

ELEMENTS OF ECONOMIC ANALYSIS OF REMOVING INDUSTRIALLY PRODUCED TRANS FAT FROM THE FOOD SUPPLY

Economic analysis, e.g. cost-effectiveness analysis (CEA) or cost-benefit analysis (CBA), may be a required or supportive part of the policy process for eliminating industrially produced trans-fatty acids (TFA) from a country's food supply. CEA compares the relative costs and outcomes (i.e., cost per lives saved or heart attacks prevented) of different courses of action (i.e., implementing a TFA limit or ban on partially-hydrogenated oils [PHO] or taking no action). CBA takes the analysis further and assigns monetary values to the outcome measures. Comparing the costs of removing TFA with its expected health outcomes allows policymakers to determine estimated net benefits of implementing policy over a specified timeframe.

This document outlines elements that may be considered when conducting an economic analysis of removing industrially produced TFA from a country's food supply. This guide will be useful for government officials tasked with creating the necessary evidence to support TFA policy action. It will be important to consult an economist or other relevant expert throughout the process. Conducting an economic analysis can be an expensive and cumbersome undertaking and should only be done if the policy process requires it.

EXAMPLES

Cost-effectiveness analysis: European Commission¹

The European Commission completed an assessment of the added value of European Union (EU)-level action on TFA by estimating the cost-effectiveness of three possible EU-level policy measures: mandatory limits, voluntary agreements with industry, and mandatory labeling. These three options were compared to not implementing any EU-level policy (i.e., by assuming only national or self-regulatory measures). They found that both imposing an EU-level legal limit and making voluntary agreements were cost-effective, preventing the loss of 3.73 and 2.19 million disability-adjusted life-years (DALYs) and saving >51 and 23 billion euros, respectively. Implementing mandatory TFA labeling can also avoid the loss of 0.98 million DALYs, but this option incurs more costs than it saves compared with the reference option. Estimations of the following costs were included in the analysis: production losses due to mortality and morbidity, informal care, primary care, outpatient care, accident and emergency care, in-patient care, medications, school-based intervention, worksite intervention, mass media campaigns, physician counseling, and food inspection program.

Cost-benefit analysis (CBA): United States²

The United States completed a cost-benefit analysis (CBA) of the removal of partially-hydrogenated oils (PHO) over a 20-year time interval, estimating the net present value (NPV) of quantified costs to be \$6.2 billion, with a 90% confidence interval of \$2.8 billion to \$11 billion. An estimated NPV of 20 years of benefits totaled \$140 billion, with a 90% confidence interval of \$11 billion to \$440 billion. Thus, the expected NPV of 20 years of net benefits—benefits minus cost—was estimated to be \$130 billion, with a 90% confidence interval of \$5 billion to \$430 billion. Estimations of the following costs were included in the analysis: reformulating products, relabeling products, increased costs of substitute ingredients, costs to consumers from changing recipes, reduced product acceptances and shorter product shelf life, and restaurants and bakeries learning how to operate without PHOs.

See the annex for details.

BASIC ELEMENTS OF AN ECONOMIC ANALYSIS³

➤ Define the problem and initiative objectives.

Increased intake of TFA is associated with increased risk of coronary heart disease events and mortality. WHO recommends that total TFA intake be limited to less than 1% of total energy intake, which translates to less than 2.2g/day in a 2,000-calorie diet.⁴ Elimination of industrially produced TFA from the food supply is critical to achieving this aim. The objective of the initiative is to eliminate industrially produced TFA from the national food supply, thereby reducing premature disease and deaths.

➤ Identify the options for achieving those objectives.

The most effective and consistent way to reduce TFA in the food supply is to implement policy actions to limit or prohibit industrially produced TFA. The WHO REPLACE action package recommends the following best practice policies: 1) national mandatory 2% limit of industrially produced TFA in all foods, or 2) national mandatory ban on the production or use of PHO as an ingredient in all foods. Mandatory labelling of TFA is a recommended complementary approach to any policy option.

➤ Decide how thorough an analysis is needed.

Economic analyses can be done to varying degrees of comprehensiveness. This level of analysis would depend on the evidence required to pass the selected policy option, on the availability of data, and the availability of resources to carry out the analysis. In general, it is recommended to do the minimum necessary to meet the requirements of the policy process.

➤ Estimate the costs of each option.

Before identifying relevant costs and benefits, it's important to determine the perspective of the analysis, as well as its timeframe. For example, should the analysis only consider costs to government, or should costs to industry, consumers and/or other stakeholders also be included? This decision would be based on the requirements of the policy process and other country-specific considerations. Estimated costs of eliminating industrially produced TFA will differ from country to country, but may include the following:

- Direct healthcare costs of TFA-associated disease, e.g. medications, doctor visits, hospitalizations and emergency care.
- Indirect costs related to the disease, e.g. loss of productivity and informal care.
- Costs to enforce the policy, e.g., food inspections, laboratory testing, and media campaigns.
- Costs to industry may be considered for inclusion in the analysis, including costs for reformulating and relabeling products. Costs to consumers may be related to changes in recipes.

➤ Estimate the benefits or effectiveness of each option.

Health benefits of removing industrially produced TFA from the food supply come from the prevention of harm that would occur over a specified period of time from continued consumption of high levels of TFA. This includes attributable deaths and disease. Quality-adjusted life years (QALYs) and other measures that combine death and disability into a single measure can be used but are often more difficult for policy makers to interpret. In a CBA, monetary values are assigned to these estimates.

➤ Analyze the relationship between costs and benefits (or effectiveness).

The analysis can be conducted at different levels of complexity, depending on factors such as the desired analytic perspective (e.g. societal vs program), the time horizon for the analysis, the level of cost detail, and the number of input assumptions. Economic analyses rely on assumptions to generate costs and benefits. Running sensitivity analyses to test the assumptions is important.

REFERENCES

- 1 Martin-Saborido, C., Mouratidou, T., Livanou, A., Caldeira, S., & Wollgast, J. (2016). Public health economic evaluation of different European Union-level policy options aimed at reducing population dietary trans fat intake. *The American journal of clinical nutrition*, 104(5), 1218-1226.
- 2 M Burns, R. (2015). Estimate of Costs and Benefits of Removing Partially Hydrogenated Oils (PHOs) from the US Food Supply. Department of Health and Human Services, Food and Drug Administration. Memorandum from the Office of the Commissioner to the Office of Food Additive Safety. Available on: <https://www.regulations.gov/docketBrowser?rpp=50&po=0&dct=SR&D=FDA-2013-N-1317>. Accessed on April 1 2019.
- 3 Steps have been adapted from the World Bank Group guide on "Groundwork for Economic Analysis". Accessed on 2/28/2019, <http://siteresources.worldbank.org/NUTRITION/Resources/Tool3-Chap4.pdf>
- 4 WHO. Draft Guidelines: Saturated fatty acid and trans-fatty acid intake for adults and children. 2018. Geneva: WHO.



Memorandum

Date: 11 June, 2015

From: Richard Bruns, Economist, Office of the Commissioner

Subject: Estimate of Costs and Benefits of Removing Partially Hydrogenated Oils (PHOs) from the US Food Supply

To: Mical Honigfort, Supervisory Consumer Safety Officer, Office of Food Additive Safety, CFSAN (HFS-265)

Executive Summary

We estimated the 20-year costs and benefits of removing partially hydrogenated oils (PHOs) from the US food supply, an outcome that could result from the determination that they are not generally recognized as safe (GRAS). We estimated the costs of all significant effects of the removal, including packaged food reformulation and relabeling, increased costs for substitute ingredients, and consumer, restaurant, and bakery recipe changes. We monetized the expected health gains from the removal of PHOs from the food supply using information presented in the FDA PHO safety assessment and the peer-reviewed literature, and added this to expected medical expenditure savings to determine the estimated benefits of this action.

We estimate the net present value (NPV) of 20 years of quantified costs of this action to be \$6.2 billion, with a 90 percent confidence interval of \$2.8 billion to \$11 billion. We estimate the NPV of 20 years of benefits to be \$140 billion, with a 90 percent confidence interval of \$11 billion to \$440 billion. Expected NPV of 20 years of net benefits (benefits reduced by quantified costs) are \$130 billion, with a 90 percent confidence interval of \$5 billion to \$430 billion.

Table 1 - Costs and Benefits¹ of PHO removal, USD Billions

20-Year NPV	Low Estimate	Mean	High Estimate
Costs*	\$2.8	\$6.2	\$11
Benefits	\$11	\$140	\$440
Net Benefits*	\$5	\$130	\$430
* This does not include some unquantified costs, see the "Costs to Consumers" section for discussion.			

¹ All numbers in this table come from Monte Carlo simulations, and are rounded to two significant figures as explained in the "Uncertainty" section.

Description of FDA Action

FDA has determined that PHOs are not GRAS for any use in food based on current scientific evidence establishing the health risks associated with the consumption of *trans* fatty acids (“TFA” or “*trans* fat”). PHOs are the dietary source of an estimated average 1.0g per person per day intake of industrially-produced *trans* fat (Ref. 1). Although FDA has not listed the most commonly used PHOs in its GRAS regulations, they have been used in food for many years. As a result of this action, PHOs will effectively be eliminated from the US food supply except as may be otherwise authorized by FDA. The determination will have a compliance date three years after its publication.

The estimate below assumes that FDA does not authorize new uses of PHO via issuance of new food additive regulations. If FDA were to issue such regulations, then fewer reformulations would be needed and the costs and benefits would be lower than what we estimate.

Changes from Previous Version

The previous version of this memo from November, 2013, estimated the costs and benefits of an action that would have a compliance date of one year in the future instead of three years. Because there will be more time to adjust to the removal of PHOs and develop substitutes and new recipes, many costs are lower than in the previous estimate. In addition, this document incorporates additional information from public comments and further research. Several numbers have been updated to match the most recent data. This version also compares costs to a baseline of gradual removal, instead of assuming that current usage will continue indefinitely. This lowers both the costs and the benefits that can be attributed to this action.

Baseline

The baseline for this estimate is the gradual voluntary removal of PHOs from the food supply as a result of consumer demand for healthier food. We calculate costs and benefits relative to this baseline. We do not know how quickly PHOs would be phased out without FDA action. At one extreme, they might be completely removed within ten years. At another extreme, the current usage might continue indefinitely. Our best estimate, based on public comments (Ref. 2) and past declines in PHO use (Ref. 3), is that PHOs would be removed from the food supply in twenty years in the absence of FDA action.

Uncertainty

When presenting our estimates of input values, we use average values for readability. The actual probability distribution used in the model is included in parentheses. In the ‘Costs’ and ‘Benefits’ sections, all results presented are for average values of inputs, rounded to two significant figures. The ‘Net Benefits with Confidence Intervals’ section presents the Monte Carlo simulation that we use to form our final estimates.

Costs

The estimated costs of removing PHOs from the food supply come from

- 1) reformulating products currently produced with PHOs.
- 2) relabeling products currently produced with PHOs.

- 3) increased costs of substitute ingredients.
- 4) costs to consumers from changing recipes, reduced product acceptance, and shorter product shelf life.
- 5) restaurants and bakeries learning how to operate without PHOs.

