



**World Health
Organization**

REGIONAL OFFICE FOR **Europe**

**Natural Experiments for
Evaluating Chronic Disease
Policy Interventions**

Natural Experiment Studies Project

**Helping to build capacity for high-quality
evaluations of public health interventions
for the prevention and control
of noncommunicable diseases**





Abstract

Natural experiments are events in which an observer or researcher does not have control of the event. Most public health interventions, such as the implementation of tobacco-control policies, can be considered natural experiments. The WHO Regional Office for Europe worked with a number of national ministries of health and their nominated research teams to develop natural experiment studies looking at national interventions for the prevention and control of noncommunicable diseases. Four studies reached completion and publication. Summaries of these studies are presented in this report, with discussion on the reasons some studies were not completed and description of lessons learned through the process.



Keywords

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Acronyms

CHD	coronary heart disease
CVD	cardiovascular disease
EU	European Union
GNAT	Grand National Assembly of Turkey
NCD	noncommunicable disease
OECD	Organisation for Economic Co-operation and Development
TCL	Tobacco Control Law (Russian Federation)
TFA	trans-fatty acid



Natural Experiment Studies Project: A SUMMARY¹

Natural Experiment Studies

Public health interventions, including those to prevent and control noncommunicable diseases, have traditionally suffered from a lack of high-quality and influential evaluation, making it difficult to build the case for investment and to learn about what works best to improve population health.

Natural experiments are events in which an observer or researcher does not have control of the event. Most public health interventions, such as the implementation of tobacco-control policies, can be considered natural experiments.

New epidemiological techniques to study natural experiments in a more rigorous and robust way are being developed. This project takes a pragmatic approach to using some of these techniques to help to build a culture and capacity for high-quality evaluation.

The studies in this series

The WHO Regional Office for Europe worked with a number of national ministries of health and their nominated research teams to develop natural experiment studies looking at national interventions for the prevention and control of NCDs. Four studies reached completion and publication:

- **Austria: impact on cardiovascular disease of the 2009 law regulating the trans-fatty acids content in foods;**
- **Romania: subnational variation in impact of the large tobacco tax increases in 2009 and 2010 to test for the influence of illicit tobacco trade;**
- **the Russian Federation: impact on cardiovascular disease of the comprehensive and large-scale tobacco-control law implemented in 2013; and**
- **Turkey: changes in political discourse associated with changes in the long-term trend of tobacco consumption between 1960 and 2016.**

¹ Adapted from the paper: Grabovac I, Hochfellner L, Rieger M, Jewell J, Snell A, Weber A et al. Impact of Austria's 2009 trans fatty acids regulation on all-cause, cardiovascular and coronary heart disease mortality. *Eur J Public Health* 2018;28(Suppl. 2):4–9. doi:10.1093/eurpub/cky147.



Natural Experiment Studies Project: **WHY AND HOW IT WAS DONE²**

The rationale

Fiscal, legislative and regulatory interventions comprise the main WHO recommended best buys for the prevention and control of noncommunicable diseases (NCDs). In the real world, only around one in 10 of these important interventions are ever evaluated, making them vulnerable to weak implementation without improvement cycles and liable to challenge from parties with vested interests.

They are not amenable to evaluation through conventional clinical trial methods, which sit high on the hierarchies of evidence. New epidemiological methods, however, evaluate policies as natural experiments that reshape approaches used in clinical trials, such as control or randomization, to fit real-world implementation.

The WHO Regional Office for Europe's Natural Experiment Studies Project is an exercise in deploying these methods to begin building a stronger culture of evaluation and capacity for a more influential evidence base for the control of NCDs.

The process

The Regional Office invited the ministries of health for Austria, Finland, Hungary, Norway, Romania, the Russian Federation, Turkey and Ukraine to send a public health research team to a workshop in Copenhagen in March 2017, at which the principles of natural experiment studies were presented. Teams at the workshop proposed an existing national policy on NCD control for evaluation and were supported to design a natural experiment study to evaluate it.

Feasible studies were taken from design to publication over the subsequent 18 months, with remote support from external and WHO experts and up to US\$ 5000 funding per team. Of the eight original studies proposed, covering the control of alcohol, tobacco and nutrition (salt, sugar and trans fats), four were completed. Summaries of these studies are presented in this report, with discussion on the reasons some studies were not completed and description of lessons learned through the process.

² Adapted from the paper: Snell A, Stuckler D, Reeves A, Rieger M, Galea G, Mauer-Stender K et al. WHO Regional Office for Europe's Natural Experiment Studies Project: an introduction to the series. *Eur J Public Health* 2018;28(Suppl. 2):1–3. doi:10.1093/eurpub/cky195.



