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Use of 1-year intervals in graphic plots of age-period-cohort trends suggests a role for Influenza in secular variations (period and cohort) of all-causes mortality

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Context/ Background

- I am a Medical Doctor and Epidemiologist, not a demographer
- Still, in the 1980s, my interest was to understand why CHD mortality was declining...
- Life styles modifications and more intensive medical care - dominant hypotheses then (and now?) - seemed to me largely insuficient...
  - life-stiles did not change so much and so widespreadly;
  - medical care of individual patients (except maybe for vaccines and antibiotics) hardly translates into gains at the population level. Access would need to be granted to all, which we know does not happen...
  - the simultaneity of the decline in CHD mortality across so many different countries, for example, United States and Brazil, speaks against both ideas;
- Other diseases like tuberculosis and peptic ulcer/ gastric cancer had been significant causes of death in the past, and declined without medical intervention
- Challenge: to find an alternative explanation...

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This figure is a good metaphor for a paradigm...

Within this "totality", what do you see?

The young lady?
The old women?
Both?
Neither?

Context / Background

- *It took me almost 10 years to figure out missing elements in our causal modeling of variations in diseases mortality. They are as follows:*
  - *the importance of vulnerability , besides exposure*
  - *that vulnerability to die from a disease at the individual level (1 or 0) emerges, at the population, as patterns of vulnerability evolving over time*
  - *that the denominator of our mortality equation ("population at risk") is in fact a mixture of vulnerable and non-vulnerable individuals, where only the proportion of vulnerable individuals is in fact "at risk" of becoming a case (or death) given a particular exposure*
  - *That, for this reason, variations in the distribution vulnerability in the population should be expected to play a major (or even the main) role in explanations to temporal trends in mortality*
  - *That whatever the cause of a hypothesized change in population patterns of vulnerability over time it had to be acquired, not inherited, and it would be expected to have wide and almost synchronous occurrence over the world*

A wish...

I am pretty conscious that the hypothesis that I will advance is very different from the hegemonic (but not satisfactory) ideas of modernization and epidemiologic transition...

So, I wish that you may listen to it as once recomended by Francis Bacon:

*"... **not to contradict** and confute, **nor** to believe and take for granted, but to weight and consider..."*

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Hypothesis

short version:

Variations in APC patterns and main causes of mortality (and fertility) result of variations (for “better” and “worse”) in our immune-inflammatory phenotypes, built as a result of a co-evolution between the human population and the emergence/re-circulation of influenza A virus subtypes (H1N1, H2N2, H3N2,…). As we change, the viruses recycle immune antigens, and as they recycle antigens, we change.

Long version available at the BAJ 2010 supplement of a 2009 Conference

https://www.researchgate.net/publication/222093732_Influenza_Recycling_and_Secular_Trends_in_Mortality_and_Natality

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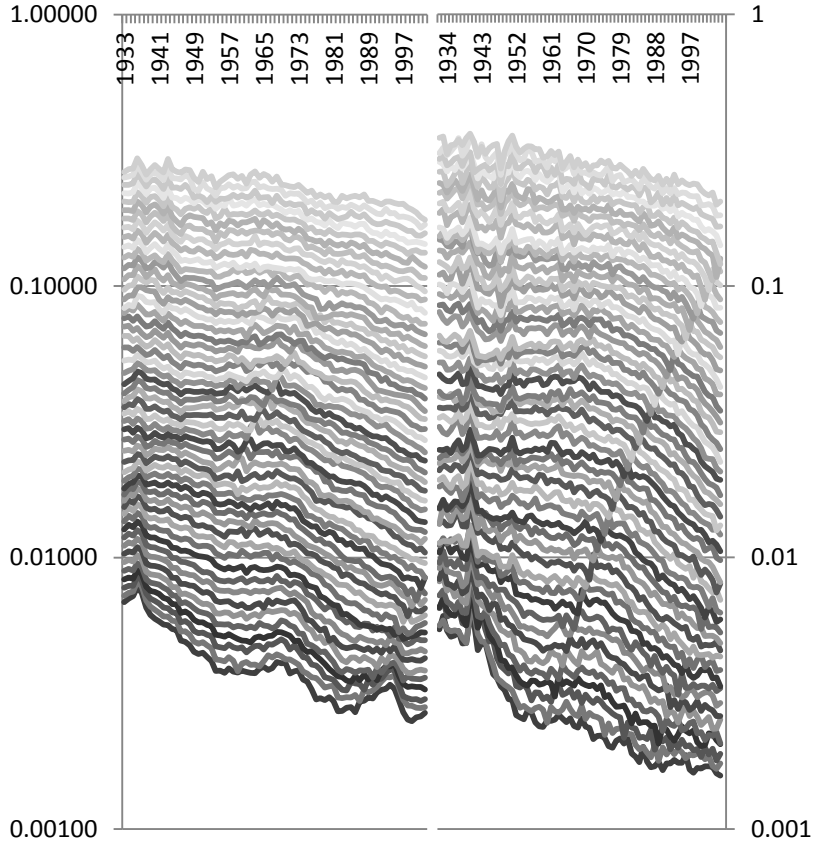
Objectives - why I am here?

I am here because I wanted to share with you, "specialists in mortality", some extraordinary things that appear in population data displayed as mortality lanscapes by 1-y intervals of age, period and cohort, when we keep this influenza idea in mind...

Objectives
Why am I here?

I believe that, in the same way that immunologists look at old serum samples and attempt to establish the time of circulation of previos sub-types of influenza viruses measuring antibodies to different sub-types over time, we can look at secular patterns of mortality - how mortality changed according to period and birth cohorts, and how consistent (or divergent) these patterns appears across different populations – and learn which and when influenza subtypes circulated in the past and how timing and sequences of recycling of influenza subtypes may be defining patterns of population vulnerability to different diseases over time (and espace, for example, what explains the similarities and differences in US and UK patterns of mortality seen in the figure on the right?)

In other words, I believe that, If the recycling of influenza sub-types is related to changes in patterns of mortality (and fertility), then the information about the history of the recycling (and of our co-evolving immuno-inflamatory phenotypes) is stored within our population mortality experience, and can be retrieved by interdisciplinary work.



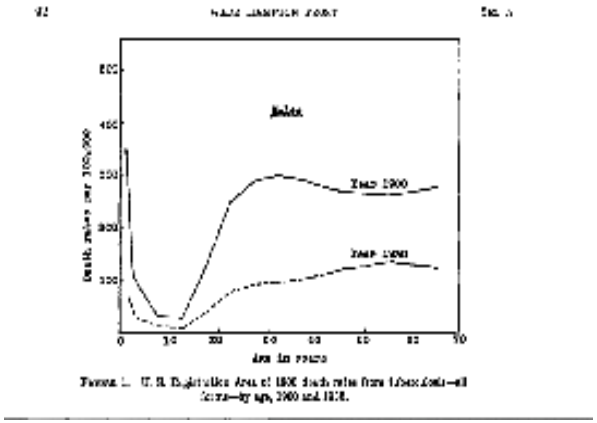
Aknowledgement

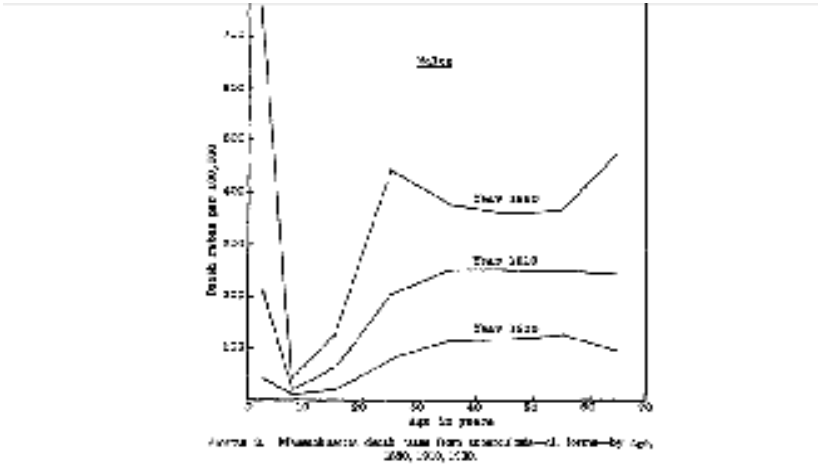
- My work could had never been possible if it were not by the availability of mortality data in different formats and for different countries provided by the continued effort of the Human Mortality Database team

Thank you very much!