We estimate each cost separately in the sections below. For all costs, we calculate the difference in costs between the baseline scenario of gradual removal and the removal required by this action. For each type of initial cost, we spread the cost out equally over the three years between the publication date and the compliance date.

The baseline removal costs are determined as follows: Each year, a certain percentage of the current PHOs are removed from the market. In the average case, this is five percent. Then, that percentage of removal costs are assigned to the year. Then, the costs are decreased, to account for the fact that removal will be less costly in the future as technology improves and substitutes become more readily available. We do not know how much these costs will decrease, but based on past trends, we assume an annual price decrease of between 10% and 30% each year. In the average case, each year in the future that the baseline costs are incurred reduces the costs by 20% per year.

All costs reported are the differences in 20-year Net Present Values of the estimated costs required by this action and the estimated baseline costs.

1. Reformulation Costs

Over two-thirds of *trans* fats from industrially produced partially hydrogenated oils have already been taken out of the American diet (Refs. 3, 4), likely as a result of greater health awareness and the industry's reaction to FDA's 2003 *trans* fat labeling rule. The 2006 Report of the *Trans* Fat Conference Planning group (Ref. 5) describes the available substitutes for PHOs, describes considerations for reformulation, and presents case studies of successful reformulations. A major producer of processed foods reported that reformulating in less than a year cost \$25 million for 187 product lines, or \$134,000 per product, and after the reformulation the products were fully competitive, with no significant change in price, consumer acceptance, or shelf life (Ref. 5).

It is possible that there would be no serious difficulties with replacing the remaining PHOs in processed, packaged foods, and that the knowledge gained in past reformulations and research into alternatives could be used to reformulate the remaining products at a low cost. However, the persistence of a significant number of products using partially hydrogenated oils, even after so many products have been reformulated to remove such oils, may indicate that reformulation of the remaining products is less economically feasible or technologically possible. We estimate the middle-ground assumption that reformulation is possible but expensive, that half of the products (triangular distribution 0%; 50%; 100%) would require a critical reformulation and the remaining products a noncritical reformulation. A critical reformulation is one that requires extensive work, and a noncritical reformulation is a relatively simple ingredient substitution.

We searched the FoodEssentials database (Ref. 6) for products that contain PHOs, and found 26,000 such products, or about 12 percent of all packaged foods. This yields 13,000 noncritical reformulations and 13,000 critical reformulations. We also added 15,000 (triangular distribution 0; 15,000; 30,000) noncritical reformulations to account for industry

comments (Refs. 2, 4) that PHOs are used as processing aids in many products without appearing on the labels.

We used the FDA reformulation cost model (Ref. 7) to calculate the average cost of a change in critical and noncritical minor ingredients. The average cost of these reformulations over a three-year time is about \$46,000 for a non-critical reformulation and \$130,000 for a critical reformulation.² We multiply the number of reformulated products by the average reformulation cost to estimate one-time reformulation costs of about \$3 billion, spread out over the next three years. The estimated baseline costs are about \$0.6 billion, and the NPV of costs attributable to this action is about \$2.5 billion.

2. Relabeling Costs

All 26,000 reformulated products where a PHO appears on the label as an ingredient would have to be relabeled. The average cost of relabeling is about \$1,400 per stock-keeping unit (SKU) if the change must be made in three years, according to the FDA relabeling model (Ref. 8). We have received comments suggesting that costs may be higher, but we note that this is an average; some firms will face higher costs and others will face lower costs.

This results in a one-time cost of about \$37 million, spread out over the next three years. The estimated baseline costs are about \$7 million, and the NPV of costs attributable to this action is about \$28 million.

3. Substitute Ingredient Costs

Substitutes for the partially hydrogenated oils currently used by food manufacturers, consumers, restaurants, and others (including bakeries) will likely cost more as a result of this action (Ref. 5). Although the prices for PHOs and their substitutes are currently about the same, it is likely that the expansion in demand for substitutes will cause their price to increase.

The FDA's Categorical Exclusion memo for this action (Ref. 9) shows that about 2.5 billion pounds of partially hydrogenated oils were used in the United States in 2012. Given the many possible replacement fats and oils, we do not have the data required to properly analyze replacement ingredient costs, but we estimate, based on past fluctuations in market prices of palm oil (Ref. 10) and other commodities, that the price of replacement ingredients could be between 0 and 20 cents per pound higher than current PHO prices. The average prices for soy oil and lard in 2013 were about 40 cents per pound, so we are estimating an average 25 percent increase in substitute ingredient prices as a result of this action.

² As noted above, a major producer of processed foods reported that reformulation cost \$25 million for 187 product lines (Ref. 5), or an average of \$134,000 per product across critical and non-critical reformulations. We assume that these results reflect reformulated products being equally good, in terms of taste, texture and other attributes, as the preceding products with PHOs. As described in a later section of this memorandum, we anticipate that, upon implementation of this GRAS determination notice, post-reformulation products will not be as good as they were previously, which will reduce costs. In other words, if competitors' products are also not using PHOs, then producers do not have to incur as much cost to try to match quality that was achieved with PHO ingredients.

We therefore estimate the average annual cost of replacing current PHO usage at about \$250 million. The net present value of 20 years of replacement caused by this action, relative to a baseline of 20-year linear elimination of PHOs, is \$1.3 billion at a seven percent discount rate and \$1.7 billion at a three percent discount rate. It is also possible, as suggested in public comments (Ref. 2), that the substitutes may cost the end users more as a result of changes in supply chains and transportation systems, an effect not included in these rough quantitative estimates.

4. Costs to Consumers (Of changing recipes and of reduced utility due to inconvenience of shorter product shelf-life and unfamiliarity with new replacement products)

Substitute ingredients may require different cooking methods or recipes. Although we expect that most at-home recipes using PHOs can be cooked with substitute ingredients at a negligible increased cost in time or money, there are many recipes, especially for baked goods, where replacing PHOs could require research or experimentation. If 50 million households currently cook or bake with PHO-containing ingredients, and it takes an average of 1.5 hours (uniform distribution 0; 3) per household to learn how to cook all dishes with the replacement ingredients that will be on the market in 3 years, then consumers would spend 75 million hours adjusting to the removal of PHO-containing ingredients from the food supply. If this time is valued at the average hourly compensation of \$33 (Ref. 11), then the cost of this adjustment would be \$2.5 billion, spread out over the next three years. The estimated baseline costs are about \$0.5 billion, and the NPV of costs attributable to this action is about \$1.8 billion.

Although previous reformulations resulted in products of similar consumer acceptance and shelf life, it is likely that some reformulations required by this action will result in products that do not have similar consumer acceptance and shelf life. This could lead to a loss in access to familiar products and a loss from being able to store goods for less time.

In the categories of dry grocery, dairy, and frozen foods, total annual sales were about \$150 billion according to Nielsen scanner data. Because about 11.4 percent of packaged food products are made with PHOs (Ref. 6), we estimate that about \$17 billion is spent on such foods. Based on public comments describing the side effects of reformulation (Refs. 2, 4), there could be some loss of consumer utility from reduced familiarity and shelf life as that proportion of remaining foods made with PHOs come into compliance. It is difficult to develop any sound quantification of the proportion of the total volume of products made with PHOs which would actually lose some value for consumers upon reformulation, and how great that loss would be for any given product. Given past experience with consumer acceptance of reformulated products, it is not likely that all reformulated products would reduce consumers' utility. The costs could be quite low in the light of experience with reformulation to date. On the other hand, there will be some cost to consumers from their loss of products with familiar tastes and textures, becoming accustomed to substitutes, and getting used to different storage practices for some reformulated foods. Because we do not have a basis to make a reasonable estimate of such costs, we simply identify them qualitatively here for purposes of transparency.

5. Cost to Restaurants (Including Retail Bakeries) for Changing Recipes

Many restaurants have adapted to local regulations restricting use of PHOs at little or no cost (Ref. 12). However, as noted in a public comment from the National Federation of Independent Business (Ref. 13), we know that some restaurants, including retail bakeries, will bear costs related to the time to learn new recipes. As with consumers, we expect that most recipes can be updated at a negligible cost, but that some recipes will require research or experimentation to adjust to substitute ingredients. Some types of restaurants (such as retail bakeries) are likely to be affected more than others. We estimate that, on average, several recipes per restaurant (other than retail bakeries) and several dozen recipes per retail bakery will have to be adjusted.

There are about 616,000 restaurants (other than retail bakeries) in the US (Ref. 14), and about 6,000 retail bakeries (Ref. 15). Based on our qualitative understanding of the situation, we estimate that it will take the chefs and head cooks an average of 20 hours (triangular distribution 0; 10; 50) per restaurant to revise their recipes and procedures to use alternate ingredients, and that it will take the head bakers an average of 200 hours (triangular distribution 0; 100; 500) per bakery. With a \$21 value of time (Ref. 16) doubled for benefits and overhead, the hourly cost is \$42 and total costs are about \$570 million, spread out over the next three years. The estimated baseline costs are about \$110 million, and the NPV of costs attributable to this action is about \$420 million.

Total Costs

The total quantified costs (Net Present Value of twenty years of costs) are about \$6.0 billion at a seven percent discount rate and \$6.5 billion at a three percent discount rate. These costs are summarized in Table 2.

Table 2 - Cost Summary, Net Present Value of 20 years, USD Billions

Cost Category	7 percent	3 percent
1. Reformulation Costs	\$2.5	\$2.5
2. Relabeling Costs	\$0.03	\$0.03
3. Substitute Ingredient Costs	\$1.3	\$1.7
4. Cost to Consumers (from changing recipes, reduced product acceptance, and shorter product shelf life)*	\$1.8	\$1.8
5. Cost to Restaurants and Bakeries	\$0.4	\$0.4
Total Quantified Costs*	\$6.0	\$6.5
* This does not include some unquantified costs, see the “Costs to Consumers” section for discussion.		

Benefits

The benefits of removing PHOs from the food supply come from preventing the harm that is projected to occur in the future from continued consumption of the *trans* fatty acids in

industrially produced partially hydrogenated oils. There are many different estimates of the health benefits that may be achieved by this action. We monetize the estimated numbers of lives saved and nonfatal illnesses prevented from several different harm estimates, and present these estimates separately. Our bottom-line benefit estimate comes from averaging the results of simulation runs using the ranges of benefits presented in the five highest-quality methods, four methods from the FDA quantitative assessment (Ref. 1) and an academic paper (Ref. 17). The sections below present the ranges of lives saved and other benefits for each method, and Table 3 shows the expected monetary benefit for each method.

We chose these five methods because they are the most thoroughly documented and represent good understanding of current science. For further information about the science and methods involved in the quantitative assessment, and why these methods should be chosen over other methods, see the text of the quantitative assessment. The academic paper (Ref. 17) is the only study we have that isolates the impact of an implemented regulation restricting use of PHOs and studies its impact. As a sensitivity analysis, we also present an estimate that averages together all eight estimates.

The benefits of this action all occur in the future, so the monetized values of these future benefits must be converted into present values. We use 7 percent and 3 percent discount rates for this conversion in our estimate. Some example calculations are presented only at the 7 percent discount rate for clarity. However, all calculations were also done with a 3 percent discount rate, and we present the results of the 3 percent calculations in all tables.

