Denmark's Policy on Artificial Trans Fat and Cardiovascular Disease

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Introduction: The consumption of trans fat is associated with cardiovascular disease (CVD). In January 2004, Denmark became the first country in the world to regulate the content of artificial trans fat in certain ingredients in food products, which nearly eliminated artificial trans fat from the Danish food supply. The goal of this study was to assess whether Denmark's trans fat policy reduced deaths caused by CVD.

Methods: Annual mortality rates in Organisation for Economic Co-operation and Development (OECD) countries from 1990 to 2012 were used to estimate the effect of Denmark's food policy on CVD mortality rates. Synthetic control methods were employed to simulate the CVD mortality trajectory that Denmark would have witnessed in the absence of the policy and to measure the policy's impact on CVD mortality rates. Analyses were conducted in 2015.

Results: Before the trans fat policy was implemented, CVD mortality rates in Denmark closely tracked those of a weighted average of other OECD countries (i.e., the synthetic control group). In the years before the policy, the annual mean was 441.5 deaths per 100,000 people in Denmark and 442.7 in the synthetic control group. In the 3 years after the policy was implemented, mortality attributable to CVD decreased on average by about 14.2 deaths per 100,000 people per year in Denmark relative to the synthetic control group.

Conclusions: Denmark's food policy, which restricted the content of artificial trans fat in certain ingredients in its food supply, has been followed by a decrease in CVD mortality rates.
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Introduction

Cardiovascular disease (CVD) is a major cause of death in most Organisation for Economic Co-operation and Development (OECD) countries, accounting for about one third of all deaths in 2011.[1] Trans fat, which is present, notably, in partially hydrogenated oils (PHOs), has been found to be associated with CVD. Trans fat intake may affect cardiovascular health through several channels, including serum lipid levels, inflammation, and endothelial cell function. For example, the consumption of trans fat increases the ratio of low-density lipoprotein to high-density lipoprotein cholesterol, which increases the risk of developing coronary heart disease (CHD).[2–5] It has been estimated that the consumption of about 5 grams of trans fat per day is associated with a 25% increase in the risk of CHD.[6] The association between CVD and trans fat appears to be causal, but no RCTs with hard endpoints have been reported.[7]

Denmark responded to the adverse cardiovascular health effects of trans fat consumption by mandating that the content of artificial trans fat in oils and fats not exceed 2 grams per 100 grams of oil or fat.[8] Comparisons of food samples taken before and after the policy have shown reductions in trans fat content. It was possible to consume 30 grams of artificial trans fat in Denmark in 2001 "by eating two or three popular food products such as biscuits, microwave popcorn, chicken nuggets, and French fries," and the corresponding amount in 2005 was less than 1 gram.[9] The mean daily intake of artificial trans fat in Denmark was about 1 gram in 2001. The Danish Nutrition Council estimated that 1% of the Danish population or 50,000 people consumed more than 5 grams daily, which in part led the Danish government to

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regulate the content of artificial trans fat in certain ingredients in the food supply.[10]

In recent years, Denmark has seen a marked reduction in CVD mortality rates. Between 2003 and 2012, deaths attributable to CVD fell from 359.9 to 210.9 per 100,000 people, or from 34.6% to 25.1% as a percentage of all deaths (age-standardized rates are from OECD StatExtracts 2014, available at http://stats.oecd.org/). Many other OECD countries have also shown a declining trend in deaths attributable to CVD. The goal of this study was to assess whether some of the reduction in deaths caused by CVD in Denmark can be attributed to the implementation of the trans fat policy.

Methods

Data Sources and Exclusion Criteria

In our analysis, we used data from the OECD StatExtracts database, which provides comparable data for all OECD member states (http://stats.oecd.org/). The main variable of interest was the age-standardized CVD mortality rate per 100,000 people. Our sample started in 1990 and ended with the latest available year in 2012. This resulted in a balanced sample with 14 years prior to and 9 years after the policy was implemented in Denmark. Age-specific mortality rates were obtained from the WHO's Mortality Database (www.who.int/healthinfo/mortality_data/en/).