Graphic Approach to APC analysis

- Graphic approach to age-period-cohort (APC) analyses were introduced in epidemiology at the beginning of the 20th century (Frost, Andword, Brownlee) as a way to attempt to separate the contributions of age, period and birth cohort effects on mortality trends due to tuberculosis.





Frost, 1939

Derrick, 1927, source Davey-Smith and Kuh IJE 2001

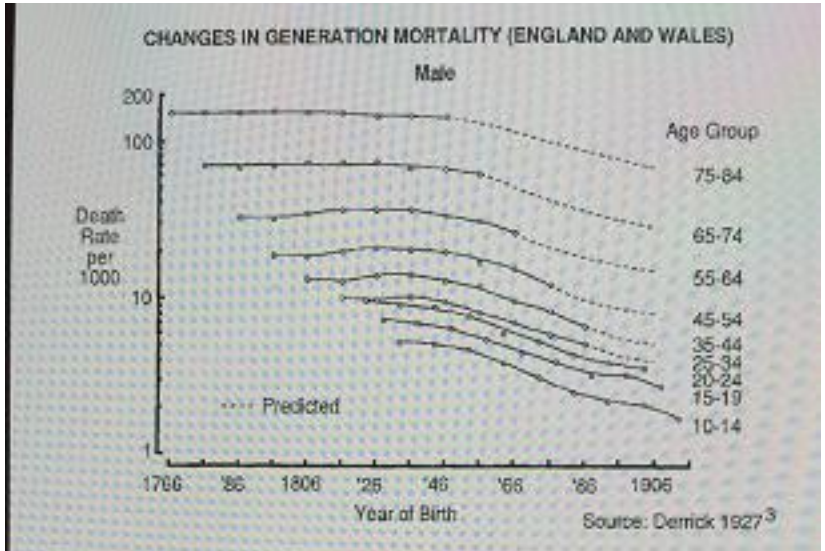


Figure 2 Generational mortality for males. Dotted lines indicate projections

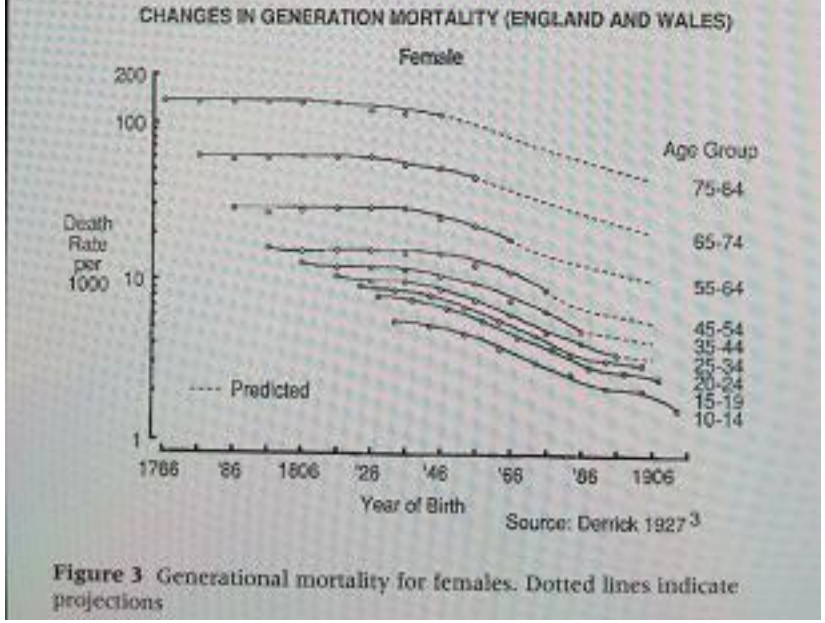


Figure 3 Generational mortality for females. Dotted lines indicate projections

In the field of demography, Derrick (1927) and Kermack et al (1934) had already published seminal papers using graphic displays of mortality trends by year of birth

The approach suggested that, for several generations until the beginning of the 20th century, each birth cohort carried with it, throughout its life, a characteristic mortality.

Kermack et al, 1934,
source Davey-Smith and Kuh IJE 2001

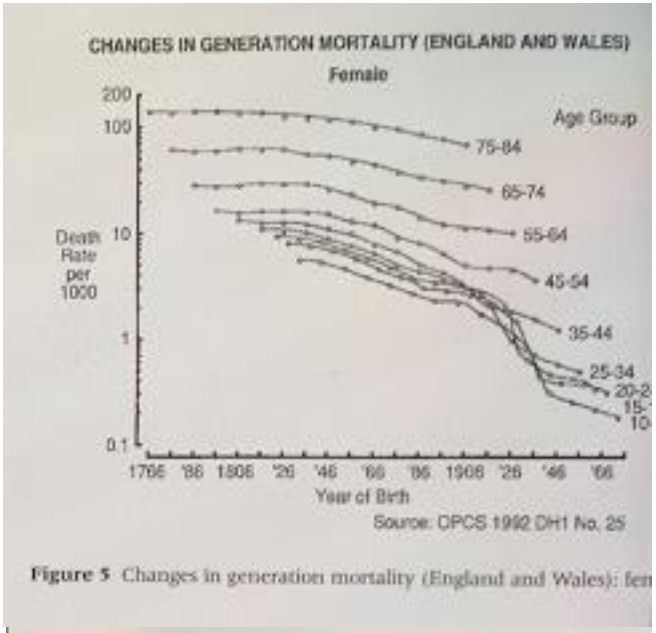
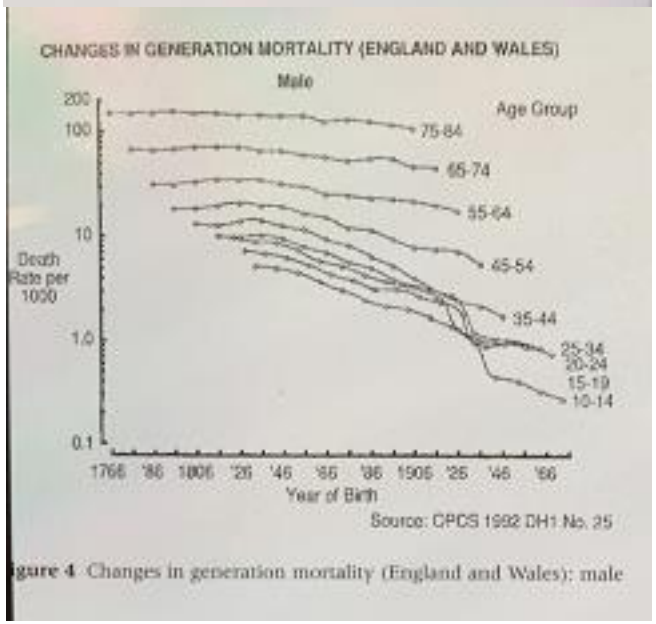