Each fatal heart attack causes an average of 13 life years to be lost (Ref. 18). We use an average Value of a Statistical Life Year (VSLY) of about \$225,000 (triangular distribution \$112,000, \$225,000, \$337,000), based on VSLY and Cost Effectiveness Analysis literature which often cites \$100,000, \$200,000 and \$300,000 as values (base year 2006). (Ref. 19) With a 7 percent discount rate, each fatal heart attack prevented has a discounted value of about \$1.8 million. With a 3 percent discount rate, each fatal heart attack prevented is valued at about \$2.5 million.

Each nonfatal heart attack causes lowered quality of life for the rest of the victim's average 13 years of life. The average annual loss in Quality Adjusted Life years (QALYs) is 0.18 (Ref. 18). The present discounted value of this QALY loss is 1.44 at 7 percent and 1.98 at a 3 percent discount rate. We multiply this by the QALY value to monetize the quality of life gained due to prevention of a nonfatal heart attack at \$370,000 at 7 percent and \$511,000 at a 3 percent discount rate. The present discounted value of medical costs incurred by each nonfatal heart attack is an additional \$38,000 at a 7 percent discount rate and \$44,000 at a 3 percent discount rate.

All benefit estimates we use are based on reducing the current consumption level of *trans* fats from industrially produced PHOs to zero. However, it is likely that baseline PHO consumption would be lower in the future even without FDA action, as industry would likely continue to voluntarily phase out PHOs. We estimate that without FDA action, the baseline amount of PHO consumed would be reduced by five percent of its current value (triangular distribution 0%, 5%, 10%) each year, decreasing linearly to zero consumption in 20 years in the most likely scenario.

In this estimate, we find and report the total NPV of the benefits of this action over the next 20 years. This action has a compliance date three years after it is published, so we estimate

zero benefits in years 1, 2, and 3. We estimate that in year 4, this action will have expected annual benefits of 85 percent of the estimates generated using current consumption levels, decreasing to 80 percent in year 5, down to 5 percent in year 20. These percentages are averages; each simulation run has a different counterfactual base rate of decline in PHO consumption, and in each simulation, this rate of decline is the same as the one used in the cost baseline calculation.

Additionally, for the purposes of this estimate, we expect a 2-year lag between the removal of PHOs and the realization of the health benefits (Ref. 20). All benefit numbers are therefore discounted an additional two years into the future, at the appropriate discount rate, to account for this.

FDA Quantitative Assessment (Methods 1-4)

FDA conducted an updated quantitative assessment of risk for PHOs, which is available as a reference to the docket of this determination (Ref. 1). This quantitative assessment presented estimates of the expected number of fatal and nonfatal heart attacks that would be prevented as a result of replacing PHOs. We use the data from the first set of scenarios, the ones that replace trans fat with other macronutrient fatty acids, and combine that with data on expected replacement fats and oils and their nutrient composition, to produce an expected health effect.

As a result of this determination, the PHOs currently used will be replaced with a replacement mix of fats and oils. Based on data from the Grocery Manufacturers Association (GMA), a report from Oak Ridge National Laboratory, and other information, we estimated that the replacement mix of fats and oils would be as follows:

- High oleic soy oil, 25 percent (triangular distribution 15%; 25%; 35%);
- Fully hydrogenated oils, 10 percent (triangular distribution 0%; 10%; 20%);
- Interesterified fats, 10 percent (triangular distribution 0%; 10%; 20%);
- High oleic sunflower oil, 5 percent (triangular distribution 0%; 5%; 10%);
- Butter, 1 percent (triangular distribution 0%; 1%; 2%);
- Lard, 5 percent (triangular distribution 0%; 5%; 10%);
- Tallow, 4 percent (triangular distribution 0%; 4%; 8%);
- Soy Oil, 5 percent (triangular distribution 0%; 5%; 10%);
- Cottonseed oil, 2.5 percent (triangular distribution 0%; 2.5%; 5%);
- Canola oil, 2.5 percent (triangular distribution 0%; 2.5%; 5%); and
- Palm oil, 30 percent (100% minus the sum of all other oils used).

The weighted average fatty acid profile of these replacement oils is about 1 percent TFA, 39 percent saturated fatty acid (SFA), 44 percent monounsaturated fatty acid (MUFA), and 16 percent polyunsaturated fatty acid (PUFA). We estimate the weighted average fatty acid profile of the PHOs currently being used to be 33 percent TFA, 22 percent SFA, 31 percent MUFA, and 14 percent PUFA. Therefore, as a result of PHO replacement, we estimate that the net change in average fatty acid profile for replacement oils compared with current PHOs will be: TFA content will decrease by about 33 percentage points, SFA will increase by about

17 percentage points, MUFA will increase by about 14 percentage points, and PUFA will increase by about 2 percentage points.

Because the average TFA content decreases by about 33 percentage points with replacement using this estimate, every three grams of PHO replacement results in one gram of TFA replacement. For every gram of TFA removed from the diet as a result of this action, we estimate that SFA will increase by 0.52 grams, MUFA will increase by 0.42 grams, and PUFA will increase by 0.06 grams. We use these numbers to generate a weighted average of the quantitative assessment's estimates of harm prevented by PHO replacement. This forms our best estimate of the likely effect of this action.³

The quantitative assessment presented four different methods of calculating these numbers. We monetize our weighted average of the risk prevention in all four of these methods in the paragraphs below.

Method 1 looks only at the health effects of trans fats on LDL cholesterol, a validated surrogate endpoint biomarker for coronary heart disease (CHD), as shown through controlled feeding trials. The Method 1 result for PHO replacement with other fats from the expected replacement ingredients is about 1,400 fatal heart attacks prevented and 2,000 nonfatal heart attacks prevented per year at current TFA consumption levels of 0.5 percent energy. This is \$3.3 billion in monetized annual benefits at a 7 percent discount rate and \$4.6 billion at a 3 percent rate. The 20-year NPV of these benefits, given the baseline of reduced consumption described earlier and adjusted for the health benefit lag, is \$12 billion at a 7 percent discount rate and \$25 billion at a 3 percent rate.

Method 2 combines the effects of Method 1 with the additional effects of trans fats on HDL cholesterol, a major CHD risk factor biomarker, as shown through controlled feeding trials. Method 2 predicts that about 4,400 fatal heart attacks and 6,300 nonfatal heart attacks would be prevented. The 20-year NPV of these monetized benefits is \$38 billion at a 7 percent rate and \$79 billion at a 3 percent rate.

Method 3 combines the effects of Method 2 with the effects of TFA on a combination of emerging CHD risk factor biomarkers (lipoprotein(a), apolipoproteinB/apolipoproteinA1 and C-reactive protein), as shown through controlled feeding trials. Method 3 predicts that about 8,500 fatal heart attacks and 12,000 nonfatal heart attacks would be prevented. The 20-year NPV of these monetized benefits is \$75 billion at a 7 percent rate and \$150 billion at a 3 percent rate.

Method 4 uses association of trans fats with CHD risk as shown through prospective observational studies. Method 4 predicts that about 19,000 fatal heart attacks and 27,000

³ A source used as a key input for the quantitative assessment does not report its estimating equation. Therefore, we do not know whether the regression analysis of the dose-response relationship between trans fat consumption and cholesterol levels in Mozaffarian and Clarke (2009) estimates its intercept empirically or sets it to zero, the latter of which would increase the slope of the regression line. However, we have no reason to question the basic results of this source, which shows a progressive and linear relationship between trans fat consumption and LDL and HDL cholesterol levels consistent with other evidence we reviewed, and thus supports this final determination.

nonfatal heart attacks would be prevented. The 20-year NPV of these monetized benefits is \$160 billion at a 7 percent rate and \$330 billion at a 3 percent rate.

Restrepo and Rieger 2014 (Method 5)

This paper (Ref. 17) analyzes county regulations in several New York State counties restricting use of PHOs. Different counties implemented regulations at different times, with no observable differences in the counties before the ban. Their identification strategy relies on the assumption that differences across counties that may affect health outcomes (other than PHO regulation) are fixed over time. The authors looked at the differences in coronary heart disease rates in the different counties and found that the regulations caused a 4.3 percent reduction in heart disease. If the paper's identification strategy is sound, the reported results would likely be underestimates, because the regulations only applied to restaurant foods and not to packaged foods, and did not include uses below 0.5g/serving.

A 4.3 percent nationwide reduction in coronary heart disease would mean approximately 16,000 fatal heart attacks and 23,000 nonfatal heart attacks prevented. The 20-year NPV of these monetized benefits is \$140 billion at a 7 percent rate and \$290 billion at a 3 percent rate.

GMA Comment (Method 6)

The Grocery Manufacturers Association (GMA) submitted a comment stating that *trans* fats cause no harm when people consume them at levels of intake at or below 2.0 percent of energy, which is about 4.9 grams a day for the average diet. FDA addresses the scientific evidence relating to this argument in the final determination (see section IV.B. of that document) and in a technical memo (Ref. 21). FDA disagrees with this comment and has concluded that the scientific evidence supports a progressive and linear cause and effect relationship between TFA intake and adverse effects on blood lipids that predict CHD risk, and FDA does not agree that a threshold at which effects would not be expected to occur has been identified based on the available science. However, for the purposes of this estimate of costs and benefits, we calculate the benefits of this action in this section using an assumption that the GMA statement were true.

We estimate that average individual consumption of *trans* fats from PHOs is currently close to 1.1 g per day, but there is variation in *trans* fat consumption. Only about 1.5 percent of the population is consuming *trans* fats at a level higher than 4.9 g per day on a given two days. (Ref. 22) We use the distribution of *trans* fat intake from PHOs, and subtract 4.9 g per day, to find the estimated consumption of *trans* fat from PHOs in the population that exceeds 4.9 g per day. We then apply methods 1-5 to this amount of consumption exceeding 4.9 g per day, to find the estimated benefits of this action incorporating the assumption that there is no increased CHD risk at TFA levels below 2.0 percent of energy. With current consumption levels, the health benefits calculated with this alternate, counterfactual method are one percent of the benefits estimated using an average of methods 1-5.

We repeat this process 20 times, each time reducing all intake numbers by 5 percent to account for the expected future decrease in consumption. This generates a 20-year path of expected benefits, with the percentage of benefit relative to the base method decreasing in later years.

When applied to the average monetized benefits of this action estimated using methods 1-5, the GMA comment counterfactual method yields a 20-year NPV of monetized benefits of \$0.9 billion at a 7 percent rate and \$1.6 billion at a 3 percent rate.

Weston Firm Comment (Method 7)

The Weston Firm submitted a comment (Ref. 23) stating that PHOs cause between 12,600 and 42,000 annual coronary deaths. FDA addresses the scientific evidence relating to this argument in the final determination (see section IV.B. of that document). For the purposes of this estimate of costs and benefits, we calculate the benefits of this action in this section using the prevention of coronary deaths as stated in the Weston comment.

Given a uniform distribution of deaths with minimum 12,600 and maximum 42,000, the comment states an average of 27,300 deaths prevented. Given that 41 percent of heart attacks are fatal (Ref. 24), these numbers imply an average of 39,000 nonfatal heart attacks prevented.

