

C. Funding: Self-funded by the authors

D. Data sharing statement: The data used in this study was obtained from the office of national statistics, United Kingdom.

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Abstract

Background: Acute myocardial infarction (AMI) is a leading cause of death globally. Increase in AMI mortality during winter has also been identified in existing literature. This has been associated with low outdoor and indoor temperatures and increasing age. The relationship between AMI and other factors such as gender and socioeconomic factors varies from study to study. Influenza epidemics have also been identified as a contributory factor.

Objective: This paper aims to illustrate the seasonal trend in mortality due to AMI in England and Wales with emphasis on excess winter mortality.

Methods: Monthly mortality rates per 10,000 population were calculated from data provided by the U.K. Office for National Statistics (ONS) for 1997 to 2005. To quantify the seasonal variation in winter, the excess winter mortality estimates (Excess Winter Mortality (EWM), Excess Winter Mortality Ratio (EWMR), Excess Winter Mortality Index (EWMI) for each year were calculated. Negative binomial regression model was used to estimate the relationship between increasing age and excess winter mortality.

Results:

The decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005. Significant trend for reduction in AMI associated mortality was observed over the period ($p<0.001$). This decline was not seen with excess winter mortality ($p<0.001$). 17% excess deaths were observed during winter. This amounted to about 20,000 deaths over the 8 year period. Increasing winter mortality was seen with increasing age for AMI.

Conclusion: Excess winter mortality secondary to AMI does occur in England and Wales. Excess winter deaths due to AMI have remained high despite decline in overall mortality. More research is needed to identify the relationship of sex, temperature, acclimatization and excess winter deaths due to AMI.

Strengths

- The data used involved a large sample size and this was able to capture relevant results in the data analysis and this data represents the population of interest.
- The paper gives further insight into the concept of excess winter mortality.

Limitations

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A study involving data from various countries in Europe found a similar association but also identified 18^{o}C as the threshold for this to occur[11]. Research carried out in Scotland[12] and in England[13] could quantify this relationship: a 1^{o}C drop in temperature resulted in a 1-2% increase in the number of deaths. This corresponds to increased odds of dying during the winter by 1.5% [10].

The effects of temperature are both direct and immediate. Time series analyses have shown that there is a minimum lag time of about 24 hours between drop in temperature and increase in mortality[14]. The impact of cold temperature could also extend over a period of 1 to 2 weeks. This lag time shows that there is a possible mechanism that is initiated by the low outdoor temperatures directly that leads to death supporting evidence from previous studies. It has also been shown that the effect of temperature is significantly potentiated by high relative humidity and strong winds[15].

There are suggestions that the influence of winters and low temperatures on the "spiked" increase in mortality rates is preventable. This is because there is ecological evidence that countries with colder winters do not have greater excess winter mortality when compared to countries with milder winters[4], for example the United Kingdom when compared to Scandinavian countries[16, 17]. This observation is referred to as the excess winter paradox. Factors that are considered to play a role include socioeconomic status[17], influenza[18,19] and age[16]. Other factors considered include housing insulation and the concept of fuel poverty both of which affect the indoor temperature. Housing in Britain has lower insulation properties compared to houses in Germany, Russia or the Scandinavian countries[20]. Due to the low insulation properties of housing in England and Wales, it is more expensive to warm these homes when compared to houses in other European states. This introduces the concept of fuel poverty. Fuel poverty is defined as a situation *"when in order to heat its home to an adequate standard of warmth a household needs to spend more than 10% of its income on total fuel use[21]."* The World Health Organization's (WHO) recommendation of adequate standard warmth is defined as 18^{o}C in occupied rooms and 21^{o}C in living room. The temperature level of 18^{o}C is remarkable because below this threshold has been identified as when significant mortality occurs. The ability to generate heat to a surrounding temperature above this identified threshold might prove necessary. The UK Government has acknowledged that excess winter mortality is a problem and currently has put in place some policies to tackle this phenomenon.

There are few studies that have taken examined the phenomenon of excess winter mortality specifically due to AMI in England and Wales. Most studies treat the subject of excess winter mortality by assessing total mortality without isolating individual diagnosis. Assessing individual diseases might produce stronger evidence on the impact seasonal variation on a particular disease condition. Due to the overwhelming global impact of this condition, it is important to identify seasonal variation of mortality due to AMI and also points of possible preventive strategies that can help in reducing the incidence of the disease.

Methodology

This study was a secondary data analysis that assessed excess winter deaths due to AMI in England and Wales. The study used anonymised mortality data provided by the office of National Statistics (ONS), United Kingdom (UK) and mean monthly temperature data provided by the Meteorological Office, UK. The database provided by the ONS consisted of anonymised data of daily mortality in England and Wales for the period from 1997 to 2005. The International Classification of Disease (ICD) was used for coding the various cause of death. The ninth edition (ICD-9) was used from 1997 to 2000 while the tenth edition (ICD-10) was used between 2001 and 2005. The cause of death considered for the study was acute myocardial Infarction (ICD-9:410; ICD-10: I21). This was presented in 3 age groups: 0 to 64 years, 65 to 74 years, and 75 years and above. There was no sex distribution provided.

Age-specific mortality rates were also calculated for each age group. The daily, monthly, and yearly mortality rates were calculated and the age specific population served as denominator. The population data for each year and each age group was extracted from ONS yearly publications. The monthly rates were standardised to 30 day months.

Adjustments in mortality rates were also made to account for changes in ICD coding. This was done using this formula: MA (y, d) = MO (y, d). R. MA is the adjusted daily mortality (deaths) for a day, d, in year, y. MO is the observed mortality. R is the comparability ratio: the ICD-10/ICD-9 comparability ratio for acute myocardial infarction 0.9889 was used to adjust ICD-9 code death counts[22].

Specifically the concept of excess winter deaths was explored in this study. The method used to analyse the excess winter deaths was first described by Curwen and it is similar to that used by the ONS[23]. The months of December to March defines the winter period. The non-winter period is defined as the months of August to November before this winter period, and the months of April to July following the winter period.

In order to quantify the seasonal variation in winter, the excess winter mortality (EWM), excess winter mortality ratio (EWMR), and the excess winter mortality index (EWMI) for each year was calculated. The EWM reflects the absolute difference in mortality between the winter season and non-winter season. Whereas the EWMR represents the relative risk of death during the winter months compared to the non-winter months. The EWMI represents a variant of relative risk reduction or "excess". The EWMR and EWMI are viable tools for comparisons between age, sex, regions or countries. These estimates were also calculated for each age group. These estimates were calculated using the following formulae:

- EWM= O –E
- EWMR = O/E
- EWMI = (O –E)/E or EWMR-1 (represented as a percentage)

Where, O is the observed death count. This is the total death counts during the winter months, a period of 4 months, (winter deaths). E is the expected death count which is the total death counts during the non-winter months, a period of 8 months, divided by 2.

Direct correlation between mean monthly temperature and monthly mortality rate was carried out with a significant level set at <0.05. Addition trend analysis with autoregressive integrated moving average (ARIMA) model and forecasting was done with a significant level < 0.05.

A regression model was used in assessing the rates of death during the winter season and non-winter seasons. The log-linear model was derived with the mortality count during winter period as the estimated outcome while age was the explanatory variable. The hypothesis was to test if there was any difference between excess winter mortality ratios amongst the various age groups. Therefore, the log of the average non-winter deaths was used as offset to fit the model. The model was fitted using a negative binomial model with a log link function due to over dispersion in the initial analysis. All analysis was carried out using the Statistical package for social sciences (SPSS) version 19. Significant p – value was defined as less than 0.05.

Results

Table: 1 Yearly mortality patterns of AMI from August 1997 to July 2005.

Year Period*	**Mortality Rate per 10,000 (Number of deaths)**			
	Age:			
	0 to 64 years	65 to 74 years	75 years and above	Total
97/98	1.96 (8184)	24.72 (14299)	83.59 (33678)	10.87 (56161)
98/99	1.81 (7581)	22.59 (13119)	79.84 (32283)	10.22 (52983)
99/00	1.64 (6924)	20.11 (11724)	74.70 (30330)	9.41 (48978)
00/01	1.52 (6435)	17.99 (10528)	67.98 (27716)	8.55 (44679)
01/02	1.40 (5964)	16.28 (9567)	65.00 (26610)	8.03 (42141)
02/03	1.35 (5784)	14.71 (8685)	64.45 (26495)	7.77 (40964)
03/04	1.21 (5189)	13.39 (7937)	60.84 (25125)	7.22 (38251)
04/05	1.16 (5005)	11.84 (7066)	55.79 (23180)	6.62 (35251)
Total	1.51 (51066)	17.70 (82925)	69.02 (225417)	8.59 (359408)

Between August 1997 and July 2005 there were 359,408 deaths due to acute myocardial infarction (AMI) with an average death count of 44,926 occurring yearly (Table 1). 62.7% of the total deaths were seen in the age group 75 years and above, 23.1% in age group 65 to 74 years and 14.2% in age group 0 to 64 years. A steady decline in the absolute death counts as well as mortality rates were seen in all age groups across the years (Figure 1). Overall, the decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005.

A sharp rise in mortality is noticed in early November and peaks between December and January (Figure 2). A second rise also occurs around the month of March but the mortality rate seen during this period is not as high as that observed during the December and January months. The lowest mortality rates occurred during July and August months.

A plot of the mean temperatures in Celsius (figure 3) showed a trough during the months of December to March and when compared to figure 2 this indicates that lower temperatures are observed during the peaks of mortality during the year. A plot of the mean monthly temperature with mortality rate showed a significant negative correlation between the two variables ($r = -0.479$; $P < 0.0001$).

Estimation of Excess Winter Mortality due to AMI

Excess winter mortality was seen in all the years observed. An average of about 2,463 excess winter deaths occurred yearly. In all year periods the highest absolute EWM occurred in those 75 years and above (Table 2). This age group also contribute an average of 70% to the excess winter deaths yearly. The excess winter mortality over the 8 year period resulted in 19,635 total deaths. This is equivalent to 5.5% of the overall yearly mortality due to AMI over the 8 year period.

The excess winter mortality ratio (winter: non-winter rate ratio) is greater than 1 in all year periods considered, indicating that there is greater mortality in winter compared to the non-winter months (Table 3). The excess winter mortality ratio describes the risk in dying during winter compared to non-winter months. This can also be represented as a percentage (Excess winter mortality index). This shows that there is an average 17% excess death yearly (Table 2).