Figure 5 Changes in generation mortality (England and Wales): fem

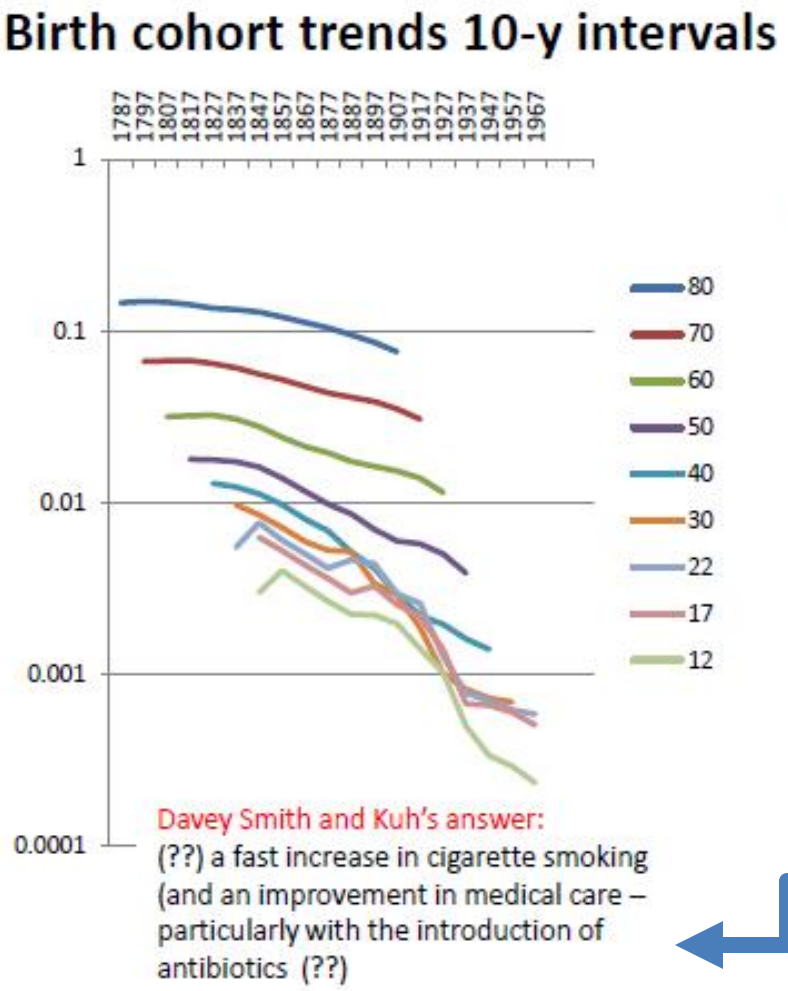


gure 4 Changes in generation mortality (England and Wales): male

But, still in the 1930s, some distortions became apparent...

With time, differences between observed and predicted mortality trends based on birth cohort trends begun to increase and the use of the generational approach to forecast mortality lost its previous strength.

England and Wales



The late 1980s evidences of possible effects of early-life exposures on late-life mortality from chronic diseases (Barkers' hypothesis) brought the 1920s-30s APC studies back to the fore.

Attempts to exlain the observed distortions in birth-cohort trends were resumed...

As registered by Davey-Smith and Kuh (2001), "at younger ages mortality fell faster than predicted on the basis of birth cohort regularities, whereas at older ages, mortality declined as much lower rate than predicted".

Why? The answers remain insufficient...

1-y intervals APC graphics

- APC graphic analysis done during the 20th Century used data aggregated by 10-year intervals.
- It is proposed here that descriptive graphic analysis of age-period-cohort mortality trends by 1 instead of 10-year intervals may help us to ***visually detect expected*** * non-random patterns of variation ***(influenza-related and others)*** closest in time to their actual occurrences (particular ranges of calendar years and/or birth-cohorts).

** Theory ladden*

(Excel database with graphics available at the site or upon request)

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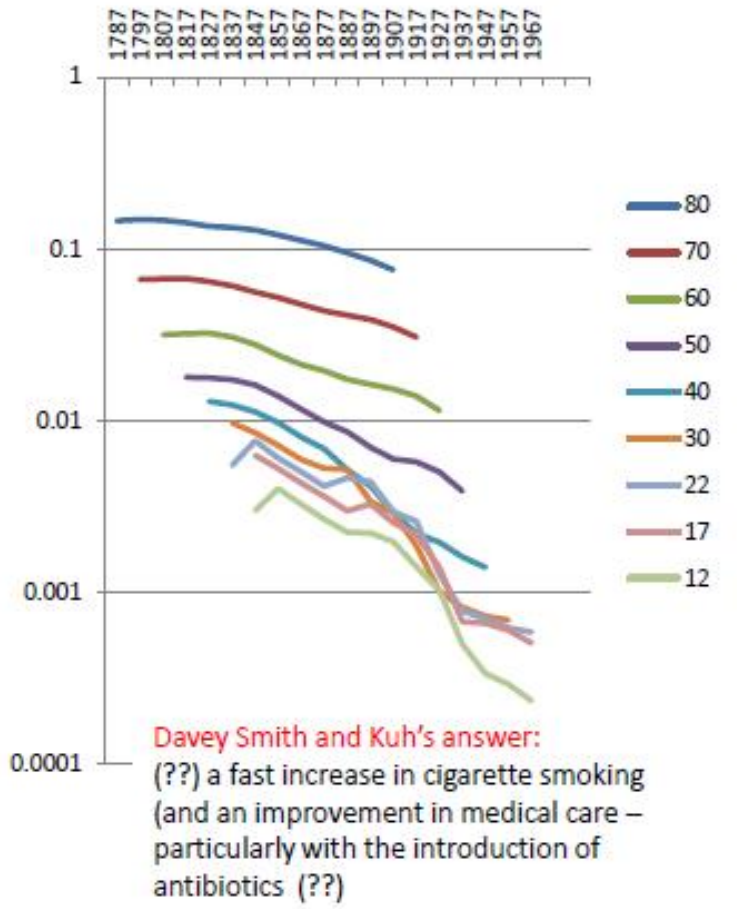
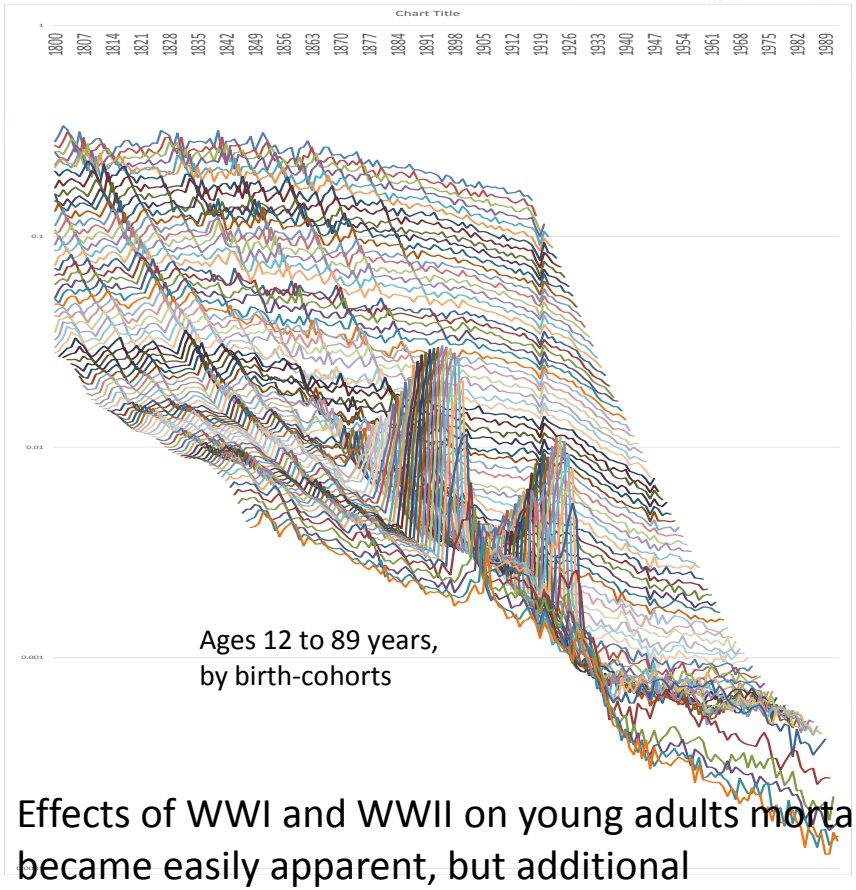
Comparing the ammount of information provided by both approaches:

Birth cohort trends 10-y intervals



Davey Smith and Kuh's answer:
(??) a fast increase in cigarette smoking (and an improvement in medical care – particularly with the introduction of antibiotics (??)