We also obtained country-level data on CVD risk factors (BMI, total cholesterol levels, and systolic blood pressure from WHO; fruit and vegetable consumption obtained from the Food and Agriculture Organization of the UN; and tobacco and alcohol consumption from OECD); economic conditions (health expenditures per capita, gross domestic product [GDP] per capita, and food price inflation defined as the percentage change over the previous year from OECD); and age structure (the percentage of the population aged >65 years from OECD). One caveat of our study is that there were no country-level data on potentially important covariates such as the use of statins and defibrillators.

Our original data set included information on all 34 OECD countries. Our goal was to estimate the impact of a national policy restricting the content of artificial trans fat in certain ingredients in the food supply, so we dropped from the sample countries that implemented other trans fat policies over the study period, such as trans fat labeling (Canada, Korea, and the U.S.) and voluntary self-regulation of trans fat content in food products in restaurants (Netherlands). Information on trans fat laws was obtained from the WHO (www.who.int/bulletin/volumes/91/4/12-111468/en/). We also dropped from the sample OECD countries that had an incomplete time series of CVD mortality rates over the study period.

We also excluded countries that implemented any policy regulating the content of artificial trans fat in food over the study period. Austria, Iceland, and Switzerland implemented laws between 2009 and 2011 similar to the Danish one. Denmark was the only case for which we had many years of pre- and post-policy data, both of which are important for synthetic control methods. And isolating the impact of a trans fat policy would have been difficult in some of the other cases because anti-smoking laws, which could have independent effects on CVD mortality rates, were implemented before their trans fat policy was implemented. Information on smoke-free laws was obtained from Americans for Nonsmokers' Rights (www.no-smoke.org/goingsmokefree.php?id=174). The analytic data set included information on Denmark and ten other OECD countries, which were used to form the synthetic control group for Denmark.

It is possible that there were spillovers resulting from Denmark's policy to other OECD countries resulting from shared transnational food supply chains, and some of these countries implemented anti-smoking laws over the study period (e.g., bans on smoking in public places). Both the spillovers and smoking laws in other OECD countries would, if anything, have worked against finding an effect of Denmark's trans fat policy on CVD mortality rates. Denmark implemented anti-smoking laws in August 2007. Fortunately, there was a post-policy period during which there were no national anti-smoking laws in place, allowing us to isolate the impact of the trans fat policy.

Statistical Analysis

Our empirical model compared Denmark's annual CVD mortality rates over time with those of a synthetic control group, which was composed of a weighted average of other OECD countries that did not implement a policy restricting the content of artificial trans fat in certain ingredients in food.[11] The weights assigned to control countries by the synthetic control estimator are non-negative, may range from zero to one, and sum to one. The estimator chose these weights in a recursive algorithm such that the synthetic Denmark most closely tracked the values of the pre-policy CVD mortality rates in Denmark. The synthetic control method's algorithm iterated through many combinations of weights until it found a single set of weights for the donor units that produced a control unit whose CVD path best approximated that of Denmark prior to the policy.

The variables used in the pre-policy matching process included CVD mortality rates (1990, 1995, 2000, and 2003) and the averages of all available information on the aforementioned CVD risk factors, health expenditures, age structure, food price inflation, and GDP. Measures of economic conditions were included because previous work indicates that they affect CVD mortality rates.[12,13] We found no evidence of abrupt changes in risk factor trends around the time of the policy using Chow tests. The model was implemented using the "synth" package in Stata, version 13.1.

The synthetic control approach offered a data-driven and objective way of choosing the control group. The use of a sample of disaggregated data and traditional methods of statistical inference would have captured uncertainty about the true aggregate values in the population. Here, the source of uncertainty was instead "the ability of the control group to reproduce the counterfactual outcome trajectory that the affected units would have experienced in the absence of the intervention."[11] The synthetic control method does not lend itself to classical methods of statistical inference, so we coupled the main analysis with placebo tests and permutation inference.