Table 2: Excess Winter Mortality and index secondary to AMI between 1997-2005

Year Period	EWM (EWMI)			
	Age: 0 to 64 years	65 to 74 years	75 years +	Total
97/98	244.5(9%)	731.5(16%)	1716.0(16%)	2692.0(15%)
98/99	281.5(12%)	756.0(18%)	2280.0(23%)	3317.5(20%)
99/00	333.0(15%)	643.5(17%)	2715.0(29%)	3691.5(24%)
00/01	148.5(7%)	368.5(11%)	1332.5(15%)	1849.5(13%)
01/02	258.0(14%)	453.0(15%)	1372.5(16%)	2083.5(16%)
02/03	196.5(11%)	423.0(15%)	1430.0(17%)	2049.5(16%)
03/04	251.0(15%)	260.0(10%)	1339.5(17%)	1850.5(15%)
04/05	140.5(9%)	466.0(21%)	1494.5(21%)	2101.0(19%)
Total	1853.5(11%)	4101.5(16%)	13680.0(19%)	19635.0(17%)

Table 3. Excess Winter Mortality Ratio secondary to AMI between 1997-2005

Year Period	Excess winter mortality ratio (CI)			
	Age: 0 to 64 years	65 to 74 years	75 years +	Total
97/98	1.09 (1.07, 1.11)	1.16 (1.15, 1.18)	1.16 (1.15, 1.17)	1.15 (1.14, 1.16)
98/99	1.12 (1.09, 1.14)	1.18 (1.17, 1.20)	1.23 (1.22, 1.24)	1.20 (1.19, 1.21)
99/00	1.15 (1.13, 1.17)	1.17 (1.16, 1.19)	1.29 (1.28, 1.31)	1.24 (1.24, 1.25)
00/01	1.07 (1.05, 1.09)	1.11 (1.09, 1.13)	1.15 (1.14, 1.16)	1.13 (1.12, 1.14)
01/02	1.14 (1.11, 1.16)	1.15 (1.13, 1.17)	1.16 (1.15, 1.17)	1.16 (1.15, 1.17)
02/03	1.11 (1.08, 1.13)	1.15 (1.13, 1.17)	1.17 (1.16, 1.18)	1.16 (1.15, 1.17)
03/04	1.15 (1.13, 1.18)	1.10 (1.08, 1.12)	1.17 (1.16, 1.18)	1.15 (1.14, 1.16)
04/05	1.09 (1.06, 1.11)	1.21 (1.19, 1.23)	1.21 (1.19, 1.22)	1.19 (1.18, 1.20)
All periods	1.11 (1.10, 1.13)	1.16 (1.14, 1.17)	1.19 (1.18, 1.20)	1.17 (1.17, 1.18)

A regression analysis was carried using a negative binomial regression to estimate the excess winter mortality ratio and age (Table 4). The relative risk of excess mortality in age groups 65 to 74 years and 75 years and above was 1.36 and 2.45 respectively compared to the younger age group.

Table 4: Excess winter mortality ratio and age

Age	coefficient	EWM(%)	Relative risk	P-value
0 to 64 years	reference	11		
65 to 74 years	0.308	16	1.36 (1.18-1.57)	<0.0001
75 years +	0.894	19	2.45 (2.16-2.77)	<0.0001

Figure 4 shows the trend of mortality rate and excess winter mortality index (EWMI) secondary to AMI. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality observed over the period studied ($p<0.001$). The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change and remains relatively the same ($p<0.001$).

Discussion

The results from the data analysis showed there is a significant increase in mortality rates due to AMI during the winter period in England and Wales. In this study, the excess winter mortality ratio over the 8 year study period for all age groups was 1.17 with a resultant 17% excess winter deaths for acute myocardial infarction. This amounted to about 20,000 excess deaths due to this disease. From their analysis of 2266 deaths, Biedrzycki and Baithun[1] in their study of mortality from myocardial infarction found that December was the peak month of mortality. A decline was observed from February onwards with the lowest mortality rate observed during the month of August. This pattern is similar to what was elicited in this paper: the highest mortality rates peaked between December and January and lowest mortality rates were observed during the months of July and August.

Besides the demonstrable winter excess, the monthly mortality rate plot showed a double peak. A peak in mortality, which was clearly above the mean mortality rate, was observed around the month of March. This second peak in mortality was less than that seen in the months of December and January.

Since fluctuations in daily temperatures could not be appreciated from monthly mean temperature data, it is possible that absolute low outdoor temperatures may not be the only factor in causing mortality but rather daily changes in temperature may also be significant. It has already been established that in most countries in Europe a 1°C drop in temperature is associated in increasing in mortality[12, 13]. Carson et al, in their study found that cardiovascular diseases were more sensitive to temperature changes than respiratory disease[24.] This relationship has also been recognized in other studies: Kysely et al[14] found that fluctuations in daily temperatures resulted in increase in mortality rates of cardiovascular diseases. They also noted that a second cold spell usually had a lower excess mortality and suggested that the reason for this might be that some form of acclimatization to the previous cold spell might be protective against the next. This might explain the double peaks that were observed in this study. Large variations in temperatures between winter and non-winter months as seen in countries with warm winters such as England and Wales may also explain the winter paradox observed in Europe. It is possible that the lack of acclimatization due to the non-persistent cold weather, unlike in Iceland and Russia, may lead to a greater impact when the winter season does arrive. However, this is not conclusive and would require more research to clearly define such an association.

The study has shown that AMI has undergone a steady decline in England and Wales over the years. This is remarkable. The decline of mortality rate from 10.87 deaths per 100,000 population to 6.62 deaths per 10,000 population was observed over the 8 years study period. This was statistically significant. The reasons for this may include such factors as better diagnostic and therapeutic procedures, healthier life styles of the population, and better awareness of the public. Despite this steady decrease in total yearly mortality rate, the risk of dying from AMI during winter has remained the same. This is suggestive that excess winter mortality is not a function of the overall mortality. This has important control and prevention implications: the measures used to control overall mortality may not necessary influence winter excess.

There are several factors which could be possibly associated with excess winter mortality and this may include seasonal variations in solar ultraviolet-B (UVB) doses and serum 25-hydroxyvitamin D [25(OH)D] concentrations, gene expression, ambient temperature and humidity, UVB effects on environmental pathogen load, environmental pollutants and allergens, and photoperiod (or length of day)[25]. Amongst these factors, possibly 25(OH)D concentration (<20 ng/ml) would be modifiable risk factor and its supplementation might reduce death rates significantly in winter months. Several RCTs are ongoing and these will provide results to clarify whether vitamin D deficiency as a causal and reversible factor to prevent cardiovascular disease.

There was a gradient relationship between excess winter deaths and age: we found increasing winter deaths with increasing age. A regression model was used to estimate the relationship between age and winter mortality and we found a more than a two-fold increase in risk when the oldest age group was compared to the youngest. The older age groups seem to be more vulnerable to the effects of winter and should be an important risk targeted group for prevention policies and strategies.

The excess winter paradox observed across countries in Europe and the identified decline in winter deaths seen in some countries suggests that significant increases in death during winter are preventable. The decline observed in excess winter mortality in all age groups, as well as overall, observed during the 2000-2001 year is interesting. This period had the lowest EWMR and also observed the highest percentage drop in EWMR. It also had the least absolute excess winter death counts among all the year periods studied. A few months earlier, the UK government introduced innovative measures to tackle the burden of winter excess deaths. These measures were robust interventions incorporated in the fuel poverty strategy. This sharp drop in EWMR may suggest that these measures may have had an immediate impact. However, this study cannot conclusively confirm this. Nevertheless, if these strategies had had an immediate impact, it was definitely short-lived. This is because despite the fluctuations the trend has remained the same. In other words, the increased risk of dying during winter due to AMI has remained high in England and Wales despite the various strategies implemented by the government, and the trend analysis shows that it will remain so for a couple of years. It might be that it is too soon to evaluate the impact of these measures or they may not be effective.

Conclusion

This study has shown that increased winter mortality due to acute myocardial infarction do exist. The excess winter mortality has remained high for AMI for England and Wales over the years. The study also identified an association between increasing age and increasing excess winter mortality. There is a possibility that acclimatization may play a role in the mechanisms that initiate winter deaths.

Figure Legends

Figure 1: Showing a decline in mortality rate due to AMI over the year periods

Figure 2 Showing variation in mortality rate over the months over the year periods

Figure 3: A plot of the mean monthly temperatures in Celsius with an obvious deep in temperatures during the months of December to March

Figure 4: Trend in mortality rate and excess winter mortality index over the year period observed and forecast for the next 11 years. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality. The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change.

A. Contributor ship Statement

Find below the contribution of each author

- **Osakpolor Ogbebor**: literature review, data analysis and interpretation of data. Drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Odugbemi Babatunde**: literature review, drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Maheswaran Ravi.**: Conception and design of study, acquisition of data, literature review, revising manuscript. Approval of the version of the manuscript to be published.
- **Patel Kavya**: drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published.

B. Competing interest: None

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D. Data sharing statement: The data used in this study was obtained from the office of national statistics, United Kingdom.

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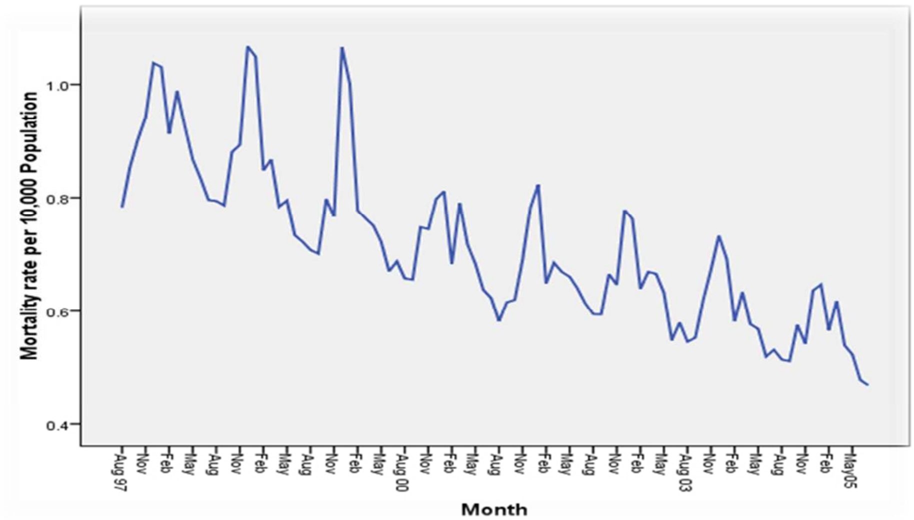

Figure 1: Mortality rate during the months of the year period

Figure 1: Showing a decline in mortality rate due to AMI over the year periods

147x98mm (150 x 150 DPI)