Birth cohort trends 1-y intervals



Ages 12 to 89 years,
by birth-cohorts

Effects of WWI and WWII on young adults mortality became easily apparent, but additional information emerges...

(Excel database with graphics available at the site or upon request)

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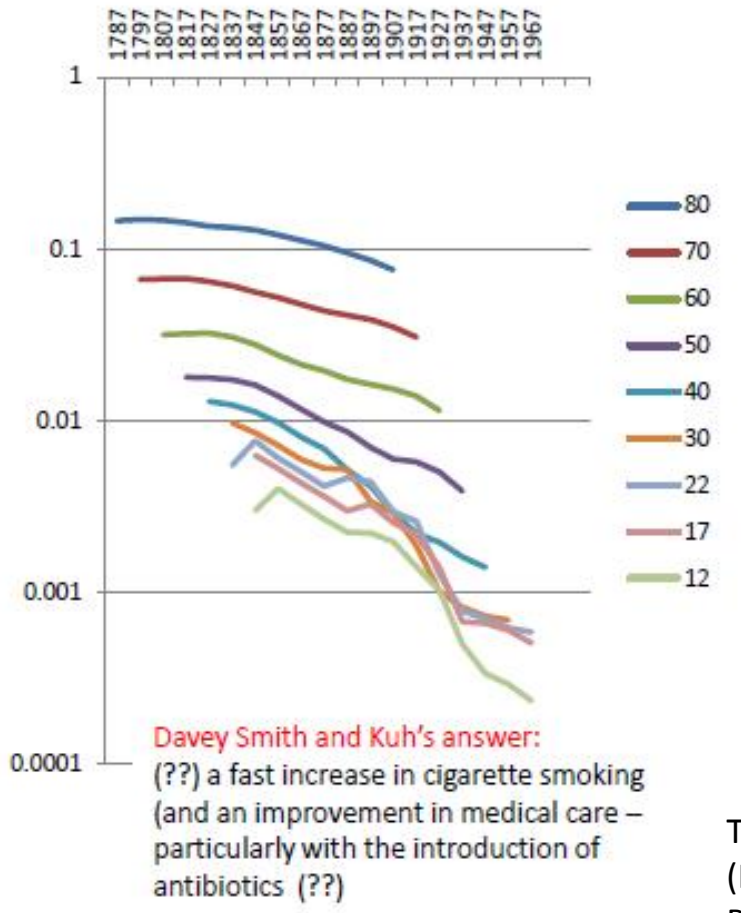
1 - At youngest ages mortality fell faster than predicted

(Davey-Smith and Kuh, 2001

Comparing the ammount of information provided by both approaches:

Birth cohort trends 10-y intervals



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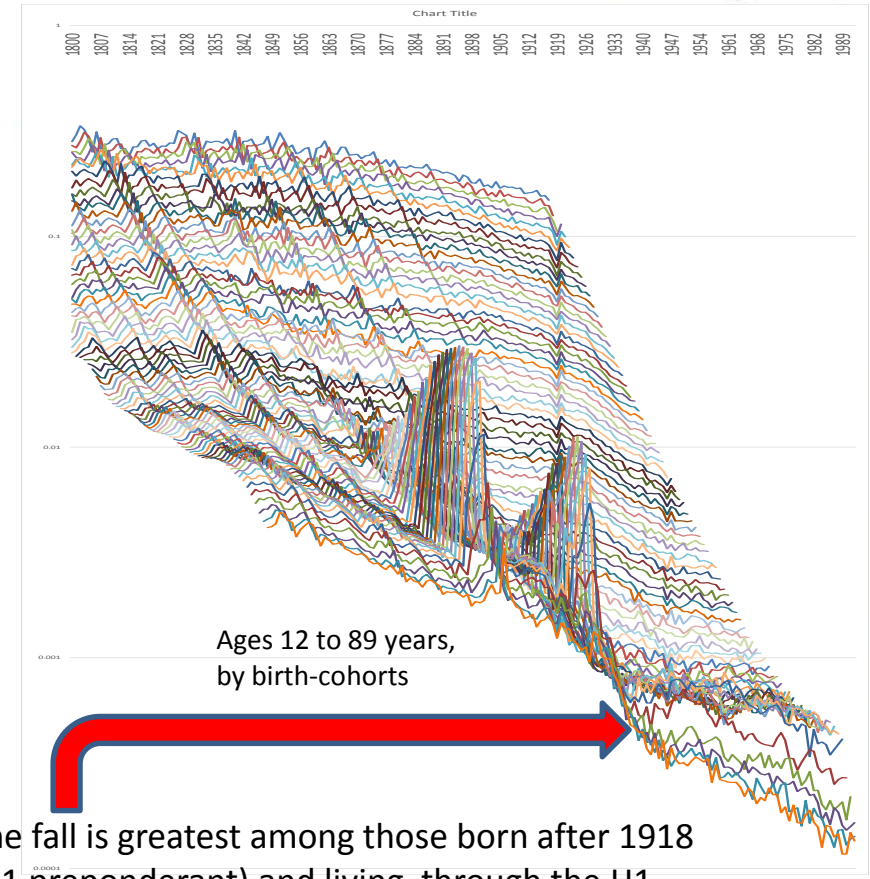
Birth cohort trends 1-y intervals



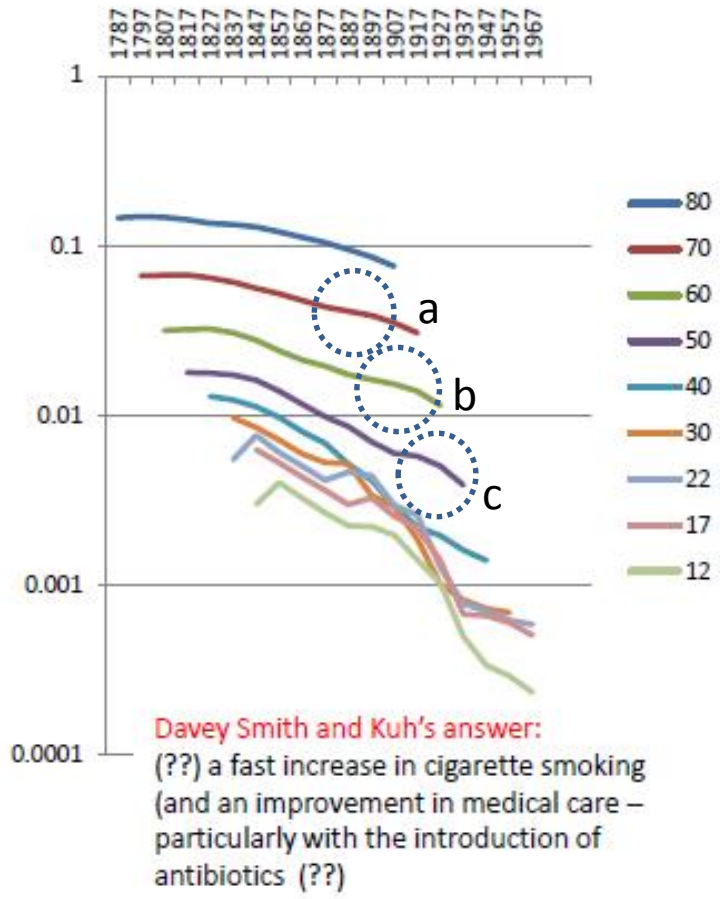
The fall is greatest among those born after 1918 (H1 preponderant) and living through the H1 Period (until 1959). It changes among H1 primed cohorts with the emergence of H2.

(Excel database with graphics available at the site or upon request)

At older ages, mortality declined at much lower rates than predicted (Davey-Smith and Kuh, 2001).