Results

In Panel A of Table 1, we show the weights that the synthetic control estimator assigned to each of the ten

OECD countries in our sample. The pre-policy trend in CVD mortality rates in Denmark was best reproduced by a combination of five countries: Estonia, Finland, Luxembourg, Mexico, and Spain. The other five OECD countries were assigned a weight of zero by the estimator. Panel B of Table 1 shows that the means of the predictors of CVD mortality rates for Denmark were generally much closer to those of the synthetic Denmark than to those of an equally weighted average of all ten OECD countries.

Panel A of Figure 1 displays annual CVD mortality rates in Denmark, synthetic Denmark, and other OECD countries from 1990 to 2012. There was a downward-sloping trend in CVD mortality rates in Denmark and in other OECD countries. Figure 1 also shows that Denmark and synthetic Denmark, unlike the equally weighted average of all ten OECD countries, tracked each other closely prior to the intervention period.

Panel A of Figure 1 illustrates that after the trans fat policy was implemented in 2004, Denmark's CVD mortality rates displayed a clear shift downward. In comparison, the trend of synthetic Denmark remained stable after this period. We focused on the differences in CVD mortality rates in 2004–2006, which was before Denmark implemented anti-smoking laws. In 2004, the difference between Denmark and synthetic Denmark was negligible, but grew to –18 in 2005 and grew further still to –22 in 2006. The average effect of the policy over the short run (3 years) is estimated to be a reduction in CVD mortality of 14.2 deaths per 100,000 people per year. Compared with synthetic Denmark during the 2004–2006 period, this is a reduction of about 4.3%. To put this number in perspective, consider that for road traffic accidents in 2012, the male age-adjusted death rate was 7.5 per 100,000 people in Denmark (www.who.int/substance_abuse/publications/global_alcohol_report/profiles/dnk.pdf?ua=1).

The difference in CVD mortality rates between Denmark and synthetic Denmark was even larger in 2007 and afterwards, but it is difficult to know how much of the difference was attributable to the trans fat policy versus how much of it was attributable to anti-smoking laws. Many studies have found that smoke-free laws reduce fatal CVD events.[14] If we attribute half of the CVD mortality gap in 2007–2012 to the anti-smoking laws, we obtain a reduction of 22 deaths per 100,000 people per year.

In line with the mixed evidence on the association between trans fat intake and stroke,[15] our results indicate that the impact on CVD is driven by diseases of the heart and not stroke, as can be seen in graphs that include all CVD and graphs that exclude stroke (Figure 1, Panels A and B). For CHD, the estimated reduction over the 2004–2006 period was 26.5 deaths per 100,000 people per year. By contrast, the corresponding estimated reduction in all CVD was 14.2 deaths per 100,000 people per year. Relative to averages for synthetic Denmark in 2004–2006, these were reductions of 10.4% and 4.3%, respectively. We could not further disaggregate CVD because the synthetic control approach was designed for case studies at aggregate levels (e.g., country level) and works best for data with smooth time trends. Naturally, the more one disaggregates the data, the more volatile the time series, and the harder it is to find a good synthetic Denmark given the small pool of control countries.

The policy reduced male and female CVD deaths by 24.4 per 100,000 (Figure 1, Panel C) and 14.3 per 100,000 (Figure 1, Panel D) per year over the 2004–2006 period, respectively. Relative to averages for synthetic Denmark in 2004–2006, these were estimated reductions of 5.8% or 5.2%. Figure 1 reports similar patterns for CVD net of stroke (Panels E and F, respectively).