The Weston comment also states that PHOs cause many illnesses not accounted for in the FDA estimate. FDA addresses the scientific evidence relating to this argument in the final determination (see section IV.B. of that document). FDA's science review found that, for the association of *trans* fat intake with human health effects other than cardiovascular diseases, such as various types of cancer, metabolic syndrome and diabetes, and adverse effects on fertility, pregnancy outcome, cognitive function and mental health, the literature reports remained limited or inconclusive. However, for the purposes of this estimate of costs and benefits, we calculate the benefits of this action in this section using an assumption that the Weston statement were true. The comment included many statements about other types of illnesses prevented, which we estimate to be the QALY equivalent of about 40,000 nonfatal heart attacks.

Taken together, the monetized deaths and illnesses prevented yield a 20-year NPV of \$300 billion at a 7 percent rate and \$620 billion at a 3 percent rate.

Center for Effective Government Comment (Method 8)

The Center for Effective Government submitted a comment (Ref. 25) stating that FDA should use a Value of Statistical Life (VSL) methodology. In this section, we present a benefit calculation using a VSL of \$8.3 million for each fatal heart attack prevented.

We recalculate all seven of the methods presented above with this VSL, while keeping the same numbers for the nonfatal heart attacks and medical care. The average benefits are then \$370 billion at a 7 percent discount rate and \$580 billion at a 3 percent discount rate.

Average Expected Benefits

Our base estimate is the average of the five best methods: the four methods presented in the FDA quantitative assessment and the Restrepo and Rieger paper.

As a sensitivity analysis, we also present an average of all eight methods: FDA's five best methods in addition to the three methods presented in the public comments. The benefits found by each method, and the two averages, are in Table 3:

Table 3 - Benefit Estimates, Net Present Value of 20 years, USD Billions

Effect Calculation Method	7 percent discount rate	3 percent discount rate
FDA Quantitative Assessment (Method 1)	\$12	\$25
FDA Quantitative Assessment (Method 2)	\$38	\$79
FDA Quantitative Assessment (Method 3)	\$75	\$150
FDA Quantitative Assessment (Method 4)	\$160	\$330
Restrepo and Rieger 2014 (Method 5)	\$140	\$290
Average Best Methods (1-5)	\$86	\$180
GMA Comment applied to Methods 1-5 (Method 6)	\$1	\$2
Weston Firm Comment (Method 7)	\$300	\$620
Center For Effective Government Comment applied to Methods 1-7 (Method 8)	\$380	\$580
Average All Methods (1-8)	\$140	\$260

Trade Effects

We expect that this action will increase imports, as domestically-produced PHOs are replaced in part by foreign-produced palm oil. The current estimated annual consumption of PHOs is 2.5 billion pounds, and we expect that about 30% of this will be replaced with palm oil. Over the past few years, the average palm oil price has been about 40 cents per pound. We anticipate that increased demand could increase the average price. Assuming an average palm oil price of 50 cents a pound, 760 million pounds of palm oil imports would be about \$380 million a year.

We expect that many of these imports would happen in the absence of FDA action, as PHOs are phased out of the food supply. Compared to expected baseline replacement of PHOs (described in the Benefits section above), we expect that this action will be responsible for an average increase of about \$150 million in annual imports.

Distribution Effects

Soy oil futures fell by 1.6 percent on the day that FDA announced its tentative determination that PHOs were not GRAS. (Ref. 26) We assume that commodity traders are acting rationally and have accurate knowledge of their market, that nothing else caused significant market movement that day, and that market traders expected the determination to be finalized with near 100% probability, meaning that the market movement is an accurate prediction of the expected effects of this action. We combine this information with UDSA statistics to form a prediction of market effects of this action.

The 2012 production of soy oil was about 20 billion pounds, and the price on the announcement date was about 40 cents a pound. An estimated 1.6 percent reduction in these

calculated revenues implies that the soy oil industry will lose about \$130 million in revenues annually as a result of the action. We believe this is an upper limit on the amount that soybean farmers will lose, because the estimated \$130 million revenue reduction will likely be split between American soybean farmers and soy oil processors.

Net Benefits with Confidence Intervals

We find the expected net benefits of the action, with a 90 percent confidence interval, by running a Monte Carlo simulation. In each simulation run, we do the following:

- 1) Randomly determine the annual baseline PHO reduction without FDA action (triangular distribution 0, 5%, 10%). The reduction is a percentage of current usage each year, generating a linear decrease.
- 2) Choose a discount rate to use. The 3 percent and 7 percent rates are each used in 1/4th of the simulation runs, respectively; in one-half of the runs, a random discount rate is chosen between 0 percent and 10 percent.
- 3) Draw a random number from all distributions used as inputs to estimate costs, and recalculate the cost of the action.
- 4) Choose a harm calculation method at random from the methods used.
- 5) For the method chosen, draw the health gains from the distribution provided by the method.
- 6) Choose a VSLY to use from the specified distribution.
- 7) Randomly determine the replacement ingredients used.
- 8) Calculate benefits using the chosen variables, and subtract the costs.

The results of the 100,000 simulation runs are shown in Table 4:

Table 4 - Net Benefits of PHO removal, USD Billions

20-Year NPV	5th Percentile	Mean	95th Percentile
Net Benefits, Best Methods*	\$5	\$130	\$430
Net Benefits, All Methods*	\$-6	\$160	\$600
* This does not include some unquantified costs, see the “Costs to Consumers” section for discussion.			

Bibliography

1. **Memorandum from J. Park to M. Honigfort**, A Quantitative Assessment of Coronary Heart Disease Risk in U.S. Adults Associated with Current Mean Intake of Industrially-Produced Trans Fatty Acids in Partially Hydrogenated Oils (PHO), Dated June 11, 2015
2. Comment from **Grocery Manufacturers Association**, FDA-2013-N-1317-0172
3. **D. Doell, D. Folmer, H. Lee, M. Honigfort & S. Carberry**. Updated estimate of *trans* fat intake by the US. *Food Additives & Contaminants*. 2012.
4. Comment from **American Bakers Association**, FDA-2013-N-1317-0173
5. **Robert H. Eckel, Susan Borra, Alice H. Lichtenstein and Shirley Y. Yin-Piazza**. Understanding the Complexity of *Trans* Fatty Acid Reduction in the American Diet. *Circulation*. 2006.
6. **FoodEssentials**. Product Label Database. [Online]
<http://labelbase.foodessentials.com/index.jsp>.
7. **RTI International**. FDA Reformulation Cost Model. 2015.
8. **RTI International**. Model to Estimate Costs of Using Labeling as a Risk Reduction Strategy for Consumer Products Regulated by the Food and Drug Administration. 2011.
9. **Memorandum from Environmental Review Team to M. Honigfort**, Determination that Partially Hydrogenated Oils (PHOs) are not GRAS, Dated June 11, 2015
10. **Index Mundi**. Palm oil Monthly Price - US Dollars per Metric Ton,
<http://www.indexmundi.com/commodities/?commodity=palm-oil&months=120>
11. **Bureau of Labor Statistics, U.S. Department of Labor (USDL)**. EMPLOYER COSTS FOR EMPLOYEE COMPENSATION –MARCH 2015,
<http://www.bls.gov/news.release/pdf/ecec.pdf>
12. **A Tan**. “A Case Study of the New York City Trans-Fat Story for International Application.” *Journal of Public Health Policy*, 30(1): 3-16. 2009
13. Comment from **National Federation of Independent Business**, FDA-2013-N-1317-0110
14. **NPD Group**. U.S. Total Restaurant Count...,
<https://www.npd.com/wps/portal/npd/us/news/press-releases/us-total-restaurant-count-increases-by-4442-units-over-last-year-reports-npd/>

15. **Small Business Development Center.** Bakery Business 2014,
<http://www.sbdcnnet.org/small-business-research-reports/bakery-business-2014>
16. **Bureau of Labor Statistics, U.S. Department of Labor (USDOL).** May 2014 National Industry-Specific Occupational Employment and Wage Estimates, NAICS 722500,
http://www.bls.gov/oes/current/naics4_722500.htm
17. **Brandon Restrepo; Matthias Rieger,** Trans fat and cardiovascular disease mortality: Evidence from bans in restaurants in New York. working paper
18. **Food and Drug Administration.** *Trans Fatty Acids in Nutrition Labeling. Federal Register.* 2003, Vol. 68, 133.
19. **R. Scott Braithwaite, et al.** What Does the Value of Modern Medicine Say About the \$50,000 per Quality-Adjusted Life-Year Decision Rule? *Medical Care.* 2008, Vol. 46, 4.
20. **M R Law, N J Wald, A R Rudnicka.** Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis *British Medical Journal* Vol. 326, June 2003
21. **Memorandum from J. Park to M. Honigfort,** Scientific Update on Experimental and Observational Studies of Trans Fatty Acid Intake and Coronary Heart Disease Risk, Dated June 11, 2015.
22. **Memorandum from D. Doell to R. Bruns.** Per Capita Exposure Estimate to Trans fat from the Use of Partially Hydrogenated Oils for the U.S. Population Aged 18+Years, Dated May 8, 2015
23. Comment from **The Weston Firm,** FDA-2013-N-1317-0223
24. **A. S. Go, D. Mozaffarian, V.L. Roger, et al.,** on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee, "Executive Summary: Heart Disease and Stroke Statistics - 2014 Update: A Report from the American Heart Association," *Circulation*, 129:399-410, 2014.
25. Comment from **Center for Effective Government,** FDA-2013-N-1317-0091
26. **Julie Ingwersen, Reuters.** Trans fat ban may hit 15 pct of U.S. soyoil use, boosting palm oil, <http://www.reuters.com/article/2013/11/07/usa-fda-transfat-markets-idUSL2N0IS2OM20131107>

Public health economic evaluation of different European Union–level policy options aimed at reducing population dietary *trans* fat intake^{1,2}

Carlos Martin-Saborido,³ Theodora Mouratidou, Anastasia Livaniou, Sandra Caldeira, and Jan Wollgast*

European Commission, Joint Research Centre (JRC), Ispra, Italy

ABSTRACT

Background: The adverse relation between dietary *trans* fatty acid (TFA) intake and coronary artery disease risk is well established. Many countries in the European Union (EU) and worldwide have implemented different policies to reduce the TFA intake of their populations.

Objective: The aim of this study was to assess the added value of EU-level action by estimating the cost-effectiveness of 3 possible EU-level policy measures to reduce population dietary TFA intake. This was calculated against a reference situation of not implementing any EU-level policy (i.e., by assuming only national or self-regulatory measures).

Design: We developed a mathematical model to compare different policy options at the EU level: 1) to do nothing beyond the current state (reference situation), 2) to impose mandatory TFA labeling of prepackaged foods, 3) to seek voluntary agreements toward further reducing industrially produced TFA (iTFA) content in foods, and 4) to impose a legislative limit for iTFA content in foods.

Results: The model indicated that to impose an EU-level legal limit or to make voluntary agreements may, over the course of a lifetime (85 y), avoid the loss of 3.73 and 2.19 million disability-adjusted life-years (DALYs), respectively, and save >51 and 23 billion euros when compared with the reference situation. Implementing mandatory TFA labeling can also avoid the loss of 0.98 million DALYs, but this option incurs more costs than it saves compared with the reference option.