Comparing the ammount of information provided by both approaches:

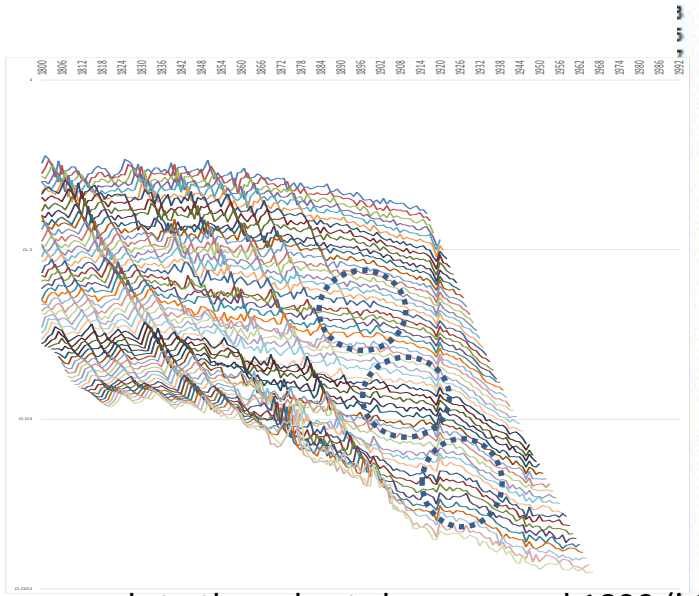
Birth cohort trends 10-y intervals



Davey Smith and Kuh's answer:
(??) a fast increase in cigarette smoking (and an improvement in medical care – particularly with the introduction of antibiotics (??)

Source: HMD

Birth cohort trends 1-y intervals



a - corresponds to the cohorts born around 1890 (h3) cursing through H1 and H2 years (until 68); **b**- corresponds to cohorts born at the beggining of the 20th century (H??) cursing through the H2 period (59-68); **c**- rise corresponds to cohorts born after 1918 (H1) cursing through the H3 (after 1969) period and the decline to the H1 cohorts entering a new H1 (co-circulating with H3) era (from 76-present) – (in UK, H1XH1 - decline in CHD mortality?)

More results from the Use of 1-year intervals in graphic plots of age-period-cohort trends and a role for Influenza in secular (period and cohort) variations of all-causes mortality

Considerations on data

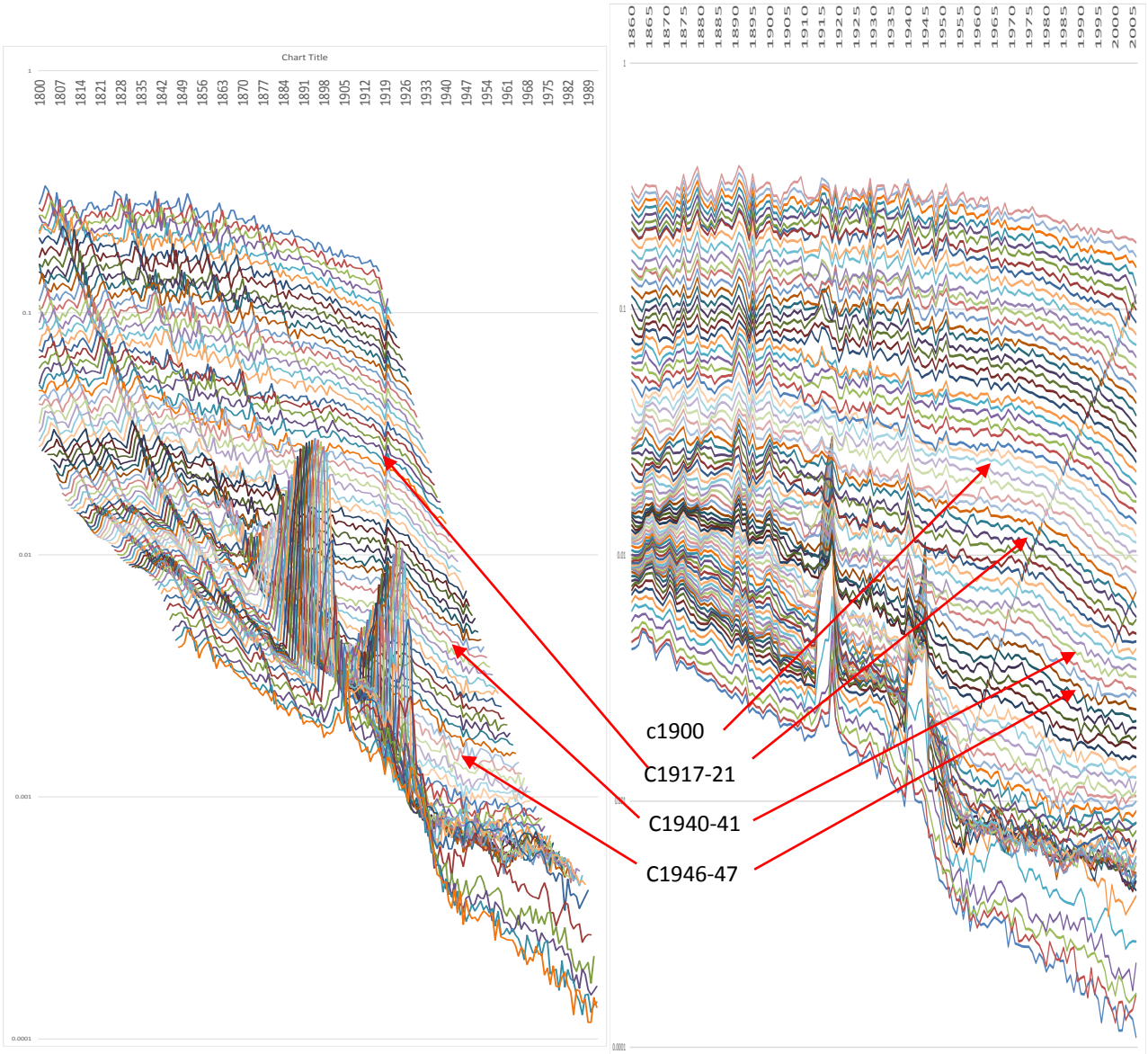
The source of data was the HMD.

I was are interested in the details...
I suposed that variations are not random, that patterns exist and can be recognized...

So, I used period data both in period x age and cohort x age plots (cohort = period less age), because it would be easier to recognize and compare age-specific patterns of change across period and cohort plots and also because, regarding influenza occurrences, I supposed (maybe wrongly?) that Period (1x1) data were more close to real occurrences than cohort (1x1) data... (I thought that as cohort estimation uses information of lexis triangles across two-year periods, contrasts might be lost?)

(Excel databases with graphics available at the site or upon request)

England and Wales population landscape of mortality trends – 1860-2011, both sexes.



Source: HMD, United Kingdom death rates (period 1x1), 1860-2011

1- pre 1910, the data is suggestive of many epidemics (localized increases of deaths) - several infectious diseases? - different intensities at different ages - maybe due to short-term period X cohort interacting effects caused by relatively frequent influenza recycling?

2- The 1890 influenza epidemic is huge and kills people at all ages. Mortality also incresases in all ages in 1896 and around 1900 (documented influenza and war?).