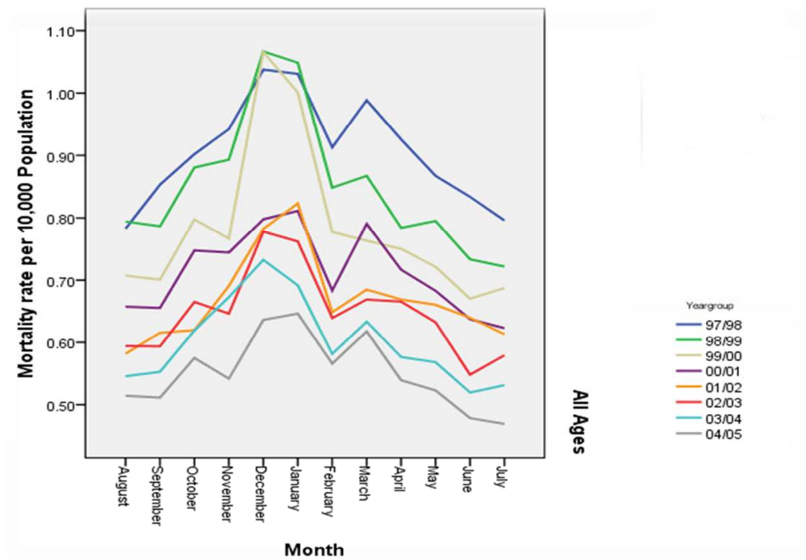

Figure 2: Mortality rate during months over the year periods

Figure 2 showing variation in mortality rate over the months over the year periods

174x128mm (150 x 150 DPI)

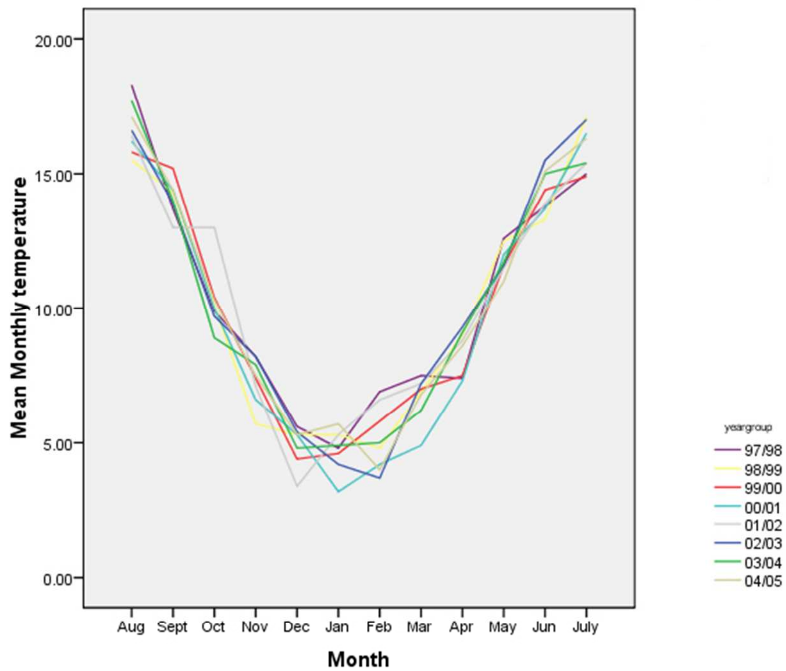

Figure 3: Mean Monthly Temperature over the year periods

Figure 3: A plot of the mean monthly temperatures in Celsius with an obvious deep in temperatures during the months of December to March

190x179mm (96 x 96 DPI)

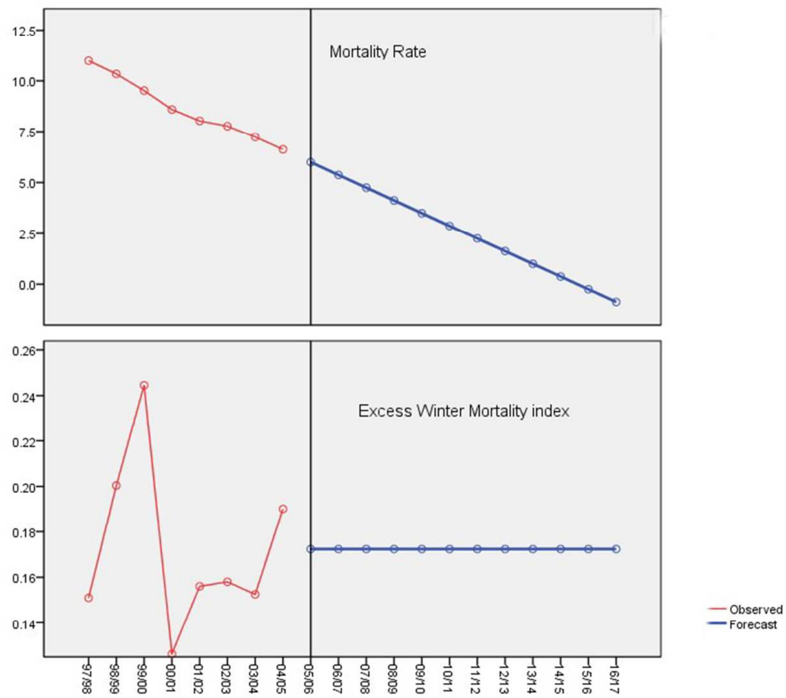

Figure 4: Trend of mortality rate and excess winter mortality index over the observed period and forecast

Figure 4: Trend in mortality rate and excess winter mortality index over the year period observed and forecast for the next 11 years. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality. The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change .

239x210mm (96 x 96 DPI)

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Seasonal variation in mortality secondary to acute myocardial infarction in England and Wales: a secondary data analysis

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Seasonal variation in mortality secondary to acute myocardial infarction in England and Wales: a secondary data analysis

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Abstract

Background: Acute myocardial infarction (AMI) is a leading cause of death globally. Increase in AMI mortality during winter has also been identified in existing literature. This has been associated with low outdoor and indoor temperatures and increasing age. The relationship between AMI and other factors such as gender and socioeconomic factors varies from study to study. Influenza epidemics have also been identified as a contributory factor.

Objective: This paper aims to illustrate the seasonal trend in mortality due to AMI in England and Wales with emphasis on excess winter mortality.

Methods: Monthly mortality rates per 10,000 population were calculated from data provided by the U.K. Office for National Statistics (ONS) for 1997 to 2005. To quantify the seasonal variation in winter, the excess winter mortality estimates (Excess Winter Mortality (EWM), Excess Winter Mortality Ratio (EWMR), Excess Winter Mortality Index (EWMI) for each year were calculated. Negative binomial regression model was used to estimate the relationship between increasing age and excess winter mortality.

Results:

The decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005. Significant trend for reduction in AMI associated mortality was observed over the period ($p<0.001$). This decline was not seen with excess winter mortality ($p<0.001$). 17% excess deaths were observed during winter. This amounted to about 20,000 deaths over the 8 year period. Increasing winter mortality was seen with increasing age for AMI.

Conclusion: Excess winter mortality secondary to AMI does occur in England and Wales. Excess winter deaths due to AMI have remained high despite decline in overall mortality. More research is needed to identify the relationship of sex, temperature, acclimatization, vitamin D and excess winter deaths due to AMI.

Strengths

- The data used involved a large sample size and this was able to capture relevant results in the data analysis and this data represents the population of interest.
- The paper gives further insight into the concept of excess winter mortality.

Limitations

- Although the data provided by the ONS was complete and considered accurate, the data characteristics however restricted the number of variables that could be controlled such as sex distribution.
- The population data which was used as denominator would reduce in accuracy as the year of study moved away from the recent census (29^{th} April 2001). This is because the midyear populations after this date were extrapolated using birth and death data; these data are prone to their own type of error. However, it is anticipated that the brief period used in the research was unlikely to experience any dramatic changes in population.

Background

Studies over time have observed an increase in mortality rate during winter months[1-3]. This appears to be a global phenomenon with evidence of excess winter mortality occurring in a number of countries, including the United Kingdom[4,5], Japan[6] , Brazil[7] , Canada[2], the United States[3] and New Zealand [8].

The relationship between mortality and temperature observes a U shape[9]: an increase in mortality is seen with extremes in temperature. Excess winter mortality which is defined as "a significant increase in the number of deaths during winter compared with the average of the non-winter seasons" has been linked to the drop in temperature[10]. Low temperatures have been implicated in the increase in number of deaths during the winter months; however, they are not due to hypothermia. There is evidence to suggest that low temperatures trigger pathological mechanisms that lead to increase in blood pressure and thrombus formation[2]. The consequence of this is the initiation of physiological stress that results in the development of a myocardial infarction or a stroke. A study involving data from various countries in Europe found a similar association but also identified 18°C as the threshold for this to occur[11]. Research carried out in Scotland[12] and in England[13] could quantify this relationship: a 1°C drop in temperature resulted in a 1-2% increase in the number of deaths. This corresponds to increased odds of dying during the winter by 1.5% [10].

The effects of temperature are both direct and immediate. Time series analyses have shown that there is a minimum lag time of about 24 hours between drop in temperature and increase in mortality[14]. The impact of cold temperature could also extend over a period of 1 to 2 weeks. This lag time shows that there is a possible mechanism that is initiated by the low outdoor temperatures directly that leads to death supporting evidence from previous studies. It has also been shown that the effect of temperature is significantly potentiated by high relative humidity and strong winds[15].

There are suggestions that the influence of winters and low temperatures on the increase in mortality rates is preventable. This is because there is ecological evidence that countries with colder winters do not have greater excess winter mortality when compared to countries with milder winters[4], for example the United Kingdom when compared to Scandinavian countries[16, 17]. This observation is referred to as the excess winter paradox.

Housing insulation and the concept of fuel poverty, both of which affect the indoor temperature, are some of the factors thought to be responsible for the paradox. Housing in Britain has lower insulation properties compared to houses in Germany, Russia or the Scandinavian countries[18]. Due to the low insulation properties of housing in England and Wales, it is more expensive to warm these homes when compared to houses in other European states. This introduces the concept of fuel poverty. Fuel poverty is defined as a situation *"when in order to heat its home to an adequate standard of warmth a household needs to spend more than 10% of its income on total fuel use[19]."* The World Health Organization's (WHO) recommendation of adequate standard warmth is defined as 18^oC in occupied rooms and 21^oC in living room. The temperature level of 18^oC is remarkable because below this threshold has been identified as when significant mortality occurs. The ability to generate heat to a surrounding temperature above this identified threshold might prove necessary. A behavioural component may also be contributory to the paradox. For example people living in warmer winters such as United Kingdom and Portugal were less likely to heat the living and bedroom to recommended levels when outdoor temperature drops[11]. This is a marked contrast to persons leaving in countries like Russia[20] who maintained their indoor temperatures at 20.9^oC and 24.2^oC when the temperature outside was 7^oC. Studies also show that people in the United Kingdom were also less likely to wear protective clothing such as hats, heavy jackets and gloves[11]. The UK Government has acknowledged that excess winter mortality is a problem and currently has put in place policies to tackle this phenomenon.