Conclusions: The model indicates that there is added value of an EU-level action, either via a legal limit or through voluntary agreements, with the legal limit option producing the highest additional health benefits. Introducing mandatory TFA labeling for the EU common market may provide some additional health benefits; however, this would likely not be a cost-effective strategy. *Am J Clin Nutr* 2016;104:1218–26.

Keywords: European Union, cost-effectiveness, public health, public policy, *trans* fatty acids

INTRODUCTION

trans Fatty acids (TFAs)⁴ are a type of unsaturated fatty acid that have ≥1 unsaturated, nonconjugated double bond in the *trans* configuration. TFA intake can be of industrial (mainly partially hydrogenated oils) or natural (ruminant food sources) origin (1). The detrimental effects of dietary intake of industrially produced

TFAs (iTFA) on heart health were first reported in the 1990s (2) and are now well established (3–5). Other health effects have been attributed to iTFA intake, such as on insulin sensitivity, obesity, diabetes, cancer, or early growth and development (3, 6). Most official guidelines recommend limiting daily TFA intake as much as possible within an adequate diet or to intakes of <1% or 2% of total energy (E%) (7). Many countries worldwide have policies to reduce population TFA intake (8); these are accompanied by significant reductions in food TFA content, with the largest reductions being observed in situations in which legal limits on TFAs are in place (9).

In the European Union (EU), dietary TFA intake has been decreasing since the 1980–1990s, from as high as 4.3 E% in elderly Dutch men in 1985 (9) to average population intakes <1 E% in the 2000s (1, 10, 11). These estimates include both iTFAs and TFAs from ruminant sources, with the latter contributing between 0.3 and 0.8 E% depending on dietary habits (11). Although less is known about dietary TFA intakes in Eastern Europe, data on TFA content of selected foods sampled between 2005 and 2014 suggest somewhat higher amounts than in most other parts of Europe (12–14). Recent data also suggest that the reduction in iTFAs in foods continued in some, but not all, European countries from 2006 to 2013 (13) and 2012 to 2014 (12).

Several health economic models suggest that reducing population iTFA intakes provides health benefits [i.e., reductions in cardiovascular disease or coronary artery disease (CAD)–related events and deaths as well as cost savings] (15–18). Restrepo and

¹ The authors reported no funding received for this study. This is an open access article distributed under the CC-BY license (<http://creativecommons.org/licenses/by/3.0/>).

² Supplemental Tables 1–4 are available from the “Online Supporting Material” link in the online posting of the article and from the same link in the online table of contents at <http://ajcn.nutrition.org>.

³ Present address: Health Technology Assessment Unit–Universidad Francisco de Vitoria, Madrid, Spain.

*To whom correspondence should be addressed. E-mail: jan.wollgast@ec.europa.eu.

⁴ Abbreviations used: CAD, coronary artery disease; DALY, disability-adjusted life-year; E%, percentage of total energy; EU, European Union; GDP, Gross Domestic Product; ICER, incremental cost-effectiveness ratio; iTFA, industrially produced *trans* fatty acid; PHO, partially hydrogenated oil; PSA, probabilistic sensitivity analysis; TFA, *trans* fatty acid.

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Rieger (19) estimated that the 2004 legal limit on iTFAs in Denmark has prevented ~ 14.2 deaths $\cdot 100,000$ persons $^{-1} \cdot y^{-1}$. Another study suggests that introducing a legal limit on iTFAs in England would prevent ~ 7200 deaths from CAD (or 2.6% of all predicted CAD deaths) between 2015 and 2020, providing the greatest health benefits and reduction in the inequality gap when compared with improved TFA labeling or TFA removal from restaurants and fast foods (20). Because the EU and its member states are currently evaluating the impact of possible measures at the EU level (21, 22), this study presents an economic evaluation to compare the cost-effectiveness of 3 different policy options against the option of taking no action at the EU level (reference situation).

METHODS

Model development

We developed a computer-simulated, Markov, state-transition model with the use of Excel (Microsoft Office 2010). This type of model is appropriate because Markov models are suitable for changing systems (i.e., where there is movement or transitions between different states). In this case, the different states are the conditions in which an individual can be, such as “well,” with “CAD” or “history of CAD,” or “dead” (see **Figure 1**). In addition, because the available data are population-based, discrete simulation models cannot be used and a cohort model such as Markov should be chosen instead. The International Society for Pharmacoeconomics and Outcome Research-Society for Clinical Decision Making (ISPOR-SMDM) Modeling Good Research Practices Task Force recommends Markov models for this kind of analysis (23, 24).

The TFA intake, defined as E%, as a starting point for the model (“today”) was calculated as described in **Supplemental Tables 1–3**. The model was applied to the EU population and accounts for all costs and effects applicable or resulting from the following policy options over the course of a lifetime (85 y) (25):

- 1) Reference situation (no action at the EU level): The reference situation is described by the highest cumulative TFA intake (i.e., the highest population TFA intake when summing up yearly population TFA intakes over the modeled time horizon of 85 y) in all of the 4 options, and therefore it also entails the highest risk of CAD. Nevertheless, even for this case of “no action at EU level,” in the model we assume a continued decrease in TFA consumption that leads to a removal of iTFAs from the food supply over 10 y due to continuous innovation in the industry and efforts at the national or regional levels. In terms of costs, there are no added public costs from implementing this policy option; all costs result from CAD-associated morbidity and loss of productivity.
- 2) Voluntary agreements: With this option policy makers actively seek agreements at the EU level, such as with the food industry and retailers to introduce measures that reduce TFA amounts in foods and/or between EU member states, to agree on a common framework toward reducing TFAs in foods and diets similarly to the EU salt reduction framework (26). In this case, public costs are CAD-associated and are also related to food inspection programs to monitor

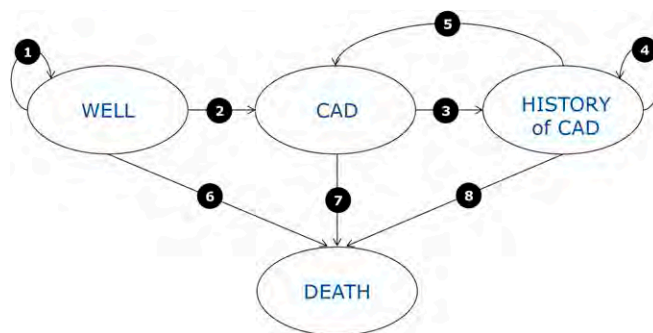


FIGURE 1 Schematic representation of the Markov model used to simulate how people move in yearly cycles through 4 health states in each of the policy options. The 4 health states are as follows: “Well” (the state for each individual with no history of CAD; a person can remain here until death or move to “CAD”); “CAD” (individuals who have CAD move to this state for a maximum of 1 y; from this state, individuals can move either to “History of CAD” or “Death” but not back to the “Well” state); “History of CAD” (post-acute CAD health state; survivors from a “CAD” state move to this state until death or until they suffer a new CAD event, in which case they move to the “CAD” state); and “Death” [this is an absorbing state (once a person enters this state, they cannot leave it); any individual can move to “Death” at any time]. The meaning of each transition probability between health states is as follows: 1) probability of keeping well (in this context, staying alive and not having a CAD event), 2) probability of experiencing a CAD event for persons without a previous CAD event, 3) probability of surviving a CAD event, 4) probability of staying alive in the post-acute CAD state, 5) probability of experiencing a new CAD event when in the post-acute CAD state, 6) probability of death from any cause (except from CAD) for persons without a previous CAD event, 7) probability of death from a CAD event, and 8) probability of death from any cause except for CAD for individuals with a history of CAD. CAD, coronary artery disease.

and evaluate the agreements. We assume a faster reduction in TFA consumption than in option 1, leading to a quicker removal of iTFAs from the food supply due to the additional private-public commitments. For this strategy in the model we assume the total removal of iTFAs from the food supply after 5 y, half the time needed in the absence of EU-level action (reference situation), albeit acknowledging that the rare use of iTFA-containing raw materials by some producers and imports of iTFA-containing foods from countries in which the iTFA issue has not been addressed cannot be excluded.

- 3) Mandatory TFA labeling: With this strategy the existing rules for the nutrition declaration on foods as governed by EU regulation 1169/2011 would be changed to require the disclosure of the TFA contents in all prepackaged foods. This provides an incentive for food reformulation toward reducing or replacing iTFAs, but only for prepackaged foods. Because this option requires legislative action, in addition to CAD-associated public costs, other non-CAD-related public costs are also considered. These are linked to the implementation of the legislation (mass media costs), worksite interventions, consumer education, and nutrition counseling as well as food inspection (9). The reduction in population TFA intake is faster than in the reference situation but slightly slower than in option 2 (voluntary agreements), because in this case there are only incentives toward reducing TFA content in prepackaged foods. The assumption in the model is that iTFA removal is faster in prepackaged foods than in options 1 (reference) and 2, but not in non-prepackaged foods, in which iTFA

removal proceeds at the same speed as in the reference option 1. The model assumes population TFA intake reductions for the first 2 y until TFA content labeling is available for all prepackaged foods, as in the reference situation (option 1), then a faster reduction in iTFA intake from prepackaged foods, which, based on the available information (see Supplemental Table 2), is assumed to contribute to 50% of population TFA intake at the start and decrease to 0% in 3 y. The model assumes that reductions in iTFAs from non-prepackaged foods continue at the same speed as in the reference situation albeit acknowledging that, in reality, some spillover effects in the efforts to remove iTFAs from prepackaged foods might also be expected for non-prepackaged foods.

- 4) Legal limit of iTFA content in foods: This option sees a restriction in the use of iTFAs in the food supply through a legislative limit, such as that already introduced by some EU member states (Denmark, Austria, Hungary, and Latvia). This measure results in a fast removal of iTFAs in all of the EU food supply and represents therefore the lowest cumulative TFA consumption of all 4 options. The model assumes the total removal of iTFAs in 2 y. This strategy implies, in addition to CAD-associated public costs, other costs that are not associated with CAD such as public costs for food inspection programs.

The model simulates how people are moving in yearly cycles through 4 health states, as shown in Figure 1. Costs (of policy implementation and CAD-related) and effects [CAD incidence and disability-adjusted life-years (DALYs)] are accounted for as the population circulates through the model. These are calculated for each policy option and then compared with one another. An

annual discount rate of 3.5% is applied to both costs and effects following best-practice guidelines (25). The economic evaluation presented here is broader than a simple evaluation focused on health system costs because it also includes a societal perspective: the costs included are not only health care–related costs but also indirect costs stemming from informal care and loss of productivity due to mortality and morbidity as well as policy implementation–related public costs.