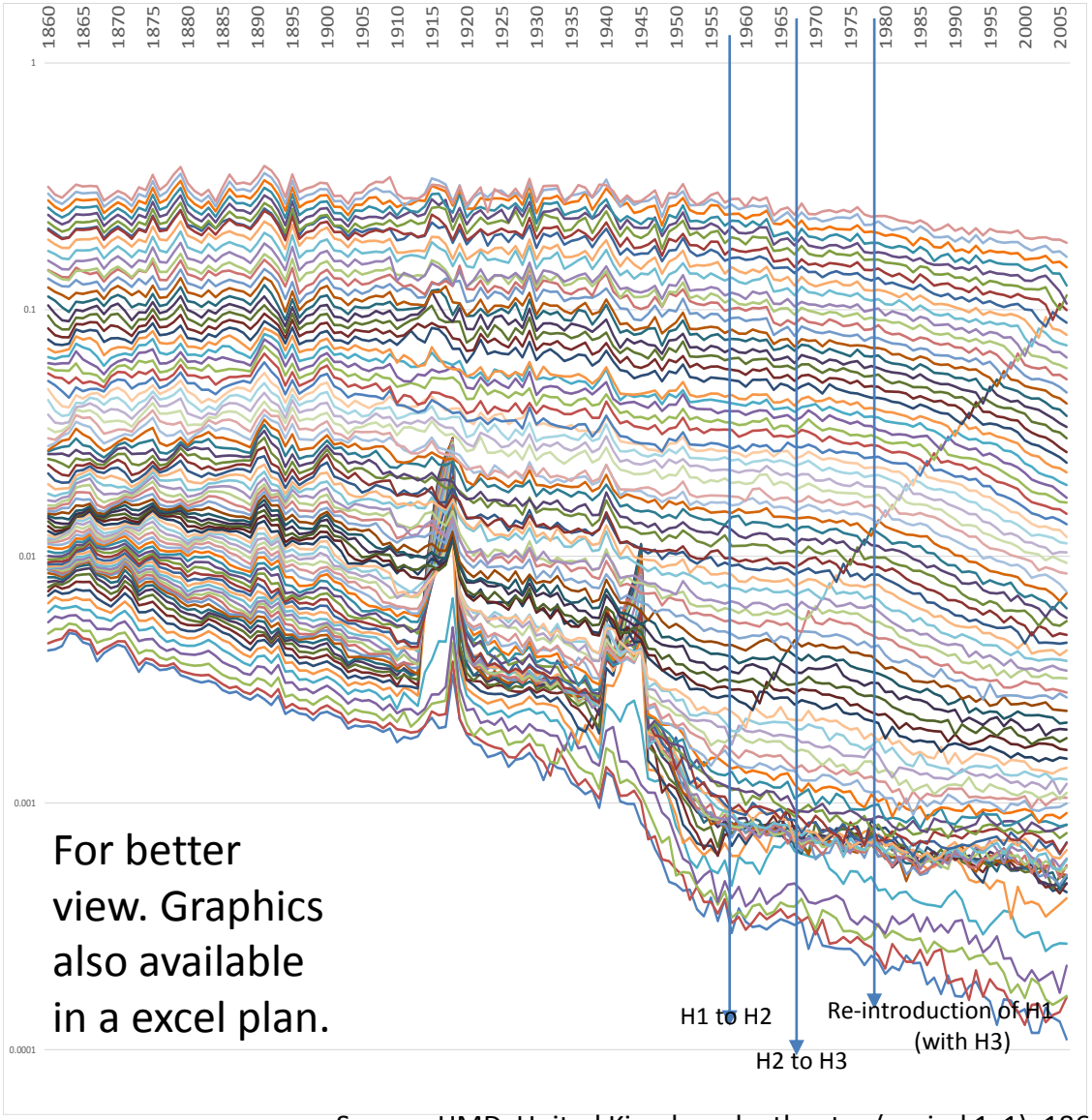
3- Around 1910 (and still more after 1918-19?) the mortality lanscape changed from cohortXperiod interacting trends to a more period-driven landscape? Mortality rises corresponding to influenza epidemics described for the years 32-33, 36-37, 40, 43, 45, 45, 51 (huge), 53, 59, 61-62, 69, 78, some with highest burdens at oldest ages, as can be seen in the data.

4- WWI and the1918-19 Influenza Pandemic appear not just as increased mortality in these period, but also as a huge cohort scar meaning an important decline in fertility across the period (war and influenza!). The transition to a decline in adults mortality is greater at this cohort mark (1918 H1 introduction), as their members re-enter a new H1 period – after 1978..)

5- cohort scars also appear corresponding to the years 1900-1901, 1940 and 1947 (all years with influenza epidemics.

6- the 1947 cohort scar is particularly intriguing because the 1947 virus – while later classified as H1 - is considered to have suffered a huge drift compared to the 1943 virus. The 1947 epidemic is described as light. But it may have resulted in fetal and neonatal deaths and immune modification of survivors. H1 cohorts, particularly after the 1947 scar, seem to show increasing mortality at young adult ages – may be associated with the AIDS deaths occurring more during years of preponderant H3 circulation? (see Azambuja,MI 2014, Researchgate)

England and Wales population landscape of mortality trends – 1860-2011, both sexes.



Source: HMD, United Kingdom death rates (period 1x1), 1860-2011

More considerations on data

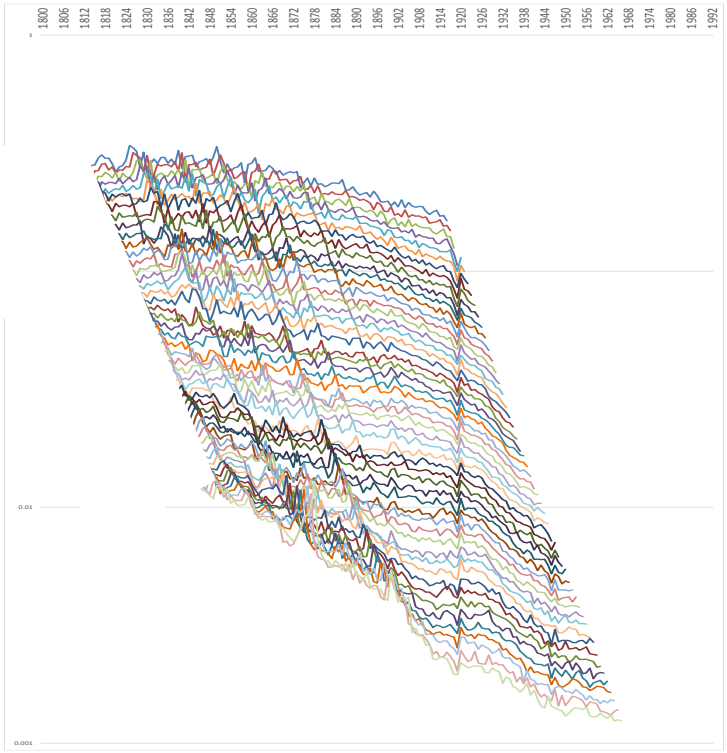
For the same reason - a better chance of pattern recognition - numbers of deaths would be much better than death rates. Population data is less reliable than desth counts when we use yearly (1x1) estimates.

Also, seing the picture of the total deaths gives us a new perpective of the mortality landscape – and of the population, source of the deaths.