Placebo Tests

To assess whether the pattern we observed for Denmark was unusual in the data, we conducted two placebo tests. First, we falsely assigned the trans fat policy to every OECD country in our sample. Because the synthetic control estimator finds a poor pre-policy fit for some donor countries, we followed the literature and kept countries whose pre-treatment root mean squared prediction error (RMSPE) was at most two times the size of the treatment group's RMSPE.[11] Panel A of Figure 2 displays these results, in which we plot the differences in CVD mortality rates over time between Denmark and synthetic Denmark, as well as those between other OECD countries and their synthetic counterparts. Denmark was unusual in the data in the sense that it was the only case in which the differences in CVD mortality rates clearly showed a downward structural break in 2004. Second, in Panel B of Figure 2, we falsely assigned Denmark's policy to start in 1999, which is well before it was actually implemented. The false post-policy period (1999–2003) did not display the pattern observed in the true post-policy period (2004–2012).

We used the results from the placebo test shown in Panel A of Figure 2 to compute a pseudo p-value. In a small sample setting such as ours, the lowest p-value that we can achieve is above the significance level used in traditional statistical inference. Denmark's ratio of post- to pre-treatment RMSPE was larger than that of each of the other five OECD countries whose pre-treatment fit was almost as good as the one we found for Denmark. The probability of obtaining the highest ratio if the intervention had been

Table 1. Weights in Synthetic Denmark and Cardiovascular Disease Mortality Predictor Means

Panel A: Optimal country weights	
Country	**Weight**
Czech Republic	0
Estonia	0.01
Finland	0.55
Germany	0
Hungary	0
Luxembourg	0.02
Mexico	0.13
Norway	0
Spain	0.29
Sweden	0

Panel B: Predictor means			
Variable	**Denmark**	**Synthetic Denmark**	**All 10 OECD countries**
Cardiovascular disease mortality rate (1990)	544.7	544.5	753.0
Cardiovascular disease mortality rate (1995)	477.2	465.8	579.2
Cardiovascular disease mortality rate (2000)	378.6	386.0	495.7
Cardiovascular disease mortality rate (2003)	359.9	361.9	481.7
Log (GDP per capita)	10.1	9.8	9.8
Log (health expenditures per capita)	8.0	7.2	7.0
Percentage of population older than 65 years	15.1	13.4	13.9
Food price inflation	1.9	3.3	5.0
Log (alcohol consumption per capita)	2.5	2.2	2.2
Log (tobacco consumption per smoker per day)	2.6	2.8	2.8
Log (BMI)	3.2	3.3	3.3
Log (total cholesterol)	1.7	1.7	1.7
Log (systolic blood pressure)	4.9	4.9	4.9
Log (fruit/veg consumption per person per day)	5.1	5.1	5.0

Note: The weights in Panel A were chosen by an iterative computational procedure. The recursive algorithm searches for a vector of weights that forms a control unit that best reproduces the treatment group's outcome path in terms of predictor variables. The data in Panel B come from the following sources: WHO: BMI, total cholesterol levels, and systolic blood pressure; FAO: fruit and vegetable consumption; OECD: tobacco and alcohol consumption, health expenditures, GDP per capita, food price inflation, and the percentage of the population older than 65 years.
FAO, Food and Agriculture Organization; GDP, gross domestic product; OECD, Organisation for Economic Co-operation and Development.

randomly assigned in the data is 1/6 or 16.7%. Coupled with the placebo tests, we take this as evidence that the effect observed for Denmark is attributable to its trans fat policy.

Sensitivity Checks by Age and Other Causes of Death

A larger reduction in CVD was observed for older individuals. We estimate that Denmark's trans fat policy averted an average of 1 CVD death per 100,000 people aged <55 years (Figure 2, Panel C) and 75 CVD deaths per 100,000 people aged ≥ 55 years per year between 2004 and 2006 (Figure 2, Panel D). Relative to averages for synthetic Denmark in 2004–2006, these are estimated reductions of 5.0% and 6.4%, respectively.