Other factors that are considered to play a role in excess winter mortality include socioeconomic status[17], influenza[21, 22], age[16] and vitamin D deficiency. Vitamin D levels less than 20ng/ml is considered an independent additional risk factor for AMI[23.24] and is not just a reflection of poor health. Dietary sources of vitamin D are usually insufficient and deficiency occurs with inadequate sun exposure. Seasonality in Vitamin D levels have been observed and levels are usually lower around winter[23,25] creating an extra burden on the cardiovascular system by various postulated mechanisms leading to significant coronary artery disease[26] and poor collateral circulation[27]. This seasonality is attributed to variability in UVB exposure during the seasons[28]. There is the suggestion that correction of vitamin deficiency may reduce the cardiovascular risk.

There are few studies that have taken examined the phenomenon of excess winter mortality specifically due to AMI in England and Wales. Most studies treat the subject of excess winter mortality by assessing total mortality without isolating individual diagnosis. Assessing individual diseases might produce stronger evidence on the impact seasonal variation on a particular disease condition. Due to the overwhelming global impact of this condition, it is important to identify seasonal variation of mortality due to AMI and also points of possible preventive strategies that can help in reducing the incidence of the disease.

Methodology

This study was a secondary data analysis that assessed excess winter deaths due to AMI in England and Wales. The study used anonymised mortality data provided by the office of National Statistics (ONS), United Kingdom (UK) and mean monthly temperature data provided by the Meteorological Office, UK. The database provided by the ONS consisted of anonymised data of daily mortality in England and Wales for the period from 1997 to 2005. The International Classification of Disease (ICD) was used for coding the various cause of death. The ninth edition (ICD-9) was used from 1997 to 2000 while the tenth edition (ICD-10) was used between 2001 and 2005. The cause of death considered for the study was acute myocardial Infarction (ICD-9:410; ICD-10: I21). This was presented in 3 age groups: 0 to 64 years, 65 to 74 years, and 75 years and above. There was no sex distribution provided.

Age-specific mortality rates were also calculated for each age group. The daily, monthly, and yearly mortality rates were calculated and the age specific population served as denominator. The population data for each year and each age group was extracted from ONS yearly publications. The monthly rates were standardised to 30 day months.

Adjustments in mortality rates were also made to account for changes in ICD coding. This was done using this formula: MA (y, d) = MO (y, d). R. MA is the adjusted daily mortality (deaths) for a day, d, in year, y. MO is the observed mortality. R is the comparability ratio: the ICD-10/ICD-9 comparability ratio for acute myocardial infarction 0.9889 was used to adjust ICD-9 code death counts[29].

Specifically the concept of excess winter deaths was explored in this study. The method used to analyse the excess winter deaths was first described by Curwen and it is similar to that used by the ONS[30]. The months of December to March defines the winter period. The non-winter period is defined as the months of August to November before this winter period, and the months of April to July following the winter period.

In order to quantify the seasonal variation in winter, the excess winter mortality (EWM), excess winter mortality ratio (EWMR), and the excess winter mortality index (EWMI) for each year was calculated. The EWM reflects the absolute difference in mortality between the winter season and non-winter season. Whereas the EWMR represents the relative risk of death during the winter months compared to the non-winter months. The EWMI represents a variant of relative risk reduction or "excess". The EWMR and EWMI are viable tools for comparisons between age, sex, regions or countries. These estimates were also calculated for each age group. These estimates were calculated using the following formulae:

- EWM= O –E
- EWMR = O/E
- EWMI = (O –E)/E or EWMR-1 (represented as a percentage)

Where, O is the observed death count. This is the total death counts during the winter months, a period of 4 months, (winter deaths). E is the expected death count which is the total death counts during the non-winter months, a period of 8 months, divided by 2.

Direct correlation between mean monthly temperature and monthly mortality rate was carried out with a significant level set at <0.05. Addition trend analysis with autoregressive integrated moving average (ARIMA) model and forecasting was done with a significant level < 0.05.

A regression model was used in assessing the rates of death during the winter season and non-winter seasons. The log-linear model was derived with the mortality count during winter period as the estimated outcome while age was the explanatory variable. The hypothesis was to test if there was any difference between excess winter mortality ratios amongst the various age groups. Therefore, the log of the average non-winter deaths was used as offset to fit the model. The model was fitted using a negative binomial model with a log link function due to over dispersion in the initial analysis. All analysis was carried out using the Statistical package for social sciences (SPSS) version 19. Significant p – value was defined as less than 0.05.

Results

Table: 1 Yearly mortality patterns of AMI from August 1997 to July 2005.

Year Period*	Mortality Rate per 10,000 (Number of deaths)			
	Age:			
	0 to 64 years	65 to 74 years	75 years and above	Total
97/98	1.96 (8184)	24.72 (14299)	83.59 (33678)	10.87 (56161)
98/99	1.81 (7581)	22.59 (13119)	79.84 (32283)	10.22 (52983)
99/00	1.64 (6924)	20.11 (11724)	74.70 (30330)	9.41 (48978)
00/01	1.52 (6435)	17.99 (10528)	67.98 (27716)	8.55 (44679)
01/02	1.40 (5964)	16.28 (9567)	65.00 (26610)	8.03 (42141)
02/03	1.35 (5784)	14.71 (8685)	64.45 (26495)	7.77 (40964)
03/04	1.21 (5189)	13.39 (7937)	60.84 (25125)	7.22 (38251)
04/05	1.16 (5005)	11.84 (7066)	55.79 (23180)	6.62 (35251)
Total	1.51 (51066)	17.70 (82925)	69.02 (225417)	8.59 (359408)

Between August 1997 and July 2005 there were 359,408 deaths due to acute myocardial infarction (AMI) with an average death count of 44,926 occurring yearly (Table 1). 62.7% of the total deaths were seen in the age group 75 years and above, 23.1% in age group 65 to 74 years and 14.2% in age group 0 to 64 years. A steady decline in the absolute death counts as well as mortality rates were seen in all age groups across the years (Figure 1). Overall, the decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005.

A sharp rise in mortality is noticed in early November and peaks between December and January (Figure 2). A second rise also occurs around the month of March but the mortality rate seen during this period is not as high as that observed during the December and January months. The lowest mortality rates occurred during July and August months.

A plot of the mean temperatures in Celsius (figure 3) showed a trough during the months of December to March and when compared to figure 2 this indicates that lower temperatures are observed during the peaks of mortality during the year. A plot of the mean monthly temperature with mortality rate showed a significant negative correlation between the two variables ($r = -0.48$; $P < 0.0001$).

Estimation of Excess Winter Mortality due to AMI

Excess winter mortality was seen in all the years observed. An average of about 2,463 excess winter deaths occurred yearly. In all year periods the highest absolute EWM occurred in those 75 years and above (Table 2). This age group also contribute an average of 70% to the excess winter deaths yearly. The excess winter mortality over the 8 year period resulted in 19,635 total deaths. This is equivalent to 5.5% of the overall yearly mortality due to AMI over the 8 year period.

The excess winter mortality ratio (winter: non-winter rate ratio) is greater than 1 in all year periods considered, indicating that there is greater mortality in winter compared to the non-winter months (Table 3). The excess winter mortality ratio describes the risk in dying during winter compared to non-winter months. This can also be represented as a percentage (Excess winter mortality index). This shows that there is an average 17% excess death yearly (Table 2).

Table 2: Excess Winter Mortality and index secondary to AMI between 1997-2005

Year Period	**EWM (EWMI)**			
	Age: 0 to 64 years	65 to 74 years	75 years +	Total
97/98	244.5(9%)	731.5(16%)	1716.0(16%)	2692.0(15%)
98/99	281.5(12%)	756.0(18%)	2280.0(23%)	3317.5(20%)
99/00	333.0(15%)	643.5(17%)	2715.0(29%)	3691.5(24%)
00/01	148.5(7%)	368.5(11%)	1332.5(15%)	1849.5(13%)
01/02	258.0(14%)	453.0(15%)	1372.5(16%)	2083.5(16%)
02/03	196.5(11%)	423.0(15%)	1430.0(17%)	2049.5(16%)
03/04	251.0(15%)	260.0(10%)	1339.5(17%)	1850.5(15%)
04/05	140.5(9%)	466.0(21%)	1494.5(21%)	2101.0(19%)
Total	1853.5(11%)	4101.5(16%)	13680.0(19%)	19635.0(17%)

Table 3. Excess Winter Mortality Ratio secondary to AMI between 1997-2005

Year Period	**Excess winter mortality ratio (CI)**			
	Age: 0 to 64 years	65 to 74 years	75 years +	Total
97/98	1.09 (1.07, 1.11)	1.16 (1.15, 1.18)	1.16 (1.15, 1.17)	1.15 (1.14, 1.16)
98/99	1.12 (1.09, 1.14)	1.18 (1.17, 1.20)	1.23 (1.22, 1.24)	1.20 (1.19, 1.21)
99/00	1.15 (1.13, 1.17)	1.17 (1.16, 1.19)	1.29 (1.28, 1.31)	1.24 (1.24, 1.25)
00/01	1.07 (1.05, 1.09)	1.11 (1.09, 1.13)	1.15 (1.14, 1.16)	1.13 (1.12, 1.14)
01/02	1.14 (1.11, 1.16)	1.15 (1.13, 1.17)	1.16 (1.15, 1.17)	1.16 (1.15, 1.17)
02/03	1.11 (1.08, 1.13)	1.15 (1.13, 1.17)	1.17 (1.16, 1.18)	1.16 (1.15, 1.17)
03/04	1.15 (1.13, 1.18)	1.10 (1.08, 1.12)	1.17 (1.16, 1.18)	1.15 (1.14, 1.16)
04/05	1.09 (1.06, 1.11)	1.21 (1.19, 1.23)	1.21 (1.19, 1.22)	1.19 (1.18, 1.20)
All periods	1.11 (1.10, 1.13)	1.16 (1.14, 1.17)	1.19 (1.18, 1.20)	1.17 (1.17, 1.18)

A regression analysis was carried using a negative binomial regression to estimate the excess winter mortality ratio and age (Table 4). The relative risk of excess mortality in age groups 65 to 74 years and 75 years and above was 1.36 and 2.45 respectively compared to the younger age group.

Table 4: Excess winter mortality ratio and age

Age	coefficient	EWM(%)	Relative risk	P-value
0 to 64 years	reference	11		
65 to 74 years	0.31	16	1.36 (1.18-1.57)	<0.0001
75 years +	0.89	19	2.45 (2.16-2.77)	<0.0001

Figure 4 shows the trend of mortality rate and excess winter mortality index (EWMI) secondary to AMI. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality observed over the period studied ($p<0.001$). The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change and remains relatively the same ($p<0.001$).

Discussion

The results from the data analysis showed there is a significant increase in mortality rates due to AMI during the winter period in England and Wales. In this study, the excess winter mortality ratio over the 8 year study period for all age groups was 1.17 with a resultant 17% excess winter deaths for acute myocardial infarction. This amounted to about 20,000 excess deaths due to this disease. From their analysis of 2266 deaths, Biedrzycki and Baithun[1] in their study of mortality from myocardial infarction found that December was the peak month of mortality. A decline was observed from February onwards with the lowest mortality rate observed during the month of August. This pattern is similar to what was elicited in this paper: the highest mortality rates peaked between December and January and lowest mortality rates were observed during the months of July and August.