Natural Experiment Studies Project: **THE STUDIES**

Austria's regulation of trans-fatty acid content in foods³

Background

Unhealthy diet, especially consumption of trans-fatty acids (TFAs), is a known risk factor for cardiovascular disease (CVD), which is a leading cause of death globally. WHO has recommended reducing the intake of TFA among children and adolescents to under 1% of total energy intake. In 2003, Denmark became the first country globally to introduce a trans-fat ban, setting limits for industrial TFA in the food supply (< 2 g TFA per 100 g total fat). Austria also introduced a law regulating TFAs in 2009. Prior to this, monitoring of the food supply showed that food products available on the Austrian market contained very high levels of TFA. This was particularly pronounced in margarines, convenience food products and fast foods, which contained on average 7.83%, 3.64% and 2.17% TFA/fatty acids, respectively. The aim of this study was to assess the impact of the Austrian TFA regulation on CVD-related outcomes.

Methods

This study evaluated the TFA regulation as an intervention in a natural experiment. Two study periods were assessed: pre-intervention (1995–2009) and post-intervention (2010–2014). The study compared the age-standardized death rates per 100 000 population for CVD outcomes (all-cause mortality, CVD mortality and coronary heart disease (CHD) mortality rates) in Austria with those of a so-called synthetic control.

The control population was created from data of Organisation for Economic Co-operation and Development (OECD) countries in which TFA regulation has not been implemented, but where the population is comparable. As tobacco is a major risk factor and potential confounder, sensitivity analysis was used to assess its influence by excluding OECD countries with full implementation of bans on smoking in public places.

³ Adapted from the paper: Grabovac I, Hochfellner L, Rieger M, Jewell J, Snell A, Weber A et al. Impact of Austria's 2009 trans fatty acids regulation on all-cause, cardiovascular and coronary heart disease mortality. *Eur J Public Health* 2018;28(Suppl. 2):4–9. doi:10.1093/eurpub/cky147.

Results

There was a remarkable and significant decrease of TFA contents in total, as well as in vegetable fats, margarines, vegetable oils and fine bakery products, following implementation of the 2009 TFA regulation in Austria.

The pre-intervention trend for all-cause, CVD and CHD mortality in the synthetic control tracked that of Austria closely, providing a good comparison group. There was a continuous decrease in CVD-related mortality throughout the study period in both the synthetic control population and the Austrian population, with no significant change in the trend observed as an effect of TFA regulation.

Implications

While the results are counterintuitive, given the established link between TFA consumption and increased risk of CVD, there are many possible explanations for the findings: concurrent high prevalence of tobacco-smoking; changes in comparator countries' TFA content in foods due to international guidance, rather than formal regulation; and the beneficial impact of TFA regulation on subgroups of the population that might not be detected with nationally aggregated data.

TFA should continue to be considered an important intervention for preventing and controlling CVD and other NCDs, but this study might support the idea that it should be a part of a wider programme of control rather than a single intervention. Wider control should include more comprehensive approaches to reducing unhealthy diet, tobacco use, physical inactivity and other key risk factors.



Natural Experiment Studies Project: **THE STUDIES**

Romania's brief period of intensive tobacco excise tax hikes⁴

Background

Tobacco is the leading preventable cause of death globally. Tobacco taxation that results in an increase in the price of tobacco products for the consumer is a cost-effective method of reducing tobacco use in countries and increasing revenue. The tobacco industry and the research it funds, however, suggest that rather than having any benefit, taxation results in an increase in illicit tobacco trade, including smuggling cheap tobacco. There is also debate around whether taxation alone is enough to produce a beneficial impact on public health.

Romania sharply increased its tobacco excise taxes in 2009 (by 28%) and 2010 (16%). Consequently, consumers paid 52% more for a pack of cigarettes in 2010 than in 2009, and 17% more in 2011 than in 2010. Annual increases in excise tax since 2011 have been less than 5%.

The study tested subnational variations in the health impact of these sharp tobacco tax increases to establish if regions that are prone to cigarette smuggling realize less benefits.

Methods

This is a pragmatic natural experiment study of the period 2009–2015. Findings from data of adult hospital episodes relating to seven smoking-attributable conditions – ischaemic heart disease, stroke, chronic obstructive pulmonary disease, asthma, tuberculosis, lung cancer and all other cancers – were analysed nationally and compared across six regional subgroups:

- a central region with no border countries, where smuggling has been reported to be low;
- three regions that border countries not in the European Union (EU), where cigarette prices are around four times cheaper than in Romania; and
- two regions that border EU countries and which have tighter tobacco regulations more akin to those in Romania.