Unlike a previous cohort-level study,[16] we did not find evidence of a relationship between trans fat intake and all-cause mortality rates (Figure 2, Panel E). Note

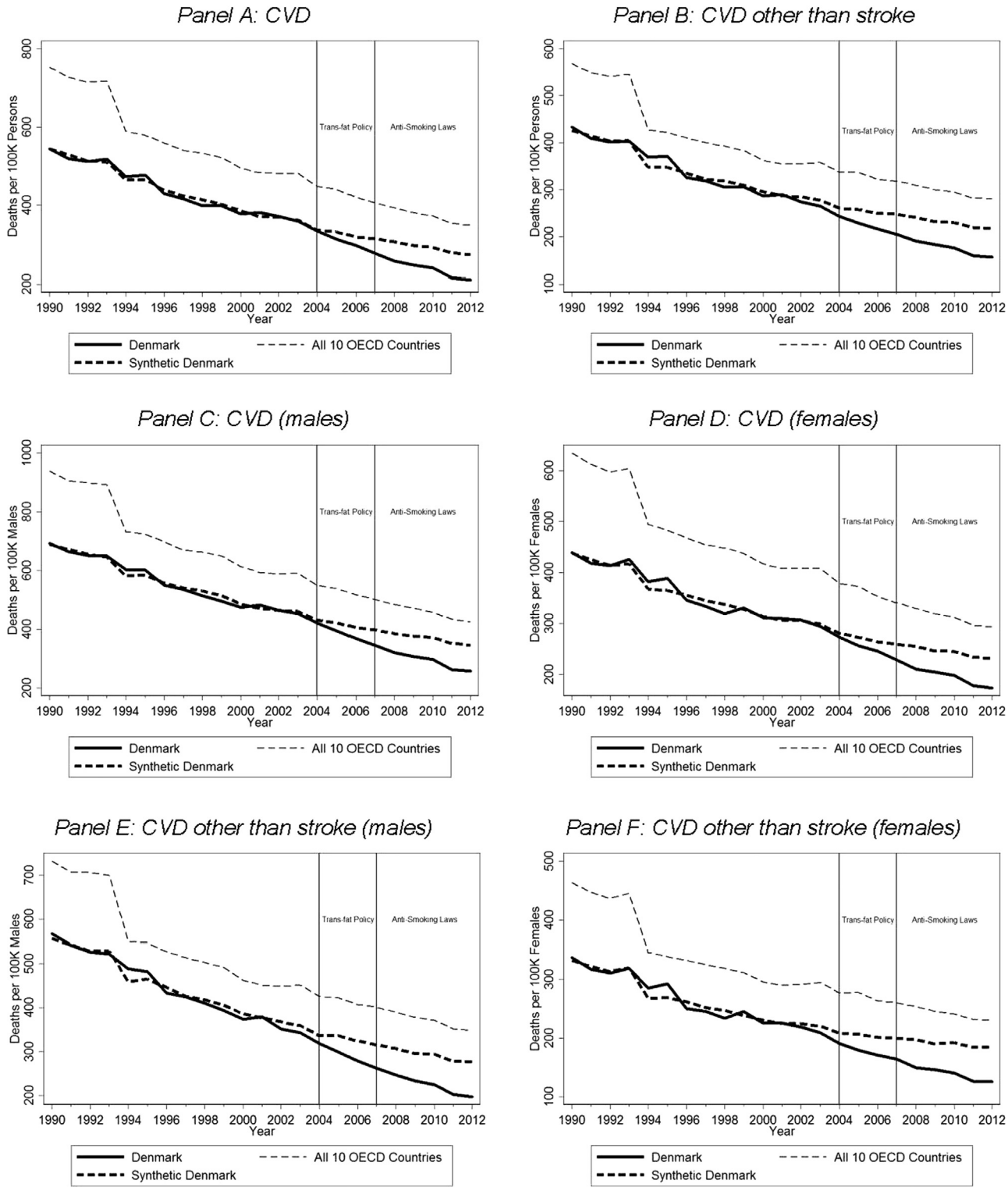

Figure 1. The impact of Denmark's trans fat policy on CVD mortality rates.
Note: Age-standardized death rates per 100,000 people using the 2010 OECD population as the reference population.