Besides the demonstrable winter excess, the monthly mortality rate plot showed a double peak. A peak in mortality, which was clearly above the mean mortality rate, was observed around the month of March. This second peak in mortality was less than that seen in the months of December and January.

Since fluctuations in daily temperatures could not be appreciated from monthly mean temperature data, it is possible that absolute low outdoor temperatures may not be the only factor in causing mortality but rather daily changes in temperature may also be significant. It has already been established that in most countries in Europe a 1^{o}C drop in temperature is associated in increasing in mortality[12, 13]. Carson et al, in their study found that cardiovascular diseases were more sensitive to temperature changes than respiratory disease[31.] This relationship has also been recognized in other studies: Kysely et al[14] found that fluctuations in daily temperatures resulted in increase in mortality rates of cardiovascular diseases. They also noted that a second cold spell usually had a lower excess mortality and suggested that the reason for this might be that some form of acclimatization to the previous cold spell might be protective against the next. This might explain the double peaks that were observed in this study. Large variations in temperatures between winter and non-winter months as seen in countries with warm winters such as England and Wales may also explain the winter paradox observed in Europe. It is possible that the lack of acclimatization due to the non-persistent cold weather, unlike in Iceland and Russia, may lead to a greater impact when the winter season does arrive. However, this is not conclusive and would require more research to clearly define such an association.

The study has shown that AMI has undergone a steady decline in England and Wales over the years. This is remarkable. The decline of mortality rate from 10.87 deaths per 100,000 population to 6.62 deaths per 10,000 population was observed over the 8 years study period. This was statistically significant. The reasons for this may include such factors as better diagnostic and therapeutic procedures, healthier life styles of the population, and better awareness of the public. Despite this steady decrease in total yearly mortality rate, the risk of dying from AMI during winter has remained the same. This is suggestive that excess winter mortality is not a function of the overall mortality. This has important control and prevention implications: the measures used to control overall mortality may not necessary influence winter excess.

One of such measures could be vitamin D supplementation. There are several factors which could be possibly associated with excess winter mortality and this may include seasonal variations in solar ultraviolet-B (UVB) doses and serum 25-hydroxyvitamin D [25(OH)D] concentrations, temperature and humidity[28]. Amongst these factors, possibly 25(OH)D concentration (<20 ng/ml) would be modifiable risk factor and its supplementation to levels greater than 36 ng/mL might reduce death rates significantly in winter months. In a Study in Iran[32], supplementation of vitamin to levels greater than 20ng/mL was effective in reducing the cholesterol level by about 16mg/dl. The clinical significance of this result needs to be investigated. Several clinical trials as well as observational and ecological studies are on-going and these will provide results to clarify whether vitamin D deficiency is a modifiable factor to prevent cardiovascular disease.

There was a gradient relationship between excess winter deaths and age: we found increasing winter deaths with increasing age. A regression model was used to estimate the relationship between age and winter mortality and we found a more than a two-fold increase in risk when the oldest age group was compared to the youngest. The older age groups seem to be more vulnerable to the effects of winter and should be an important risk targeted group for prevention policies and strategies.

The excess winter paradox observed across countries in Europe and the identified decline in winter deaths seen in some countries suggests that significant increases in death during winter are preventable. The decline observed in excess winter mortality in all age groups, as well as overall, observed during the 2000-2001 year is interesting. This period had the lowest EWMR and also observed the highest percentage drop in EWMR. It also had the least absolute excess winter death counts among all the year periods studied. A few months earlier, the UK government introduced innovative measures to tackle the burden of winter excess deaths. These measures were robust interventions incorporated in the fuel poverty strategy. This sharp drop in EWMR may suggest that these measures may have had an immediate impact. However, this study cannot conclusively confirm this. Nevertheless, if these strategies had had an immediate impact, it was definitely short-lived. This is because despite the fluctuations the trend has remained the same. In other words, the increased risk of dying during winter due to AMI has remained high in England and Wales despite the various strategies implemented by the government, and the trend analysis shows that it will remain so for a couple of years. It might be that it is too soon to evaluate the impact of these measures or they may not be effective.

Conclusion

This study has shown that increased winter mortality due to acute myocardial infarction does exist. The excess winter mortality has remained high for AMI for England and Wales over the years. The study also identified an association between increasing age and increasing excess winter mortality. There is a possibility that acclimatization may play a role in the mechanisms that initiate winter deaths.

Figure Legends

Figure 1: Showing a decline in mortality rate due to AMI over the year periods

Figure 2 Showing variation in mortality rate over the months over the year periods

Figure 3: A plot of the mean monthly temperatures in Celsius with an obvious deep in temperatures during the months of December to March

Figure 4: Trend in mortality rate and excess winter mortality index over the year period observed and forecast for the next 11 years. There is a steady decline in mortality rate with a

significant trend for reduction in AMI associated mortality. The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change.

A. Contributor ship Statement

Find below the contribution of each author

- **Osakpolor Ogbebor**: literature review, data analysis and interpretation of data. Drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Odugbemi Babatunde**: literature review, drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Maheswaran Ravi.**: Conception and design of study, acquisition of data, literature review, revising manuscript. Approval of the version of the manuscript to be published.
- **Patel Kavya**: drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published.

B. Competing interest: None

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D. Data sharing statement: The data used in this study was obtained from the office of national statistics, United Kingdom.

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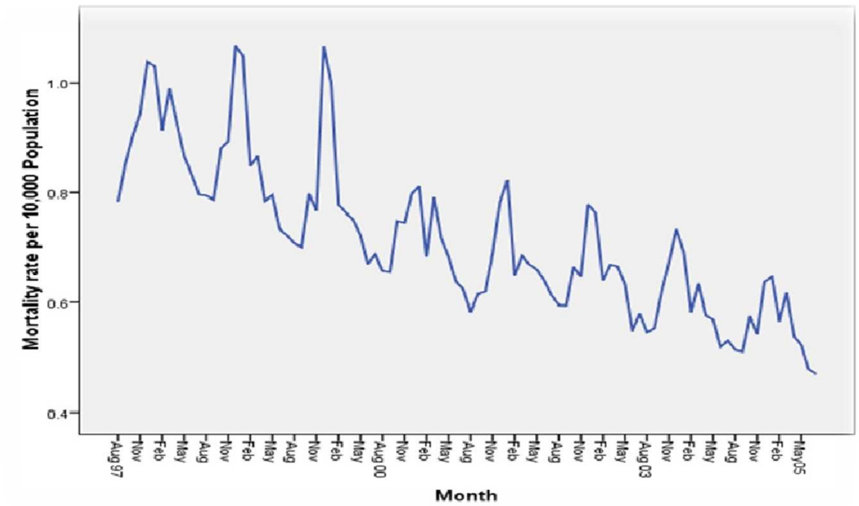

Figure 1: Showing a decline in mortality rate due to AMI over the year periods

203x114mm (144 x 144 DPI)

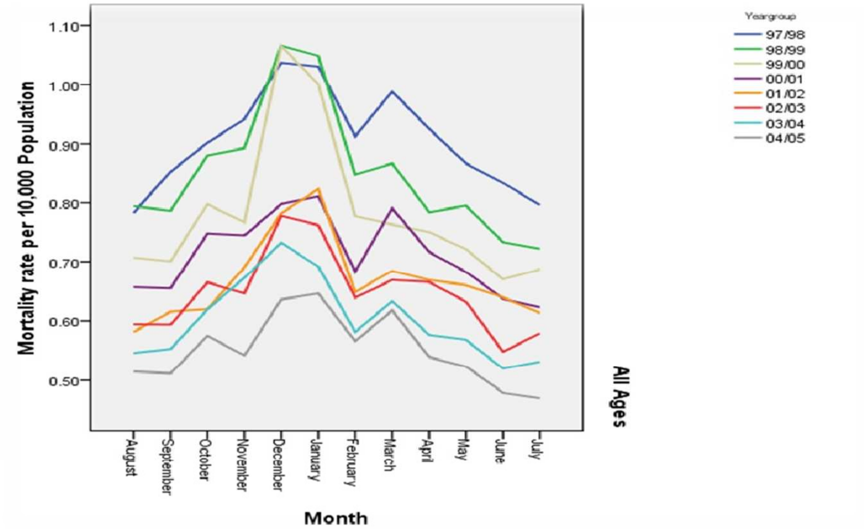

Figure 2: showing variation in mortality rate over the months over the year periods

203x114mm (144 x 144 DPI)

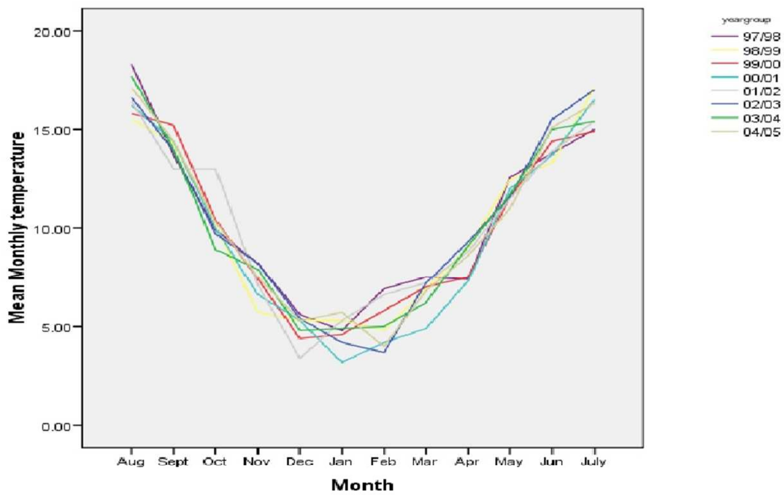

Figure 3: A plot of the mean monthly temperatures in Celsius with an obvious dip in temperatures during the months of December to March

203x114mm (144 x 144 DPI)

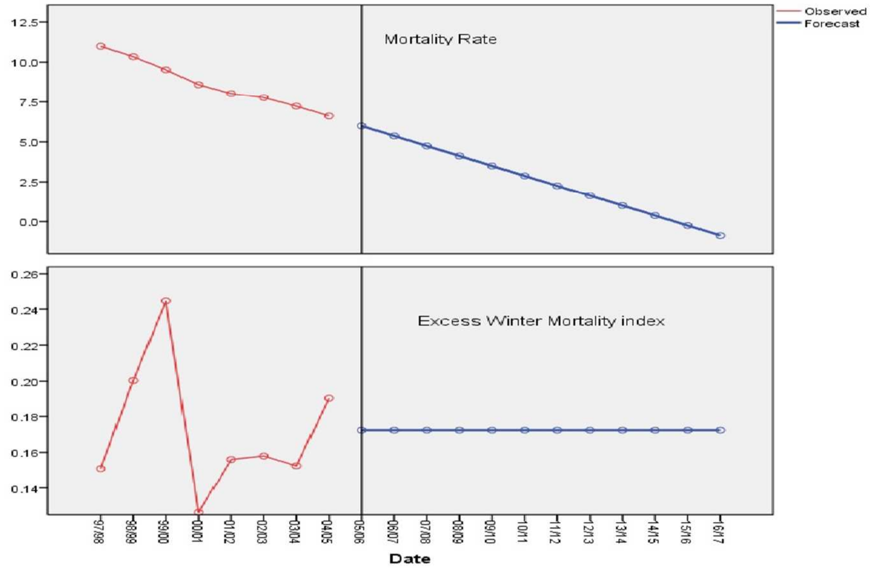

Figure 4: Trend in mortality rate and excess winter mortality index over the year period observed and forecast for the next 11 years. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality. The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change.