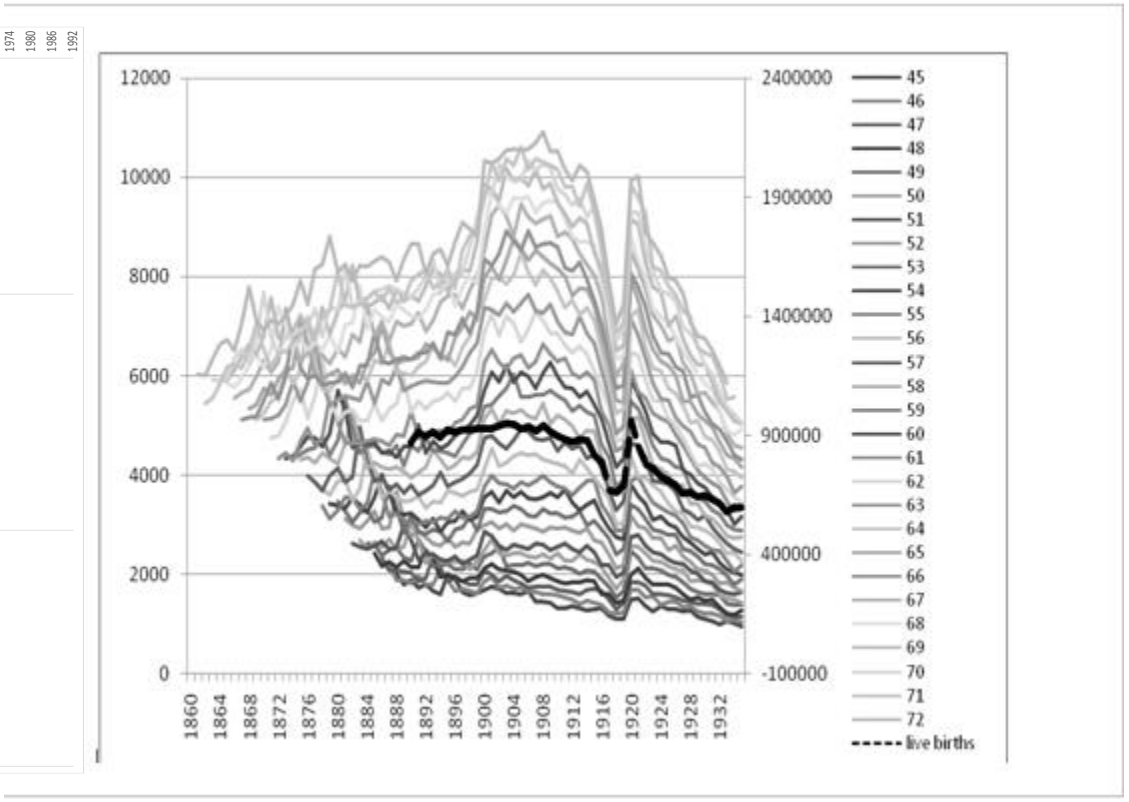
Of course that we have to be aware that trends in population numbers of deaths strongly depends on sizes of the corresponding birth-cohorts (the denominator of death-rates).

England and Wales population landscape of mortality trends – 1933-2011

UK Mortality rates 45-90 1933-2006



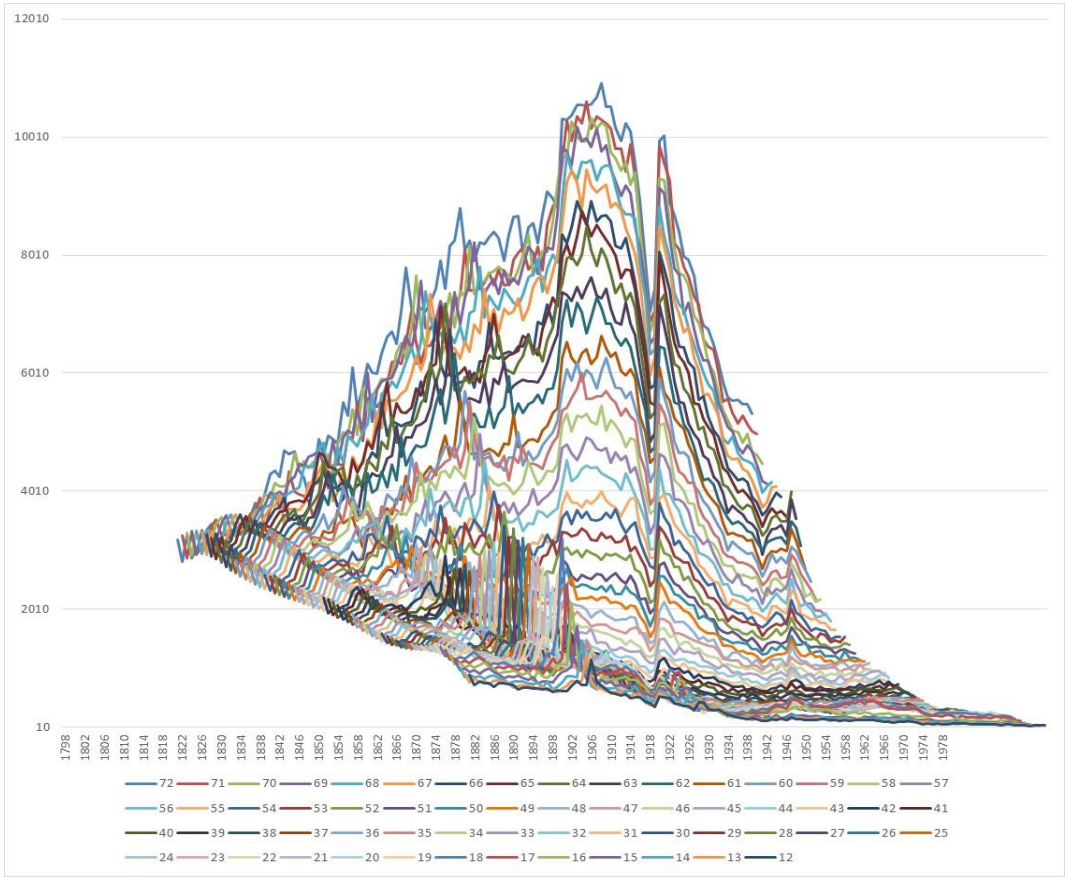
UK numbers of deaths 45-72 1933-2006



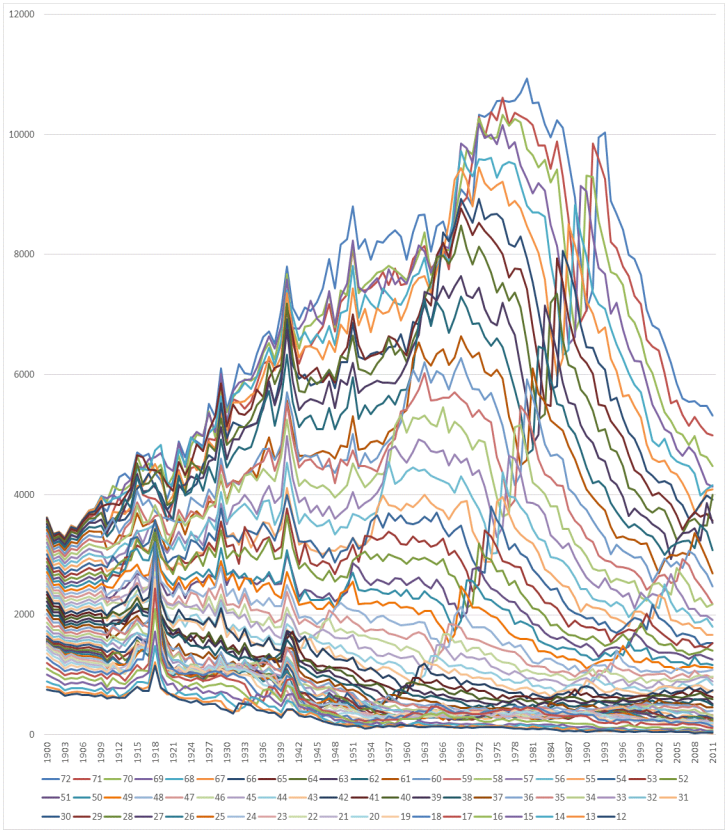
Sources: HMD, HFD

England and Wales population landscape of mortality trends – males, civilian population, 1900 -2011