that from 2004 to 2006, relative to the mean all-cause mortality rate in Denmark (980), the estimated reduction in CVD mortality rates we found (14.2) is small (14.2/980 or 1.4%). Any shifts between causes of mortality may be better captured by using individual- or cohort-level data rather than population-level data. All-cause mortality patterns suggest that there were no dramatic changes in the overall disease and mortality

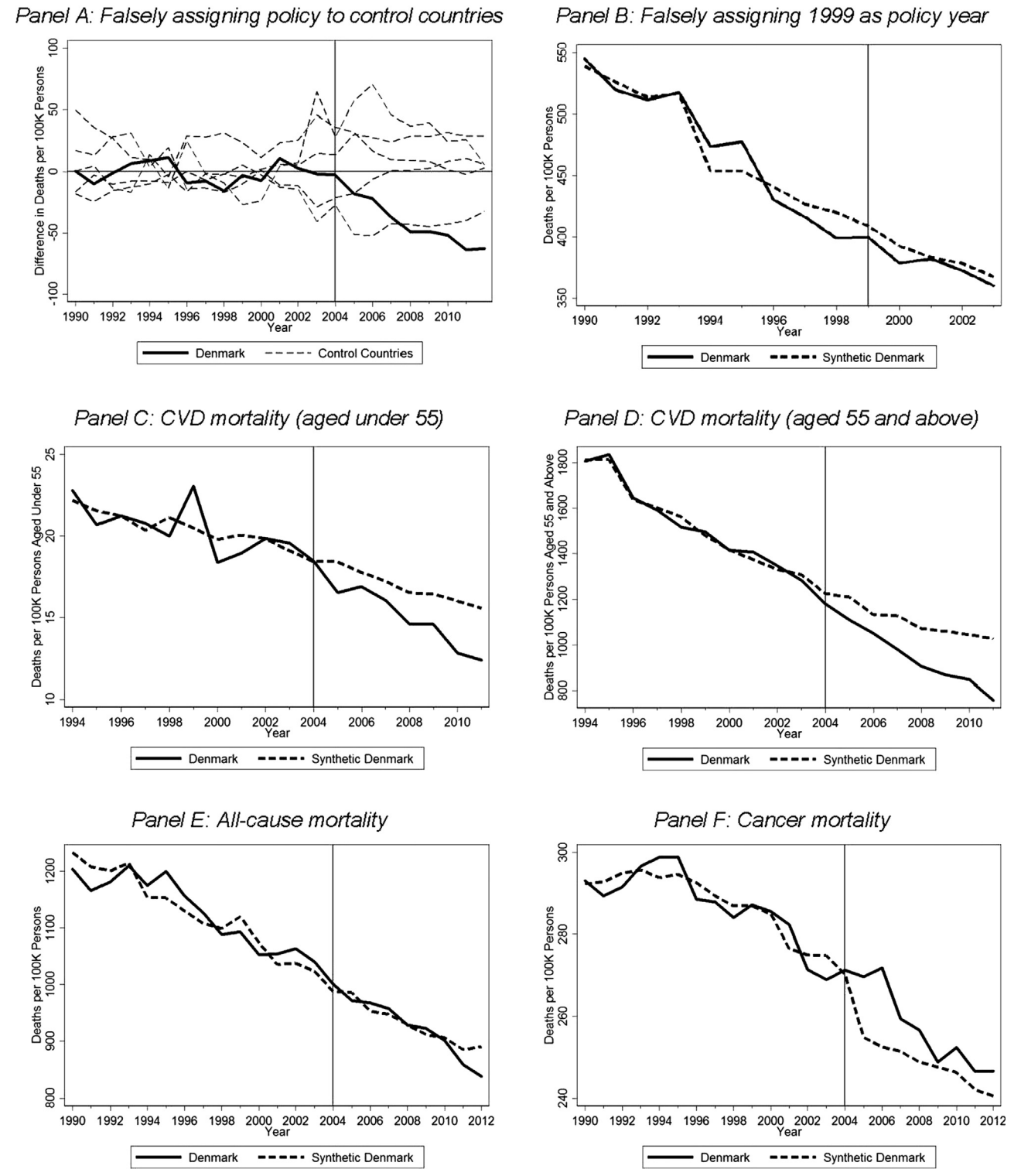

Figure 2. Robustness and sensitivity checks.

Note: Age-standardized death rates per 100,000 people using the 2010 OECD population as the reference population (Panels A, B, E, and F). Information for Denmark was missing in 1990–1993 and 2012 in WHO's Mortality Database (Panels C and D).

environments. If we had found a sizeable difference in all-cause mortality between Denmark and its synthetic counterpart, then this would have been a signal that there were other changes affecting health in addition to the reduction in trans fat content in the food supply over the policy period.

We did not observe a reduction in cancer mortality rates in the 2004–2006 trans fat policy period (Figure 2, Panel F). Cancer mortality rates stabilized in Denmark well before the implementation of Denmark's trans fat policy and, in the period of interest for our analysis (2004–2006), there was no visible break in this trend. Interestingly, we observed a reduction in cancer mortality rates starting in 2007, which may be a result of anti-smoking legislation in Denmark.

Discussion

We evaluated a Danish trans fat policy that placed an upper bound on the content of artificial trans fat that is allowed in certain ingredients in its food supply. Our paper provides the first population-level evidence on the impact of trans fat intake reductions on CVD using a counterfactual evaluation design. Our results complement the previous literature based on observational studies and plausible biological mechanisms. Previous work also noted dramatic decreases in both male and female CHD mortality rates after Denmark's trans fat policy was implemented.[17]