203x118mm (144 x 144 DPI)

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Seasonal variation in mortality secondary to acute myocardial infarction in England and Wales: a secondary data analysis

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Abstract

Background: Acute myocardial infarction (AMI) is a leading cause of death globally. Increase in AMI mortality during winter has also been identified in existing literature. This has been associated with low outdoor and indoor temperatures and increasing age. The relationship between AMI and other factors such as gender and socioeconomic factors varies from study to study. Influenza epidemics have also been identified as a contributory factor.

Objective: This paper aims to illustrate the seasonal trend in mortality due to AMI in England and Wales with emphasis on excess winter mortality.

Methods: Monthly mortality rates per 10,000 population were calculated from data provided by the U.K. Office for National Statistics (ONS) for 1997 to 2005. To quantify the seasonal variation in winter, the excess winter mortality estimates (Excess Winter Mortality (EWM), Excess Winter Mortality Ratio (EWMR), Excess Winter Mortality Index (EWMI) for each year were calculated. Negative binomial regression model was used to estimate the relationship between increasing age and excess winter mortality.

Results:

The decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005. Significant trend for reduction in AMI associated mortality was observed over the period ($p<0.001$). This decline was not seen with excess winter mortality ($p<0.001$). 17% excess deaths were observed during winter. This amounted to about 20,000 deaths over the 8 year period. Increasing winter mortality was seen with increasing age for AMI.

Conclusion: Excess winter mortality secondary to AMI does occur in England and Wales. Excess winter deaths due to AMI have remained high despite decline in overall mortality. More research is needed to identify the relationship of sex, temperature, acclimatization, vitamin D and excess winter deaths due to AMI.

Strengths

- The data used involved a large sample size and this was able to capture relevant results in the data analysis and this data represents the population of interest.
- The paper uses statistical methods that have been verified to analyse trends in mortality as well as to define the concept of excess winter mortality. The data analysis was thorough, standardising the outcomes and presenting the data in a way that can be comparable with various populations.

Limitations

- Although the data provided by the ONS was complete and considered accurate, the data characteristics however restricted the number of variables that could be controlled such as sex distribution. To reach a more robust conclusion it would have been necessary to have data to test for effects of housing, indoor temperatures, outdoor temperatures, influenza epidemics as well as other possible confounders.
- The population data which was used as denominator would reduce in accuracy as the year of study moved away from the recent census (29th April 2001). This is because the midyear populations after this date were extrapolated using birth and death data; these data are prone to their own type of error. However, it is anticipated that the brief period used in the research was unlikely to experience any dramatic changes in population.

Background

Studies over time have observed an increase in mortality rate during winter months[1-3]. This appears to be a global phenomenon with evidence of excess winter mortality occurring in a number of countries, including the United Kingdom[4,5], Japan[6] , Brazil[7] , Canada[2], the United States[3] and New Zealand [8].

The relationship between mortality and temperature observes a U shape[9]: an increase in mortality is seen with extremes in temperature. Excess winter mortality which is defined as "a significant increase in the number of deaths during winter compared with the average of the non-winter seasons" has been linked to the drop in temperature[10]. Low temperatures have been implicated in the increase in number of deaths during the winter months; however, they are not due to hypothermia. There is evidence to suggest that low temperatures trigger pathological mechanisms that lead to increase in blood pressure and thrombus formation[2]. The consequence of this is the initiation of physiological stress that results in the development of a myocardial infarction or a stroke. A study involving data from various countries in Europe found a similar association but also identified 18^{o}C as the threshold for this to occur[11]. Research carried out in Scotland[12] and in England[13] could quantify this relationship: a 1^{o}C drop in temperature resulted in a 1-2% increase in the number of deaths. This corresponds to increased odds of dying during the winter by 1.5% [10].

The effects of temperature are both direct and immediate. Time series analyses have shown that there is a minimum lag time of about 24 hours between drop in temperature and increase in mortality[14]. The impact of cold temperature could also extend over a period of 1 to 2 weeks. This lag time shows that there is a possible mechanism that is initiated by the low outdoor temperatures directly that leads to death supporting evidence from previous studies. It has also been shown that the effect of temperature is significantly potentiated by high relative humidity and strong winds[15].

There are suggestions that the influence of winters and low temperatures on the increase in mortality rates is preventable. This is because there is ecological evidence that countries with colder winters do not have greater excess winter mortality when compared to countries with milder winters[4], for example the United Kingdom when compared to Scandinavian countries[16, 17]. This observation is referred to as the excess winter paradox.

Housing insulation and the concept of fuel poverty, both of which affect the indoor temperature, are some of the factors thought to be responsible for the paradox. Housing in Britain has lower insulation properties compared to houses in Germany, Russia or the Scandinavian countries[18]. Due to the low insulation properties of housing in England and Wales, it is more expensive to warm these homes when compared to houses in other European states. This introduces the concept of fuel poverty. Fuel poverty is defined as a situation *"when in order to heat its home to an adequate standard of warmth a household needs to spend more than 10% of its income on total fuel use[19]."* The World Health Organization's (WHO) recommendation of adequate standard warmth is defined as 18°C in occupied rooms and 21°C in living room. The temperature level of 18°C is remarkable because below this threshold has been identified as when significant mortality occurs. The ability to generate heat to a surrounding temperature above this identified threshold might prove necessary. A behavioural component may also be contributory to the paradox. For example people living in warmer winters such as United Kingdom and Portugal were less likely to heat the living and bedroom to recommended levels when outdoor temperature drops[11]. This is a marked contrast to persons leaving in countries like Russia[20] who maintained their indoor temperatures at 20.9°C and 24.2°C when the temperature outside was 7°C. Studies also show that people in the United Kingdom were also less likely to wear protective clothing such as hats, heavy jackets and gloves[11]. The UK Government has acknowledged that excess winter mortality is a problem and currently has put in place policies to tackle this phenomenon.

Other factors that are considered to play a role in excess winter mortality include socioeconomic status[17], influenza[21, 22], age[16] and vitamin D deficiency. 25-hydroxyvitamin D [25(OH)D] levels less than 20ng/ml is considered an independent additional risk factor for AMI[23.24] and is not just a reflection of poor health. Dietary sources of vitamin D are usually insufficient and deficiency occurs with inadequate sun exposure. Seasonality in 25(OH)D levels have been observed and levels are usually lower around winter[23,25] creating an extra burden on the cardiovascular system by various postulated mechanisms leading to significant coronary artery disease[26] and poor collateral circulation[27]. This seasonality is attributed to variability in UVB exposure during the seasons[28]. There is the suggestion that correction of vitamin D deficiency may reduce the cardiovascular risk.

There are few studies that have taken examined the phenomenon of excess winter mortality specifically due to AMI in England and Wales. Most studies treat the subject of excess winter mortality by assessing total mortality without isolating individual diagnosis. Assessing individual diseases might produce stronger evidence on the impact seasonal variation on a particular disease condition. Due to the overwhelming global impact of this condition, it is important to identify seasonal variation of mortality due to AMI and also points of possible preventive strategies that can help in reducing the incidence of the disease.

Methodology

This study was a secondary data analysis that assessed excess winter deaths due to AMI in England and Wales. The study used anonymised mortality data provided by the office of National Statistics (ONS), United Kingdom (UK) and mean monthly temperature data provided by the Meteorological Office, UK. The database provided by the ONS consisted of anonymised data of daily mortality in England and Wales for the period from 1997 to 2005. The International Classification of Disease (ICD) was used for coding the various cause of death. The ninth edition (ICD-9) was used from 1997 to 2000 while the tenth edition (ICD-10) was used between 2001 and 2005. The cause of death considered for the study was acute myocardial Infarction (ICD-9:410; ICD-10: I21). This was presented in 3 age groups: 0 to 64 years, 65 to 74 years, and 75 years and above. There was no sex distribution provided.

Age-specific mortality rates were also calculated for each age group. The daily, monthly, and yearly mortality rates were calculated and the age specific population served as denominator. The population data for each year and each age group was extracted from ONS yearly publications. The monthly rates were standardised to 30 day months.

Adjustments in mortality rates were also made to account for changes in ICD coding. This was done using this formula: MA (y, d) = MO (y, d). R. MA is the adjusted daily mortality (deaths) for a day, d, in year, y. MO is the observed mortality. R is the comparability ratio: the ICD-10/ICD-9 comparability ratio for acute myocardial infarction 0.9889 was used to adjust ICD-9 code death counts[29].

Specifically the concept of excess winter deaths was explored in this study. The method used to analyse the excess winter deaths was first described by Curwen and it is similar to that used by the ONS[30]. The months of December to March defines the winter period. The non-winter period is defined as the months of August to November before this winter period, and the months of April to July following the winter period.

In order to quantify the seasonal variation in winter, the excess winter mortality (EWM), excess winter mortality ratio (EWMR), and the excess winter mortality index (EWMI) for each year was calculated. The EWM reflects the absolute difference in mortality between the winter season and non-winter season. Whereas the EWMR represents the relative risk of death during the winter months compared to the non-winter months. The EWMI represents a variant of relative risk reduction or "excess". The EWMR and EWMI are viable tools for comparisons between age, sex, regions or countries. These estimates were also calculated for each age group. These estimates were calculated using the following formulae:

- EWM= O –E
- EWMR = O/E
- EWMI = (O –E)/E or EWMR-1 (represented as a percentage)

Where, O is the observed death count. This is the total death counts during the winter months, a period of 4 months, (winter deaths). E is the expected death count which is the total death counts during the non-winter months, a period of 8 months, divided by 2.

Direct correlation between mean monthly temperature and monthly mortality rate was carried out with a significant level set at <0.05. Addition trend analysis with autoregressive integrated moving average (ARIMA) model and forecasting was done with a significant level < 0.05.

A regression model was used in assessing the rates of death during the winter season and non-winter seasons. The log-linear model was derived with the mortality count during winter period as the estimated outcome while age was the explanatory variable. The hypothesis was to test if there was any difference between excess winter mortality ratios amongst the various age groups. Therefore, the log of the average non-winter deaths was used as offset to fit the model. The model was fitted using a negative binomial model with a log link function due to over dispersion in the initial analysis. All analysis was carried out using the Statistical package for social sciences (SPSS) version 19. Significant p – value was defined as less than 0.05.