Costs

All of the costs considered to account for the burden of TFAs have been adjusted for inflation to 2011 prices (in €); currency exchanges, when applicable, were calculated on the basis of 1 January 2011 exchange rates to the euro. The model considers 3 types of costs (see also **Table 1**):

- Health care costs: These costs stem from the use of health resources (i.e., primary care costs, outpatient costs, emergency costs, and medication used during the hospitalization). The costs are based on the European Cardiovascular Disease Statistics 2012 (28).
- Non–health care costs: This group of costs includes all non–health care costs related to the disease, namely loss of productivity and informal care. The costs are based on the European Cardiovascular Disease Statistics 2012 (28).
- Costs of policy-associated measures: Each policy option (apart from option 1 “reference situation”) incurs costs related to the execution of measures needed for their successful implementation.

The costs associated with each of the measures are described in the Organization for Economic Cooperation and Development

TABLE 1

Model variables and their source, deterministic value, and distribution type¹

Variable description	Source (reference)	Deterministic value	Distribution ²
Probability of death from acute CAD	Data from HFA-DB (27)	Life tables	Log-normal
Probability of death from any cause	Data from HFA-DB (27)	Life tables	Log-normal
Probability of CAD	Hospital discharges by IHD; data from HFA-DB (27)	Morbidity table	Log-normal
Reduction in RR of CAD in legal limit strategy	Mozzafarian et al. (4), O’Flaherty et al. (18)	Age and sex dependent	Log-normal
Reduction in RR of CAD in voluntary agreements strategy	Mozzafarian et al. (4), O’Flaherty et al. (18)	Age and sex dependent	Log-normal
Reduction in RR of CAD in mandatory labeling strategy	Mozzafarian et al. (4), O’Flaherty et al. (18)	Age and sex dependent	Log-normal
RR of second and subsequent CAD events after the first event	Assumption	1.5	Log-normal
RR probability of death from second CAD event compared with death from the first CAD event	Assumption	1.5	Log-normal
Production losses due to mortality	Nichols et al. (28)	€5101.94	γ
Production losses due to morbidity	Nichols et al. (28)	€2158.88	γ
Informal care	Nichols et al. (28)	€6440.19	γ
Primary care	Nichols et al. (28)	€617.34	γ
Outpatient care	Nichols et al. (28)	€854.56	γ
Accident and emergency	Nichols et al. (28)	€213.78	γ
In-patient care	Nichols et al. (28)	€3557.46	γ
Medication	Nichols et al. (28)	€1605.36	γ
School-based intervention	Cecchini et al. (29), Sassi et al. (30)	€1.15	γ
Worksite intervention	Cecchini et al. (29), Sassi et al. (30)	€4.48	γ
Mass media campaigns	Cecchini et al. (29), Sassi et al. (30)	€1.90	γ
Physician counseling	Cecchini et al. (29), Sassi et al. (30)	€8.28	γ
Program of food inspection	Cecchini et al. (29), Sassi et al. (30)	€0.86	γ

¹ CAD, coronary artery disease; HFA-DB, Health for All Database; IHD, ischemic heart disease; TFA, *trans* fatty acid.

² Distributions were chosen following the recommendations in reference 31.

report entitled “Improving lifestyles, tackling obesity: the health and economic impact of prevention strategies” (30). Costs per person per year have been adapted from this report and applied to the model to best estimate the real costs to governments (costs were adjusted by using the purchasing power parity methods to adjust for cost of living between countries).

The following types of costs were considered (see also Table 1). The first 4 relate to the provision of information and counseling on TFAs, TFA-related health issues, and interpretation of food labels (if applicable).

- 1) School-based interventions costs: These include training teachers and food service staff and additional curricular activities, but exclude changes in food provision services.
- 2) Worksite interventions costs: These include costs from activities subsidized by the public sector and held in worksites by employers.
- 3) Mass media campaigns costs: These include broadcasting advertisements on national and local radio and television channels and for designing, producing, and distributing flyers and leaflets.
- 4) Physician counseling costs: These costs include counseling provided by physicians to targeted individuals.
- 5) Program of food inspection costs: These include the administration, planning, enforcement, and resources needed to manage food inspection.

Effects

The model calculates, for each option, CAD events and mortality in yearly cycles over a period of 85 y. It is based on current estimates of iTFA intake (detailed in reference 32 and as shown in Supplemental Tables 1–3) and the assumed reductions in TFA intake over the years as described above. In addition, the RRs for CAD associated with the different TFA intakes are based on the calculations in Mozaffarian et al. (4) in which the “pooled multivariable-adjusted RR for 2%E of TFA, as an isocaloric replacement for carbohydrate, was 1.23 (95% CI = 1.11–1.37).” This is then applied to the different iTFA intakes to calculate the probability of a CAD event (see probability 2 in Figure 1). For the starting point of the model (“today”) the risk of CAD is calculated on the basis of hospital discharges (see explanation below) and already includes the risks from current iTFA intakes, which are specific according to country, age, and sex (Supplemental Tables 1–3). The reduction in CAD risk linked to iTFA reductions in the following years from “today” is then calculated by using the RR above.

Subsequently, the resulting DALYs are then calculated on the basis of the modeled number of CAD events and deaths. DALYs reflect, in a single quantitative figure, years of life lost due to premature death from illness and years lived with disability. To calculate the DALYs averted in each strategy, the DALYs calculation template from the Health Statistics and Health Information Systems Office (WHO) was used, including the weightings as reported in the Global Burden of Disease 2010 study (Institute for Health Metrics and Evaluation) (33).

The model also includes the probabilities of having a CAD event for the first time, of having another CAD event after the first

one, of death at any time and of death because of a CAD event (or due to any cause; see Table 1). Other proposed beneficial effects of lowering TFA intake, such as on insulin sensitivity, obesity, diabetes, cancer, or early growth and development, were not considered in the model because of inconsistent evidence and lack of data (3, 6). The probabilities of having a CAD event were calculated on the basis of the EU hospital discharges (27), because this was the only source of relevant information and data. The lack of CAD incidence data was also highlighted in the 2012 European Cardiovascular Disease Statistics (30), in which hospital discharges were suggested as an alternative source of incidence data. The probabilities of dying at any time and of dying of CAD were extracted from the European Health for All Database (HFA-DB 2010) (27) for the EU.

Dealing with uncertainty

There is substantial uncertainty with regard to some of the data used in the model. For this reason, we ran the model for various scenarios so as to assess the robustness of the outcome in cases in which data are scarce, in particular with respect to the current EU population’s TFA intake. We included 3 scenarios in addition to the base case. In the base case we estimated different initial iTFA intakes per age group and sex (overall average: 0.3 E%):

Scenario 1 assumes an initial overall average iTFA intake of 0.15 E% (50% of our base case estimates, assuming that much improvement has been made since the latest estimates reported in Supplemental Table 1).

Scenario 2 assumes an initial overall average iTFA intake of 0.45 E% (assuming that the situation in countries where no estimates were identified is somewhat worse than in our estimate).

Scenario 3 assumes an initial overall average iTFA intake of 0.7 E% [allowing for even higher initial iTFA intakes as suggested from modeled data of total TFA intake (34) and as presented in **Supplemental Table 4** and after subtracting an estimated 0.5 E% contribution from ruminant TFAs (11)].

Population iTFA intakes in the 3 scenarios diminish in a similar manner as the base case in each of the 4 policy options. A summary of the initial iTFA population intakes for each scenario is provided in **Table 2**.

In addition, this economic evaluation includes, next to the deterministic analysis, which uses a single value for costs and for effects in the model calculations, a probabilistic sensitivity analysis (PSA). The PSA applies probabilistic distributions to every variable in the model. Each of the distributions used in the PSA were chosen following the current trends and literature recommendations (i.e., γ distribution for variables constrained to be zero or positive or log-normal distribution for variables calculated by using RRs) (31). These probabilistic distributions are based on mean values and CIs, SDs, or ranges of values detailed in the data sources. In this way, the PSA attempts to account for uncertainty in existing evidence [e.g., in the estimates of the risk of CAD linked to different TFA intakes (4)]. A summary of the deterministic values and the distributions applied to them for the PSA analysis are shown in Table 1. Both deterministic and probabilistic analyses were performed for all of the scenarios.

TABLE 2

Overview of different initial iTFA intakes as estimated in the base case and assumed in 3 alternative scenarios¹

	Initial population iTFA intakes, ² E%
Base case	0.3 ³
Scenario 1	0.15
Scenario 2	0.45
Scenario 3	0.7

¹ E%, percentage of total energy intake; iTFA, industrially produced *trans* fatty acid.

² Although the reduction speed differs between the 4 policy options, 0 E% iTFA intake will eventually be achieved in all of the options.

³ Averaged value; initial values in the model in the base case situation differ for age and sex.

RESULTS

The resulting health effects and costs linked to each of the 4 policy options from the deterministic base case analysis are presented in **Table 3**. It is important to note that the estimates should not be taken at face value given that the model is a simplification of reality and CAD events and deaths are not “competing” against any other disease. Consequently, the absolute numbers may be an overestimation of CAD events and deaths avoided. This stems from the model’s limitations.

The results shown in Table 3 indicate that implementing a legal limit at the EU level would result in the fewest costs to the public, followed by the voluntary agreements, the reference situation of no-EU-level action, and mandatory labeling. The main reason that the lowest public costs are associated with limiting iTFA contents in foodstuffs is that the reduction in the number of estimated CAD events is greatest due to the lower population intakes of cumulative iTFAs. The reduction in health care costs and in indirect costs linked to informal care and productivity loss outweighs the costs of implementing this policy, more than in any of the other policy options. In contrast, the highest public costs in the mandatory labeling options are due to the fact that the reduction in CAD cases obtained through this policy option is not sufficient to compensate for the costs of the measures implemented. When looking at the health outcomes, the results indicate that introducing an EU-level legal limit on iTFAs in foodstuffs would also result in the smallest number of DALYs. In contrast, taking no action at the EU level (reference situation) would produce the largest number of DALYs, followed by the options of voluntary agreements and mandatory labeling.

To compare the policy options, the difference in costs and DALYs of policy options 2–4 compared with the reference situation (option 1) were calculated and are presented in **Table 4**. These calculations were based on deterministic analyses and were carried out for the base case and the 3 alternative scenarios in which different initial population iTFA intakes were assumed. In addition, the incremental cost-effectiveness ratios (ICERs) for each of the 3 EU-level action policy options are presented in Table 4. The ICER is calculated by dividing the difference in costs between a policy option and the reference situation (no EU-level action) by the respective difference in effects (DALYs); the ICER is then interpreted as the cost for each DALY gained and therefore a lower ICER is preferred.

$$\text{ICER} = \frac{\text{Costs in policy option } x - \text{Costs in reference situation}}{\text{DALYs in policy option } x - \text{DALYs in reference situation}} \quad (1)$$

A policy option is considered dominant if it can save both costs and DALYs when compared with the reference situation. This is the case for the legal TFA limits and voluntary agreements policy options for the base case and in every scenario considered for our model (Table 4). The legal limit option was found to deliver the highest health benefits and largest cost savings of all EU-level policy options, which remained true in all initial TFA intake scenarios. According to the WHO definition (35), a cost-effective option is that in which the cost-effectiveness ratio is <3 times the Gross Domestic Product (GDP) per capita. Highly cost-effective options are those in which the cost-effectiveness ratio is <1 time the GDP per capita. In the case of the EU, this latter threshold corresponding to the per capita GDP is €23,300. In our evaluation, the mandatory labeling strategy would not be considered cost-effective for the base case or for scenario 1 (lower initial iTFA intakes than in the base case) due to an ICER well above €23,300 and €69,900 (3 times the per capita GDP), whereas this strategy may be cost-effective in cases in which initial iTFA intakes are still relatively high, resulting in an ICER below the threshold (scenarios 2 and 3, assuming higher initial iTFA intakes than in the base case).