Our analysis revealed a rapid effect of Denmark's trans fat policy on population-level CVD mortality rates. These effects may be operating through physiologic effects of trans fat consumption that materialize within a time frame that is shorter than the one we might expect from changes in serum lipid levels alone. Recent work showing associations between the consumption of trans fatty acids and the increased risk of arrhythmia and sudden cardiac death may help to explain the swift policy effects we observed in Denmark.[4,18]

Health-conscious consumers may have reduced their trans fat consumption as early as 1997 in response to a report produced by the Danish Nutrition Society. The effects in our analysis may be driven by less informed or poor consumers given that this group's trans fat consumption and CVD risk was likely higher at baseline. Effects that work through improvements in blood cholesterol levels are likely to materialize much slower than those working through effects on heart rate variability. Given the short window of the main analysis (2004–2006) and the many mechanisms through which trans fat intake can affect health, the full impact of Denmark's policy may have not been realized.

We estimated that over the 2004–2012 period, CVD mortality fell by 22 deaths per 100,000 people per year, as a result of a policy that reduced the presence of artificial trans fat in Denmark's entire food supply. A recent study found that regulation of PHO use in food service establishments in several New York jurisdictions caused an average reduction of 12 CVD deaths per 100,000 people per year.[19,20] Food environments and dietary behaviors differ across the globe, which are likely to shape the relative impacts of trans fat policy alternatives.

The Danish case may be considered as an example for other countries to follow. In June 2015, the U.S. Food and Drug Administration made a final determination that PHOs are not generally recognized as safe. The WHO has recently called for a Europe that is free of artificial trans fat.[21] Trans fat policies may be even more effective in other regions such as Eastern Europe and most Balkan countries, where trans fat consumption and CVD mortality rates are substantially higher.[22–24]

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