Patient and Public Involvement

Patients and public were not involved in the design study

Results

Table: 1 Yearly mortality patterns of AMI from August 1997 to July 2005.

Year Period*	Mortality Rate per 10,000 (Number of deaths)			
	Age:			
	0 to 64 years	65 to 74 years	75 years and above	Total
97/98	1.96 (8184)	24.72 (14299)	83.59 (33678)	10.87 (56161)
98/99	1.81 (7581)	22.59 (13119)	79.84 (32283)	10.22 (52983)
99/00	1.64 (6924)	20.11 (11724)	74.70 (30330)	9.41 (48978)
00/01	1.52 (6435)	17.99 (10528)	67.98 (27716)	8.55 (44679)
01/02	1.40 (5964)	16.28 (9567)	65.00 (26610)	8.03 (42141)
02/03	1.35 (5784)	14.71 (8685)	64.45 (26495)	7.77 (40964)
03/04	1.21 (5189)	13.39 (7937)	60.84 (25125)	7.22 (38251)
04/05	1.16 (5005)	11.84 (7066)	55.79 (23180)	6.62 (35251)
Total	1.51 (51066)	17.70 (82925)	69.02 (225417)	8.59 (359408)

Between August 1997 and July 2005 there were 359,408 deaths due to acute myocardial infarction (AMI) with an average death count of 44,926 occurring yearly (Table 1). 62.7% of the total deaths were seen in the age group 75 years and above, 23.1% in age group 65 to 74 years and 14.2% in age group 0 to 64 years. A steady decline in the absolute death counts as well as mortality rates were seen in all age groups across the years (Figure 1). Overall, the decline in mortality rate for acute myocardial infarction was 6.8% yearly between August 1997 and July 2005.

A sharp rise in mortality is noticed in early November and peaks between December and January (Figure 2). A second rise also occurs around the month of March but the mortality rate seen during this period is not as high as that observed during the December and January months. The lowest mortality rates occurred during July and August months.

A plot of the mean temperatures in Celsius (figure 3) showed a trough during the months of December to March and when compared to figure 2 this indicates that lower temperatures are observed during the peaks of mortality during the year. A plot of the mean monthly temperature with mortality rate showed a significant negative correlation between the two variables ($r = -0.48$; $P < 0.0001$).

Estimation of Excess Winter Mortality due to AMI

Excess winter mortality was seen in all the years observed. An average of about 2,463 excess winter deaths occurred yearly. In all year periods the highest absolute EWM occurred in those 75 years and above (Table 2). This age group also contribute an average of 70% to the excess winter deaths yearly. The excess winter mortality over the 8 year period resulted in 19,635 total deaths. This is equivalent to 5.5% of the overall yearly mortality due to AMI over the 8 year period.

The excess winter mortality ratio (winter: non-winter rate ratio) is greater than 1 in all year periods considered, indicating that there is greater mortality in winter compared to the non-winter months (Table 3). The excess winter mortality ratio describes the risk in dying during winter compared to non-winter months. This can also be represented as a percentage (Excess winter mortality index). This shows that there is an average 17% excess death yearly (Table 2).

Table 2: Excess Winter Mortality and index secondary to AMI between 1997-2005

Year Period	EWM (EWMI)			
	Age: 0 to 64 years	65 to 74 years	75 years +	Total
97/98	244.5(9%)	731.5(16%)	1716.0(16%)	2692.0(15%)
98/99	281.5(12%)	756.0(18%)	2280.0(23%)	3317.5(20%)
99/00	333.0(15%)	643.5(17%)	2715.0(29%)	3691.5(24%)
00/01	148.5(7%)	368.5(11%)	1332.5(15%)	1849.5(13%)
01/02	258.0(14%)	453.0(15%)	1372.5(16%)	2083.5(16%)
02/03	196.5(11%)	423.0(15%)	1430.0(17%)	2049.5(16%)
03/04	251.0(15%)	260.0(10%)	1339.5(17%)	1850.5(15%)
04/05	140.5(9%)	466.0(21%)	1494.5(21%)	2101.0(19%)
Total	1853.5(11%)	4101.5(16%)	13680.0(19%)	19635.0(17%)

Table 3. Excess Winter Mortality Ratio secondary to AMI between 1997-2005

Year Period	Excess winter mortality ratio (CI)			
	Age: 0 to 64 years	65 to 74 years	75 years +	Total
97/98	1.09 (1.07, 1.11)	1.16 (1.15, 1.18)	1.16 (1.15, 1.17)	1.15 (1.14, 1.16)
98/99	1.12 (1.09, 1.14)	1.18 (1.17, 1.20)	1.23 (1.22, 1.24)	1.20 (1.19, 1.21)
99/00	1.15 (1.13, 1.17)	1.17 (1.16, 1.19)	1.29 (1.28, 1.31)	1.24 (1.24, 1.25)
00/01	1.07 (1.05, 1.09)	1.11 (1.09, 1.13)	1.15 (1.14, 1.16)	1.13 (1.12, 1.14)
01/02	1.14 (1.11, 1.16)	1.15 (1.13, 1.17)	1.16 (1.15, 1.17)	1.16 (1.15, 1.17)
02/03	1.11 (1.08, 1.13)	1.15 (1.13, 1.17)	1.17 (1.16, 1.18)	1.16 (1.15, 1.17)
03/04	1.15 (1.13, 1.18)	1.10 (1.08, 1.12)	1.17 (1.16, 1.18)	1.15 (1.14, 1.16)
04/05	1.09 (1.06, 1.11)	1.21 (1.19, 1.23)	1.21 (1.19, 1.22)	1.19 (1.18, 1.20)
All periods	1.11 (1.10, 1.13)	1.16 (1.14, 1.17)	1.19 (1.18, 1.20)	1.17 (1.17, 1.18)

A regression analysis was carried using a negative binomial regression to estimate the excess winter mortality ratio and age (Table 4). The relative risk of excess mortality in age groups 65 to 74 years and 75 years and above was 1.36 and 2.45 respectively compared to the younger age group.

Table 4: Excess winter mortality ratio and age

Age	coefficient	EWM(%)	Relative risk	P-value
0 to 64 years	reference	11		
65 to 74 years	0.31	16	1.36 (1.18-1.57)	<0.0001
75 years +	0.89	19	2.45 (2.16-2.77)	<0.0001

Figure 4 shows the trend of mortality rate and excess winter mortality index (EWMI) secondary to AMI. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality observed over the period studied (p<0.001). The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change and remains relatively the same (p<0.001).

Discussion

The results from the data analysis showed there is a significant increase in mortality rates due to AMI during the winter period in England and Wales. In this study, the excess winter mortality ratio over the 8 year study period for all age groups was 1.17 with a resultant 17% excess winter deaths for acute myocardial infarction. This amounted to about 20,000 excess deaths due to this disease. From their analysis of 2266 deaths, Biedrzycki and Baithun[1] in their study of mortality from myocardial infarction found that December was the peak month of mortality. A decline was observed from February onwards with the lowest mortality rate observed during the month of August. This pattern is similar to what was elicited in this paper: the highest mortality rates peaked between December and January and lowest mortality rates were observed during the months of July and August. Besides the demonstrable winter excess, the monthly mortality rate plot showed a double peak. A peak in mortality, which was clearly above the mean mortality rate, was observed around the month of March. This second peak in mortality was less than that seen in the months of December and January.

Since fluctuations in daily temperatures could not be appreciated from monthly mean temperature data, it is possible that absolute low outdoor temperatures may not be the only factor in causing mortality but rather daily changes in temperature may also be significant. It has already been established that in most countries in Europe a 1°C drop in temperature is associated in increasing in mortality[12, 13]. Carson et al, in their study found that cardiovascular diseases were more sensitive to temperature changes than respiratory disease[31.] This relationship has also been recognized in other studies: Kysely et al[14] found that fluctuations in daily temperatures resulted in increase in mortality rates of cardiovascular diseases. They also noted that a second cold spell usually had a lower excess mortality and suggested that the reason for this might be that some form of acclimatization to the previous cold spell might be protective against the next. This might explain the double peaks that were observed in this study. Large variations in temperatures between winter and non-winter months as seen in countries with warm winters such as England and Wales may also explain the winter paradox observed in Europe. It is possible that the lack of acclimatization due to the non-persistent cold weather, unlike in Iceland and Russia, may lead to a greater impact when the winter season does arrive. However, this is not conclusive and would require more research to clearly define such an association.

The study has shown that AMI has undergone a steady decline in England and Wales over the years. This is remarkable. The decline of mortality rate from 10.87 deaths per 100,000 population to 6.62 deaths per 10,000 population was observed over the 8 years study period. This was statistically significant. The reasons for this may include such factors as better diagnostic and therapeutic procedures, healthier life styles of the population, and better awareness of the public. Despite this steady decrease in total yearly mortality rate, the risk of dying from AMI during winter has remained the same. This is suggestive that excess winter mortality is not a function of the overall mortality. This has important control and prevention implications: the measures used to control overall mortality may not necessary influence winter excess.

One of such measures could be vitamin D supplementation. There are several factors which could be possibly associated with excess winter mortality and this may include seasonal variations in solar ultraviolet-B (UVB) doses and serum 25-hydroxyvitamin D [25(OH)D] concentrations, temperature and humidity[28]. Amongst these factors, possibly 25(OH)D concentration (<20 ng/ml) would be modifiable risk factor and its supplementation to levels greater than 36 ng/mL might reduce death rates significantly in winter months. In a Study in Iran[32], supplementation of vitamin to levels greater than 20ng/mL was effective in reducing the cholesterol level by about 16mg/dl. The clinical significance of this result needs to be investigated. Several clinical trials as well as observational and ecological studies are on-going and these will provide results to clarify whether vitamin D deficiency is a modifiable factor to prevent cardiovascular disease.

There was a gradient relationship between excess winter deaths and age: we found increasing winter deaths with increasing age. A regression model was used to estimate the relationship between age and winter mortality and we found a more than a two-fold increase in risk when the oldest age group was compared to the youngest. The older age groups seem to be more vulnerable to the effects of winter and should be an important risk targeted group for prevention policies and strategies.

The excess winter paradox observed across countries in Europe and the identified decline in winter deaths seen in some countries suggests that significant increases in death during winter are preventable. The decline observed in excess winter mortality in all age groups, as well as overall, observed during the 2000-2001 year is interesting. This period had the lowest EWMR and also observed the highest percentage drop in EWMR. It also had the least absolute excess winter death counts among all the year periods studied. A few months earlier, the UK government introduced innovative measures to tackle the burden of winter excess deaths. These measures were robust interventions incorporated in the fuel poverty strategy. This sharp drop in EWMR may suggest that these measures may have had an immediate impact. However, this study cannot conclusively confirm this. Nevertheless, if these strategies had had an immediate impact, it was definitely short-lived. This is because despite the fluctuations the trend has remained the same. In other words, the increased risk of dying during winter due to AMI has remained high in England and Wales despite the various strategies implemented by the government, and the trend analysis shows that it will remain so for a couple of years. It might be that it is too soon to evaluate the impact of these measures or they may not be effective.