⁴ Adapted from the paper: Cucu A, Ciobanu M, Iosif I, Calomfirescu C, Brinduse L, Stuckler D et al. Variation across Romania in the health impact of increasing tobacco taxation. *Eur J Public Health* 2018;28(Suppl. 2):10–3. doi:10.1093/eurpub/cky180.

Results

Hospitalization rates for the seven smoking-attributable diseases combined decreased nationally overall during the study period. When considering the diseases separately, however, the only statistically significant decline was seen in asthma.

Using a regression panel model, no statistically significant correlation was found in year-on-year changes in the mean rates of hospitalizations between any of the regional groups – bordering versus central, and EU border versus non-EU border.

The general decline in all diseases combined appears to be steeper in the period covering the tax increases between 2009 and 2011. When looking across the seven diseases separately, this is most prominent in asthma, ischaemic heart disease, stroke and tuberculosis.

Implications

The study has several limitations. The study period was short, which prohibits a rigorous pre-intervention trend analysis, and it is unable to account for the varied and asymmetrical relationships between tax increases, the impact on smoking prevalence, and the impact on smoking-related hospitalizations, which are difficult to account for when using ecological data.

This is nevertheless a timely and important study that contributes to the evidence base from which Romania and other national governments can support tobacco taxes and stand firm against tobacco industry counterarguments of illicit trade.

To strengthen tobacco control and public health, more comprehensive and progressive tobacco control should be implemented in Romania in line with the WHO Framework Convention on Tobacco Control.



Natural Experiment Studies Project: **THE STUDIES**

The Russian Federation's comprehensive and widespread tobacco control law⁵

Background

The Global Adult Tobacco Survey carried out in the Russian Federation in 2009 showed that the country had one of the highest smoking prevalence rates in Europe, with 39.1% of adults smoking tobacco (60.2% of men and 21.7% of women). In response to this health and economic burden, the country adopted a tobacco-control policy in 2010 and implemented the Tobacco Control Law (TCL) in 2013.

The TCL is recognized as a comprehensive law that has been well enforced across the Russian Federation. It includes: a total ban on smoking in indoor and outdoor public places, facilities and workplaces; annual increases in excise tax; comprehensive tobacco advertising, promotion and sponsorship bans; text and pictorial warnings on tobacco packages; smoking cessation support; and information campaigns. Its introduction has been associated with a 21.5% relative decline in adult smoking prevalence between 2009 and 2016. The study aimed to look beyond evaluation of implementation and consumption rates to test the impact of the TCL on health outcomes, specifically in relation to CVD.

Methods

The study evaluated the 2013 TCL as an intervention in a natural experiment exploring the period 2003–2015. The outcomes studied were hospital discharge rates and standardized death rates for circulatory diseases and ischaemic heart disease. A synthetic control was created as a comparator, using data from countries that did not have a comparable comprehensive tobacco-control intervention but had adequate available data: 21 countries were included in the hospital discharge rates analysis and 13 in that for standardized death rates. Changes in trends in CVD outcomes were then compared to test for comparable pre-intervention trends and any divergence associated with TCL implementation that might indicate an associated impact.

⁵ Adapted from the paper: Gambaryan M, Reeves A, Deev A, Popovich M, Drapkina O, Boytsov S et al. Effects of tobacco control policy on cardiovascular morbidity and mortality in Russia. *Eur J Public Health* 2018;2(Suppl. 2): 14–6. doi:10.1093/eurpub/cky148.

Results

The trends in hospital discharge rates were similar in the Russian Federation and the synthetic control during the pre-TCL period, suggesting a good degree of comparability. From around 2012, the trend was for lower hospital discharge rates in the Russian Federation compared with the synthetic control. After TCL implementation in 2013, the curves become divergent, implying a beneficial impact on CVD in the Russian Federation compared with the synthetic control. When other predictors of hospital discharge rates for circulatory diseases were included in the analysis, such as smoking prevalence and number of hospital beds, the beneficial relationship was maintained.

There was a steady decline in standardized death rates in both groups over the study period, but with no clear differences between groups associated with the TCL. Standardized death rates were slightly lower for circulatory diseases in the periods just before and after the TCL in the synthetic control. They seemed to decline slightly faster for ischaemic heart disease after the TCL had been introduced, but the relationship between the TCL and standardized death rates is not clear and should not be considered as significant, as it was observed to be with hospital discharge rates.

Implications

While study limitations make it impossible to fully attribute the CVD-related benefits to the TCL, the study provides further evidence to support comprehensive tobacco control in line with the WHO Framework Convention on Tobacco Control. Alongside a reduction in tobacco consumption, smoking-related CVD morbidity appeared to benefit quite quickly after implementation, while smoking-related deaths may need a longer post-intervention period to be detectable. This makes intuitive sense, as disease and its severity might reasonably be expected to benefit more quickly than deaths in most cases of risk-factor reduction. The study also usefully exploits an unusual opportunity in the evaluation of NCD control: the Russian Federation's TCL presents a comprehensive, large-scale and discrete intervention, rather than the iterative approach often taken in other public health settings.