UK Numbers of deaths 1x1 age and birth cohorts
Males, civil pop, 12-72 years

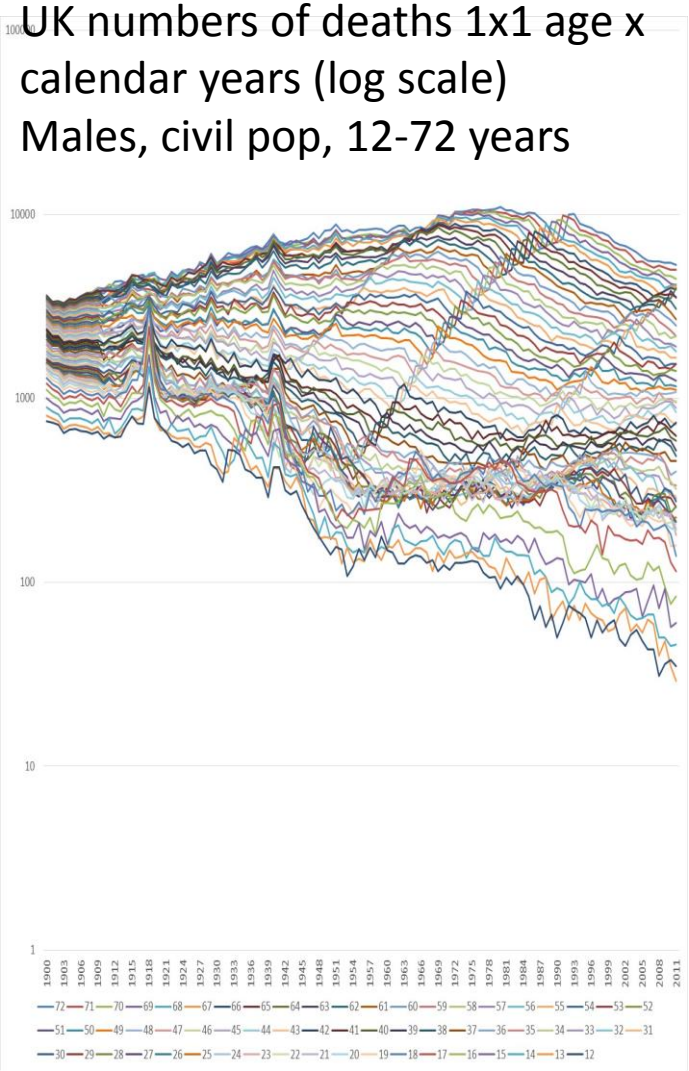


UK numbers of deaths 1x1 age x calendar years
Males, civil pop, 12-72 years

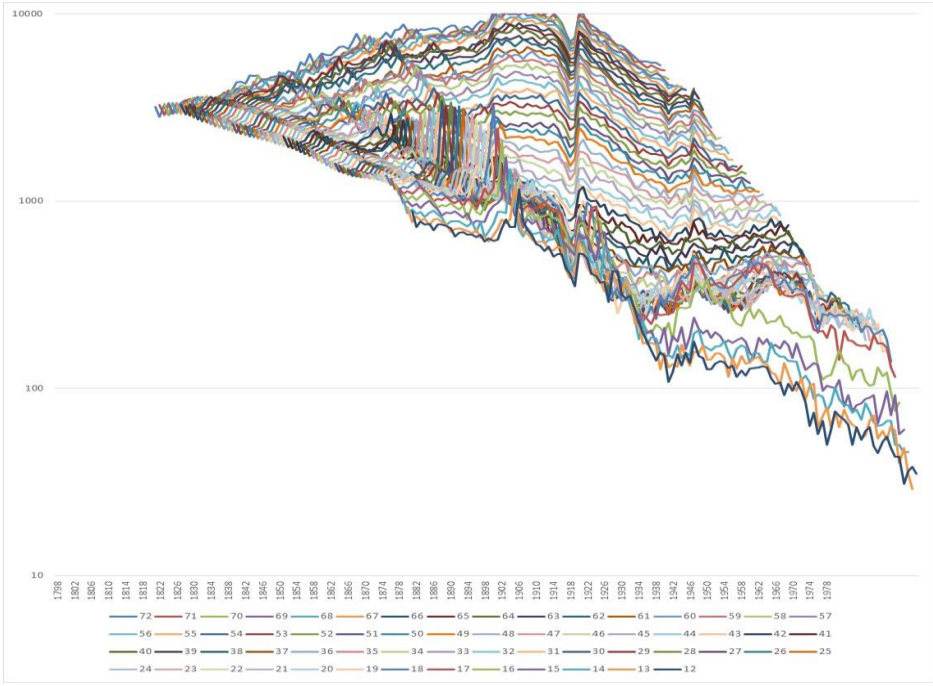


England and Wales population landscape of mortality trends – males, civilian population, 1900 -2011 (log scale)

UK numbers of deaths 1x1 age x calendar years (log scale)
Males, civil pop, 12-72 years



UK Numbers of deaths 1x1 age and birth cohorts (log scale)
Males, civil pop, 12-72 years



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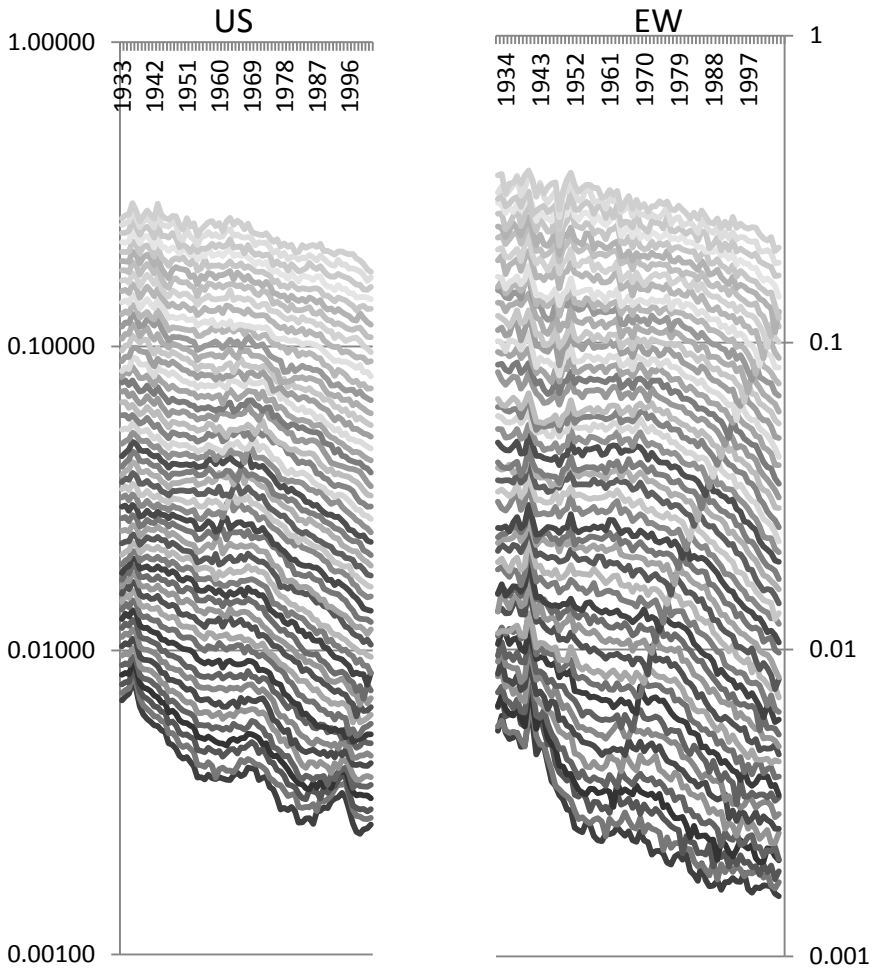
Some Final Remarks

I want to invite you to further explore this venue by looking at the population data of your countries and exchanging information on what you found...



International comparisons

Coincidences and differences to be explored

Source: HMD period (1x1), 1933-2002, ages 40-90 both sexes.

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Some Final Remarks

I understand that this is a very difficult challenge because it requires interdisciplinary knowlege and cooperation between demographers, epidemiologists, ecologistas, virologists, immunologists, history specialists, social scientists...

And to be conquered it needs many people working at different contexts...

“but difficult is good!”

Remember that Science is not the empirical, what we see...

It is the theoric explanation behind it...

I hope you consider this challenge!

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I am making available the excel files with the 1x1 age-period and age-cohort data presented here so that they could be better explored by whoever wanted.

My contact address is
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Thank you very much.

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https://www.researchgate.net/profile/Maria_Ines_Azambuja/publications