The results of this study can be generalised to any population where significant winter occurs, and an assumption can be made that a significant winter is when the temperature drops below 18^{o}C over a defined period. As elucidated in the preceding paragraphs, this has been observed in various countries in Europe, America and Asia. However, the impact in winter mortality may vary from society to society because of other ecological factors such as behavioural, housing, as well as immunisation practices.

This study was a secondary data analysis and it faced certain limitations. Although the data provided by the ONS was complete and considered accurate, the data characteristics however restricted the number of variables that could be controlled such as sex distribution. To reach a more robust conclusion it would have been necessary to have data to test for effects of housing, indoor temperatures, outdoor temperatures, influenza epidemics as well as other possible confounders. It has been identified in existing literature that these factors play a part in the complex mechanism that brings about excess winter mortality. It would have been appropriate to adjust for their effects. Also, the population data which was used as denominator would reduce in accuracy as the year of study moved away from the recent census (29th April 2001). This is because the midyear populations after this date were extrapolated using birth and death data; these data are prone to their own type of error. However, it is anticipated that the brief period used in the research was unlikely to experience any dramatic changes in population. The method used in this study to estimate excess winter mortality was first described by Curwen[4], and this method defines the winter period between December and January. It has an advantage because these months have constantly shown mortality rates greater than the mean monthly mortality rates. It is essential to note this method of assessment when comparing future studies on excess winter mortality as other studies may use calendar winter months in their analysis.

Conclusion

This study has shown that increased winter mortality due to acute myocardial infarction does exist. The excess winter mortality has remained high for AMI for England and Wales over the years. The study also identified an association between increasing age and increasing excess winter mortality. There is a possibility that acclimatization may play a role in the mechanisms that initiate winter deaths.

Figure Legends

Figure 1: Showing a decline in mortality rate due to AMI over the year periods

Figure 2 Showing variation in mortality rate over the months over the year periods

Figure 3: A plot of the mean monthly temperatures in Celsius with an obvious deep in temperatures during the months of December to March

Figure 4: Trend in mortality rate and excess winter mortality index over the year period observed and forecast for the next 11 years. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality. The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change.

A. Contributor ship Statement

Find below the contribution of each author

- **Osakpolor Ogbebor**: literature review, data analysis and interpretation of data. Drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Odugbemi Babatunde**: literature review, drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published
- **Maheswaran Ravi.**: Conception and design of study, acquisition of data, literature review, revising manuscript. Approval of the version of the manuscript to be published.
- **Patel Kavya**: drafting the manuscript, revising manuscript. Approval of the version of the manuscript to be published.

B. Competing interest: None

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D. Data sharing statement: The data used in this study was obtained from the office of national statistics, United Kingdom.

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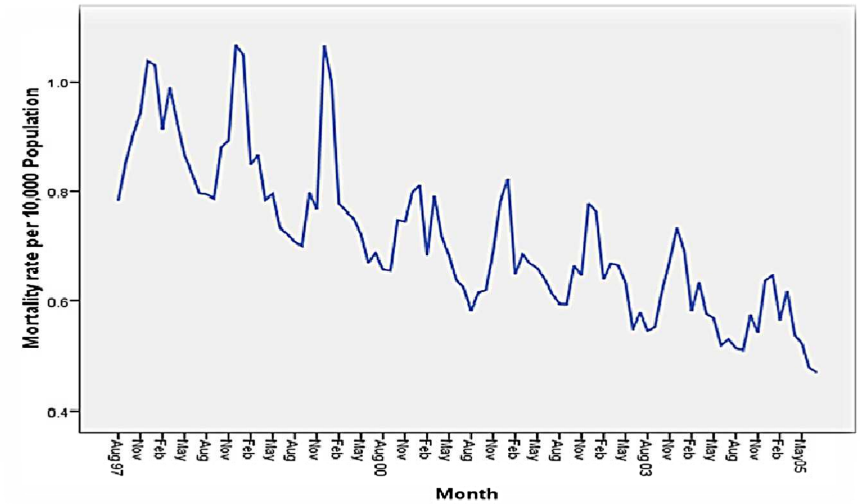

Figure 1: Showing a decline in mortality rate due to AMI over the year periods

203x114mm (300 x 300 DPI)

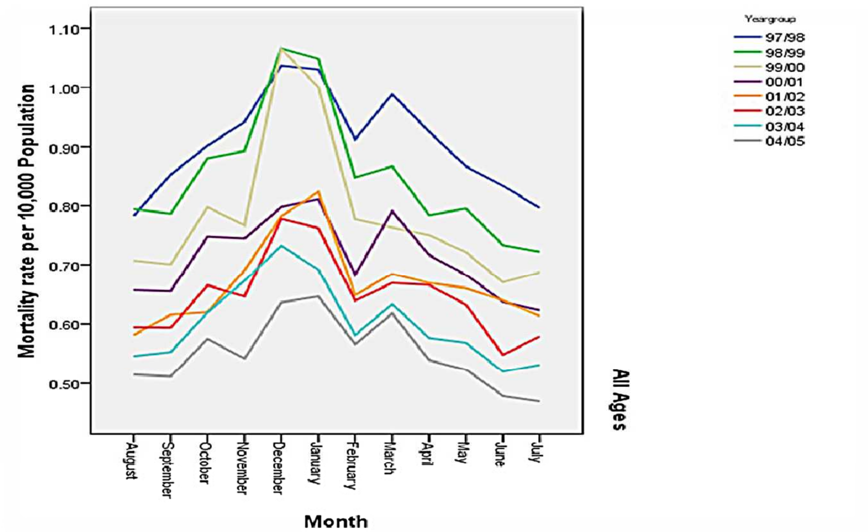

Figure 2: showing variation in mortality rate over the months over the year periods

203x114mm (300 x 300 DPI)

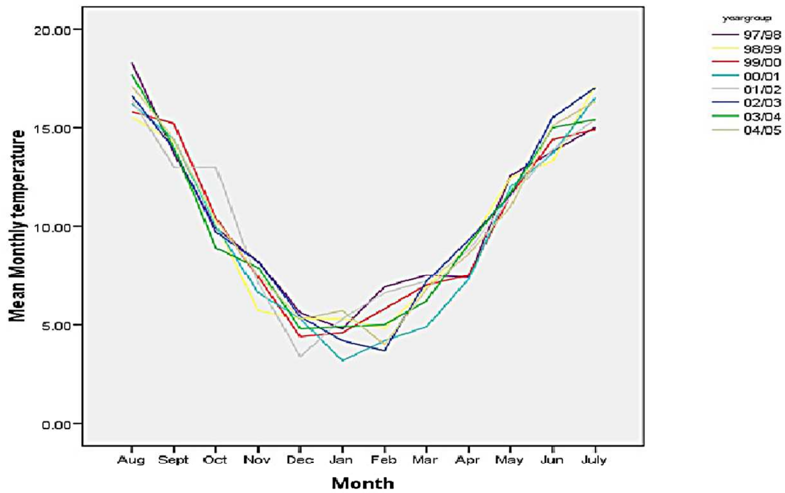

Figure 3: A plot of the mean monthly temperatures in Celsius with an obvious dip in temperatures during the months of December to March

203x114mm (300 x 300 DPI)

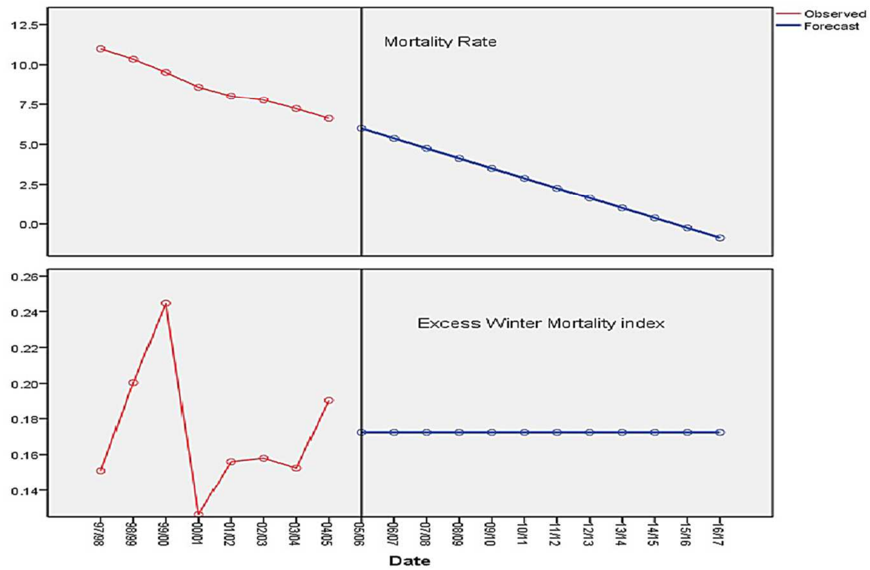

Figure 4: Trend in mortality rate and excess winter mortality index over the year period observed and forecast for the next 11 years. There is a steady decline in mortality rate with a significant trend for reduction in AMI associated mortality. The forecast for the next 11 year periods shows a continued decline. The forecast for the EWMI shows no change.

117x68mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-5	
Objectives	3	State specific objectives, including any prespecified hypotheses	5	
Methods				
Study design	4	Present key elements of study design early in the paper	5	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Not Applicable	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not Applicable	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-6*	*For example the use of comparability ratio for ICD codes*
Bias	9	Describe any efforts to address potential sources of bias	5-6	
Study size	10	Explain how the study size was arrived at	Not applicable.	

	All mortality due to AMI in England and Wales over the period studied was sampled

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6	
		(*b*) Describe any methods used to examine subgroups and interactions	5-6	For example regression model used in the data analysis
		(*c*) Explain how missing data were addressed	Not Applicable	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Not Applicable	
		(*e*) Describe any sensitivity analyses	Not Applicable	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Not Applicable	
		(b) Give reasons for non-participation at each stage	Not Applicable	
		(c) Consider use of a flow diagram	Not Applicable	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-9	
		(b) Indicate number of participants with missing data for each variable of interest	Not Applicable	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*7-9*	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*N/A*	
		Cross-sectional study—Report numbers of outcome events or summary measures	*N/A*	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9	Provided CI for estimation Excess winter mortality ratio (Table 3)

	(*b*) Report category boundaries when continuous variables were categorized	N/A
	(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-9	Regression models was described
Discussion				
Key results	18	Summarise key results with reference to study objectives	10-12	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-12	
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-12	Previous studies were compared to the results of this study in the discussion.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13	No external funding

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.