Natural Experiment Studies Project: **THE STUDIES**

Turkey's political discourse through a long and varied history of tobacco control⁶

Background

Tobacco use is a leading but preventable cause of NCDs and premature death. The legislature has a key role in setting tobacco-control policies. Smoking trends have seen some reductions associated with the introduction of effective tobacco-control policies in Turkey, but progress has not been consistent. The policies may have been shaped by how politicians interpreted social problems that were prominent during the development and implementation of tobacco regulations.

The aim of this study was to explore the long-term national relationship between tobacco consumption, tobacco-control policies and the associated political discourse in Turkey between 1960 and 2016. The study considered varying influences through national leadership on this important public health agenda.

Methods

The study compared a time-series analysis of tobacco consumption trends with a policy analysis of the minutes of deliberations at the Grand National Assembly of Turkey (GNAT), which is the Turkish parliament and unicameral Turkish legislature. It used Bayesian time-series analysis to investigate whether tobacco-control policies and related activities influenced the annual per adult cigarette consumption in Turkey. A novel method was used to identify change points in tobacco trends and whether they correspond with key policy changes intended to alter usage after adjusting for the effect of other non-policy related covariates, such as purchasing power. The policy analysis included an examination of the minutes of deliberations at the GNAT one year before and one year after the break years associated with an increase or decrease in tobacco consumption.

⁶ Adapted from the paper: Ozcebe H, Erguder T, Balcilar M, Ursu P, Reeves A, Stuckler D et al. The perspectives of politicians on tobacco control in Turkey. *Eur J Public Health* 2018;2(Suppl. 2):17–21. doi:10.1093/eurpub/cky152.

Results

Tobacco consumption increased with the encouragement of tobacco production and the entrance of multinational companies to the country in 1976 and 1993, respectively. The National Tobacco Law of 1996 and comprehensive amendments in 2008, including smoke-free public places and tax increases, appear to have helped reduce tobacco consumption in Turkey. The focus of parliamentary discussions throughout the period changed, becoming less supportive of tobacco over time, but discussions focusing on concerns about the implications for the economy and the privatization agenda, national agriculture and the welfare of farmers continued throughout the period.

Implications

Effective control appears to require certain political ingredients: politicians who are well informed on tobacco-control measures and understand the range of issues surrounding the policies (not only those that are directly health-related); and supportive public health information in the community. Evidence-based public health policy should be introduced to the politicians.

The study was limited in its exploration of causal mechanisms and the discourse is only of official political records, but it presents a useful insight into political motivations and portrays an elegant use of two methodologies to contextualize the time-series analysis.



Natural Experiment Studies Project:

WHAT HAS BEEN LEARNED FOR THE NEXT TIME⁷

The challenges

A variety of reasons explain why some of the original eight studies did not reach completion, including:

- tension between policy priorities and interventions amenable to evaluation;
- involvement of small teams that were not resilient to reduction in the capacity of their members;
- barriers to learning new techniques, including time capacity, language and baseline expertise; and
- a lack of consistent data that covered a sufficient period and confounding factors.

Two recurring challenges for teams were understanding the concept of a control in this context, and identifying data to track intervention and *control*.

Despite these challenges, the project was a valuable exercise in creating important studies evaluating public health interventions for NCD control, and in helping to build a culture of, and capacity for, high-quality evaluations moving forward.

The learning

There are three major learning points from this exercise that should be acknowledged if it were to be replicated.

1. Creating a better understanding of the work involved, greater capacity within teams, more accessible expert support and a clearer opening brief for teams would help to ensure study progress and completion.
2. Establishing a forum for capacity-pooling between teams, shared learning and reviewing each other's work would improve the process, team resilience and study quality.
3. Before inviting teams to an intensive face-to-face workshop, they should be remotely supported to select an intervention, prepare a study design and identify relevant data sources, so they can learn to apply some novel techniques through the workshop.

Ultimately, natural experiment studies should be planned ahead of policy implementation. To help shift cultures towards this, the Natural Experiment Studies Project should be reiterated, incorporating these and future lessons.

⁷ Adapted from the paper: Snell A, Stuckler D, Reeves A, Rieger M, Galea G, Mauer-Stender K et al. WHO Regional Office for Europe's Natural Experiment Studies Project: an introduction to the series. *Eur J Public Health* 2018;28(Suppl. 2):1–3. doi:10.1093/eurpub/cky195.

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