Because of the uncertainty associated with the wide distribution of some of the model variable values and data (as described in Table 1), we performed a PSA. Using the model, the analysis was repeated 1000 times, and for each time a random value within the range of values defined in the probability

TABLE 3

Costs and DALYs associated with 4 policy options to reduce TFA intake in the EU (for the base case)¹

	Both sexes		Women		Men	
	Costs (× 1 million), €	DALYs (× 1 million)	Costs (× 1 million), €	DALYs (× 1 million)	Costs (× 1 million), €	DALYs (× 1 million)
No action	10,774,890	1077	5,464,667	341	5,310,223	735
Voluntary agreements	10,752,032	1075	5,453,164	341	5,298,867	733
Mandatory labeling	10,870,004	1076	5,513,480	341	5,356,524	734
Legal limit	10,723,635	1073	5,438,734	340	5,284,900	732

¹ Values are the result of a deterministic analysis for the full time horizon of the model (85 y) and were calculated by using age and sex specifications. Although costs were similar for men and women, the number of DALYs is nearly double for men. This stems from a difference in ischemic heart disease-related mortality (higher in men), which is reflected in the calculation of DALYs only. DALY, disability-adjusted life-year; EU, European Union; TFA, *trans* fatty acid.

TABLE 4

Comparison of the differences in costs and DALYs between the 3 different EU-level action policy options and the reference situation of not acting at the EU level for the base case and the 3 scenarios (deterministic analysis)¹

	Base case		Scenario 1		Scenario 2		Scenario 3	
	Δ Costs (\times million), €	Δ DALYs (\times million)	Δ Costs (\times million), €	Δ DALYs (\times million)	Δ Costs (\times million), €	Δ DALYs (\times million)	Δ Costs (\times million), €	Δ DALYs (\times million)
Legal limit vs. no EU action	-51,255	-3.73	-10,686	-1.26	-129,684	-8.59	-279,241	-16.65
Voluntary agreements vs. no EU action	-22,858	-2.19	-2478	-0.75	-70,815	-5.15	-157,017	-10.03
Mandatory labeling vs. no EU action	95,114	-0.98	104,046	-0.42	66,159	-2.90	18,553	-5.62
ICER								
Legal limit	Dominant		Dominant		Dominant		Dominant	
Voluntary agreements	Dominant		Dominant		Dominant		Dominant	
Mandatory labeling	-96,608		-244,913		-22,840		-3301	

¹ Values are the result of a deterministic analysis for the full time horizon of the model (85 y). Negative numbers express costs saved and DALYs averted when compared with the reference situation. The absolute value of the ICER (calculated by dividing “ Δ Costs” and “ Δ DALYs”) represents the cost to the public for each DALY averted for a policy option against the reference of not acting at the EU level. A “dominant” ICER indicates that the policy option in question averts DALYs and saves money. DALY, disability-adjusted life-year; EU, European Union; ICER, incremental cost-effectiveness ratio; Δ Costs, differences in costs; Δ DALYs, difference in DALYs.

distribution (see Table 1) was used for every input variable. Costs and DALYs were calculated as outcomes for each individual analysis. Importantly, the results obtained with the PSA were similar to those obtained in the deterministic analysis, as shown in **Table 5**. This indicates that variations in the values within the ranges considered do not result in any significant differences in the outcomes of the model. **Table 6** shows the number of times (percentage) in the 1000 outcomes that each policy option was more or less effective than the reference situation. The fact that this sensitivity analysis returns such high (nearly 100%) or low (0%) probabilities reinforces the consistency of our model and the strength of the previous results. **Figure 2** depicts the cost-effectiveness plane of the PSA for the base case scenario.

The estimates confirmed that legal limit and voluntary agreements are the policy options in which more costs are saved and more DALYs are avoided than in the reference situation. These results are robust because the probability of saving costs and DALYs in the PSA is 100%. In the base case scenario,

mandatory labeling does not appear to save costs but would also avoid DALYs in 100% of the trials.

Overall, the estimates in Table 5 indicate that imposing legal limits on the iTFA content in foods could save \sim €76 billion and avoid 5.32 million DALYs over an 85-y period compared with the current situation, with a 100% of probability of being cost-effective. The similarity between the direction of the results obtained in the PSA and the deterministic analyses highlights the robustness of the model, although values in the PSA are higher than in the deterministic analysis. Both show that the 3 alternative EU-level action policy options are more effective than the reference situation of not acting at the EU level. As in the deterministic analysis, the PSA confirms that legal limits and voluntary agreements strategies are dominant (i.e., they provide health benefits and save costs), whereas mandatory labeling is highly cost-effective (in terms of GDP per capita threshold) only in scenarios 2 and 3, assuming higher (0.45 and 0.7 E%) than base case estimated initial iTFA intakes.

TABLE 5

Comparison of the mean of the differences in costs and DALYs between the 3 different EU-level action policy options and the reference situation of not acting at the EU level for the base case and 3 scenarios (probabilistic sensitivity analysis)¹

	Base case		Scenario 1		Scenario 2		Scenario 3	
	Δ Costs (\times million), €	Δ DALYs (\times million)	Δ Costs (\times million), €	Δ DALYs (\times million)	Δ Costs (\times million), €	Δ DALYs (\times million)	Δ Costs (\times million), €	Δ DALYs (\times million)
Legal limit vs. no EU action	-76,478	-5.32	-9,127	-1.13	-144,010	-9.65	-273,864	-16.67
Voluntary agreements vs. no EU action	-35,603	-2.93	-1684	-0.68	-79,067	-5.79	-153,857	-10.04
Mandatory labeling vs. no EU action	89,153	-1.39	104,736	-0.38	59,942	-3.25	20,144	-5.63
ICER								
Legal limit	Dominant		Dominant		Dominant		Dominant	
Voluntary agreements	Dominant		Dominant		Dominant		Dominant	
Mandatory labeling	-64,363		-274,163		-18,433		-3580	

¹ Values are the means of 1000 outcomes in a probabilistic sensitivity analysis for the full time horizon of the model (85 y). Negative numbers express savings when compared with the reference situation. The absolute value of the ICER (calculated by dividing “ Δ Costs” and “ Δ DALYs”) represents the cost to the public for each DALY averted for a policy option against the reference of not acting at the EU level. A “dominant” ICER indicates that the policy option in question averts DALYs and saves money. DALY, disability-adjusted life-year; EU, European Union; ICER, incremental cost-effectiveness ratio; Δ Costs, differences in costs; Δ DALYs, difference in DALYs.

TABLE 6
Probabilities of each EU-level action policy option to save costs and DALYs when compared with the reference situation in the base case and 3 scenarios¹

No EU action compared with	Base case, %		Scenario 1, %		Scenario 2, %		Scenario 3, %	
	Probability of saving costs	Probability of saving DALYs	Probability of saving costs	Probability of saving DALYs	Probability of saving costs	Probability of saving DALYs	Probability of saving costs	Probability of saving DALYs
Voluntary agreements	100	100	90.6	100	100	100	100	100
Mandatory labeling	0	100	0	100	0	100	0	100
Legal limit	100	100	100	100	100	100	100	100

¹ Values refer to the probabilistic sensitivity analysis for the full time horizon of the model (85 y). DALY, disability-adjusted life-year; EU, European Union.

DISCUSSION

The results of the model indicate that both introducing an EU-level legal limit and making voluntary agreements would save money and provide additional health benefits (avoiding DALYs) compared with not taking action at the EU level. Note also that although our analysis is focused on the EU market, it is likely that any action at the EU level would also affect the presence of iTFAs in foods and iTFA intake in other non-EU countries.

Despite a variety of uncertainties associated with some of the data included in the model, the PSA suggests that these results are robust because both policy options are dominant (saving costs and DALYs) in 100% of the trials in the PSA and the CIs are quite narrow. The same occurred for every scenario tested, except for the voluntary agreements in scenario 1, which assumed the lowest initial population iTFA intake of only 0.15 E% (90.6% probability). Although important, the cost-effectiveness of a particular policy option is not the only variable to be considered by policy makers to implement new policies. For example, our model focused on public expenditure and did not contemplate any potential costs incurred by the industry or other players when limiting iTFA content in foods. This is common practice in public health economic evaluations (25). In addition, neither EU member states nor EU stakeholders have pinpointed costs related to removing partially hydrogenated oils (PHOs) from foods (22). This is probably linked to the gradual progress in the innovation

of PHO alternatives and the fact that the EU food industry has, over time, already removed PHOs from food products to a large extent (32).

Although our model applied a lifetime horizon (85 y) for calculating health effects and costs, others used shorter time horizons (15–18). The time horizon needs to be sufficiently long to reflect all important differences in costs or outcomes between the policy options under comparison (25). We decided that a lifetime time horizon was appropriate because the varying iTFA intakes linked to the 4 policy options led to differences in survival and benefits that persist throughout a person’s life.

Introducing mandatory TFA labeling at the EU level, regardless of the scenario analyzed, also has the potential to avert DALYs but not costs. In general, the differences in costs between the different policy options are driven by the costs related to the incidence of CAD. However, in cases in which the difference in CAD incidence between an alternative option and the reference situation is low, such as the case for mandatory TFA labeling, the leading costs then stem from the costs of the measures (school-based interventions, worksite interventions, mass media campaigns, physician counseling, and food inspection programs).

With regard to the differences in DALYs, these are mostly due to the number of CAD events and related premature deaths, as well as the number of years living with disability and the number of years lost because of premature death. Small resulting differences

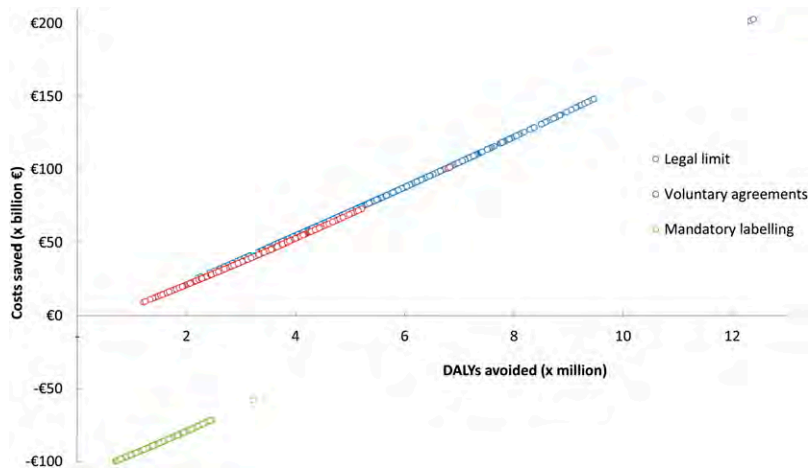


FIGURE 2 Cost-effectiveness plane. Costs saved against DALYs avoided for each EU-level action policy option against the reference of no EU-level action. The single colored circles represent the outcome of 1 single analysis in the probabilistic sensitivity analysis for each TFA-related EU-level policy option. Each set of colored circles therefore depicts the variation in costs saved against DALYs avoided as a result of the uncertainty in the model input variables. The cost-effectiveness plane is presented for the base case analysis, and values were calculated by using age and sex specifications for the full time horizon of the model (85 y). DALY, disability-adjusted life-year; EU, European Union; TFA, *trans* fatty acid.

in CAD are particularly likely in scenario 1, in which the lowest initial iTFA intakes are assumed.

In this study, we assumed a rather rapid removal of iTFAs from the EU food supply over 10 y, including in the reference situation in which no EU-level action is taken (we assumed efforts at the national level instead). This rather optimistic assumption for the reference situation means that we used a conservative approach in our conclusions on the EU-level action policy options. Health benefits would be even larger and cost savings more likely should iTFA intakes decrease more slowly than what is assumed in the reference situation in which no EU-level action is taken.

As discussed previously, some of the model variables or input data used here are rather uncertain and several assumptions had to be made. There are 3 major sources of potential errors: the estimated current TFA intake, the wide variability observed for many variables between countries, and the lack of data in some instances, such as the lack of data on the number of CAD events per year (CAD-related hospital discharges were used instead). To address the concerns related to the accuracy of estimated iTFA intake values entered in the model, we used different scenarios with different values for initial iTFA intake. In all of the scenarios and for all policy options it was assumed that, with time, iTFA intakes will eventually decrease to 0 E%. This seems reasonable given the current estimates of iTFA intakes of ~0.01 E% for Denmark, where a legal limit on iTFA contents of foods has been in place for 10 y (see Supplemental Tables 1 and 2 and reference 22). The wide variability in the data between European countries and the absence of reliable data on the incidence of CAD are addressed with the PSA. As discussed above, the robustness of the results obtained with the PSA indicates that, despite the uncertainties associated with the input data, the outcome is still valid and reliable. Again, however, we note that the absolute numbers estimated by the model are likely to overestimate the number of CAD events.

The results presented here should be interpreted as a comparison between different policy options rather than considering absolute costs, DALYs, or deaths per option. Previous work has shown the benefits of TFA intake reduction (18). Recently, the Food and Drug Administration also released a “final determination” that PHOs, the primary dietary source of iTFAs, are no longer considered to be “generally recognized as safe” products (36). This was accompanied by a memorandum that estimated costs and potential health effects of limiting iTFA content in foods in the United States (17). The authors indicated that “monetizing the lives saved, along with the value of the nonfatal illnesses and medical expenses prevented, yields an estimated benefit of \$14.7 billion/y, starting 3 y after the elimination of partially hydrogenated oils from the food supply.” Although the model used and the real costs and DALYs calculated in that memorandum differ considerably from those presented here, the conclusions are similar, namely that removing iTFAs from the US food supply would save costs and DALYs.

In conclusion, the results of this study suggest additional health benefits and reductions in public spending when taking EU-level action toward reducing population iTFA intakes. Although now introducing a mandatory TFA labeling scheme may not be a cost-effective solution in the EU, both a legal limit on the iTFA content in foods and voluntary agreements toward removing PHOs from foods produce large-enough reductions in CAD morbidity and

mortality that the related reductions in costs outweigh the costs linked to the implementation of these strategies. Finally, introducing a legal limit at the EU level would produce the greatest health benefits of all of the options included in this study.

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REFERENCES

1. European Food Safety Authority. Scientific opinion on dietary reference values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol. *EFSA J* 2010;8:1461–1567.
2. Willett WC, Stampfer M, Manson J, Colditz G, Speizer F, Rosner B, Sampson LA, Hennekens CH. Intake of trans fatty acids and risk of coronary heart disease among women. *Lancet* 1993;341:581–5.
3. Brouwer IA, Wanders A, Katan M. Trans fatty acids and cardiovascular health: research completed? *Eur J Clin Nutr* 2013;67:541–7.
4. Mozaffarian D, Aro A, Willett WC. Health effects of *trans*-fatty acids: experimental and observational evidence. *Eur J Clin Nutr*. 2009;63 Suppl 2:S5–21.
5. de Souza RJ, Mente A, Maroleanu A, Cozma AI, Ha V, Kishibe T, Uleryk E, Budylowski P, Schünemann H, Beyene J, et al. Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *BMJ* 2015;351:h3978–93.
6. European Food Safety Authority. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the presence of trans fatty acids in foods and the effect on human health of the consumption of trans fatty acids. *EFSA J* 2004;81:1–49.
7. World Health Organization. Diet, nutrition and the prevention of chronic diseases: report of a joint WHO/FAO expert consultation. *World Health Organ Tech Rep Ser* 2003;916:i–viii, 1–149, backcover.
8. L'Abbe MR, Stender S, Skeaff CM, Ghafoorunnisa TM. Approaches to removing trans fats from the food supply in industrialized and developing countries. *Eur J Clin Nutr* 2009;63(Suppl 2):S50–67.
9. Downs SM, Thow AM, Leeder SR. The effectiveness of policies for reducing dietary trans fat: a systematic review of the evidence. *Bull World Health Organ* 2013;91:262–9H.
10. Van Rossum C, Franssen H, Verkaik-Kloosterman J, Buurma-Rethans E, Ocké M. Dutch National Food Consumption Survey 2007–2010: diet of children and adults aged 7 to 69 years. Bilthoven (Netherlands): The Dutch National Institute for Public Health and the Environment (RIVM), 2011. RIVM report 350050006.
11. Hulshof KF, van Erp-Baart MA, Anttolainen M, Becker W, Church SM, Couet C, Hermann-Kunz E, Kesteloot H, Leth T, Martins I, et al. Intake of fatty acids in western Europe with emphasis on trans fatty acids: the TRANSFAIR study. *Eur J Clin Nutr* 1999;53:143–57.
12. Stender S, Astrup A, Dyerberg J. Artificial trans fat in popular foods in 2012 and in 2014: a market basket investigation in six European countries. *BMJ Open* 2016;6:e010673.
13. Stender S, Astrup A, Dyerberg J. Tracing artificial trans fat in popular foods in Europe: a market basket investigation. *BMJ Open* 2014;4:e005218.
14. Stender S, Astrup A, Dyerberg J. A trans European Union difference in the decline in trans fatty acids in popular foods: a market basket investigation. *BMJ Open* 2012;2:e000859.
15. O'Keeffe C, Kabir Z, O'Flaherty M, Walton J, Capewell S, Perry IJ. Modelling the impact of specific food policy options on coronary heart disease and stroke deaths in Ireland. *BMJ Open* 2013;3:e002837.

16. Barton P, Andronis L, Briggs A, McPherson K, Capewell S. Effectiveness and cost effectiveness of cardiovascular disease prevention in whole populations: modelling study. *BMJ* 2011;343:d4044.
17. US Department of Health and Human Services, Food and Drug Administration. Estimate of Costs and Benefits of Removing Partially Hydrogenated Oils (PHOs) from the US Food Supply. College Park, MD: US Food and Drug Administration. [memorandum from R. Bruns to M. Honigfort, June 11, 2015.]
18. O'Flaherty M, Flores-Mateo G, Nnoaham K, Lloyd-Williams F, Capewell S. Potential cardiovascular mortality reductions with stricter food policies in the United Kingdom of Great Britain and Northern Ireland. *Bull World Health Organ* 2012;90:522–31.
19. Restrepo BJ, Rieger M. Denmark's policy on artificial trans fat and cardiovascular disease. *Am J Prev Med* 2016;50:69–76.
20. Allen K, Pearson-Stuttard J, Hooton W, Diggle P, Capewell S, O'Flaherty M. Potential of trans fats policies to reduce socioeconomic inequalities in mortality from coronary heart disease in England: cost effectiveness modelling study. *BMJ* 2015;351:h4583.
21. European Commission. Report from the Commission to the European Parliament and Council regarding trans fats in foods and in the overall diet of the Union population. Brussels (Belgium): European Commission, 2015. [COM(2015) 619 final]
22. European Commission. Commission staff working document—results of the Commission's consultations on 'trans fatty acids in foodstuffs in Europe'. Brussels (Belgium): European Commission, 2015. [SWD(2015) 268 final]
23. Roberts M, Russell LB, Paltiel AD, Chambers M, McEwan P, Krahn M. Conceptualizing a model: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–2. *Value Health* 2012;15:804–11.
24. Siebert U, Alagoz O, Bayoumi AM, Jahn B, Owens DK, Cohen DJ, Kuntz KM; ISPOR-SMDM Modeling Good Research Practices Task Force. State-transition modeling: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–3. *Value Health* 2012;15:812–20.
25. Earnshaw J, Lewis G. NICE guide to the methods of technology appraisal. *Pharmacoeconomics* 2008;26:725–7.
26. Strazzullo P, Cairella G, Campanozzi A, Carcea M, Galeone D, Galletti F, Giampaoli S, Iacoviello L, Scafì L; GIRCIS Working Group. Population based strategy for dietary salt intake reduction: Italian initiatives in the European framework. *Nutr Metab Cardiovasc Dis* 2012;22:161–6.
27. European Health for All Database (HFA-DB) [Internet]. 2013. [cited 2013 June 10] Available from: <http://www.euro.who.int/en/what-we-do/data-and-evidence/databases/european-health-for-all-database-hfa-db2>.
28. Nichols MTN, Luengo-Fernandez R, Leal J, Gray A, Scarborough P, Rayner M. European Cardiovascular Disease Statistics 2012. Brussels (Belgium): European Heart Network, European Society of Cardiology; 2012.
29. Cecchini M, Sassi F, Lauer JA, Lee YY, Guajardo-Barron V, Chisholm D. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. *Lancet* 2010;376:1775–84.
30. Sassi F, Cecchini M, Lauer J, Chisholm D. Improving lifestyles, tackling obesity: the health and economic impact of prevention strategies. OECD Health working paper 48. OECD, Paris; 2009. [Internet] [cited 2013 June 10]. Available from: http://www.who.int/choice/publications/d_OECD_prevention_report.pdf
31. Briggs AH, Weinstein MC, Fenwick EA, Karnon J, Sculpher MJ, Paltiel AD. Model parameter estimation and uncertainty: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–6. *Value Health* 2012;15:835–42.
32. Mouratidou T, Livanidou A, Martin Saborido C, Wollgast J, Louro Caldeira S. Trans fatty acids in Europe: where do we stand? Luxembourg (Luxembourg): Publications Office of the European Union, 2014. [EUR 26795 EN]
33. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2197–223.
34. Micha R, Khatibzadeh S, Shi P, Fahimi S, Lim S, Andrews KG, Engell RE, Powles J, Ezzati M, Mozaffarian D; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCoDE). Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys. *BMJ* 2014;348:g2272.
35. World Health Organization. Choosing interventions that are cost effective (WHO-CHOICE). Cost-effectiveness threshold. Geneva (Switzerland): World Health Organization; 2005.
36. US Department of Health and Human Services, Food and Drug Administration. Final determination regarding partially hydrogenated oils. Federal Register. 2015;80:34650–34670.