

Estimates of costs for modelling return on investment from smoking cessation interventions

Marta Trapero-Bertran^{1,2}, Reiner Leidl^{3,4}, Celia Muñoz¹, Puttarin Kulchaitanaroaj⁵, Kathryn Coyle^{5,6}, Maximilian Präger³, Judit Józwiak-Hagymásy⁷, Kei Long Cheung⁸, Mickael Hiligsmann⁸, Subhash Pokhrel⁵ & on behalf of the EQUIPT Study Group

Centre of Research in Economics and Health (CRES-UPF) University Pompeu Fabra, Barcelona, Spain,¹ Faculty of Economics and Social Sciences, Universitat Internacional de Catalunya (UIC), Barcelona, Spain,² Institute of Health Economics and Health Care Management, Helmholtz Zentrum München (GmbH) - German Research Center for Environmental Health, Comprehensive Pneumology Center Munich (CPC-M), Member of the German Center for Lung Research (DZL), Neuherberg, Germany,³ Munich Center of Health Sciences, Ludwig-Maximilians-University, Munich, Germany,⁴ Health Economics Research Group, Institute of Environment, Health and Societies, Brunel University London, Uxbridge, UK,⁵ Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Canada,⁶ Faculty of Social Sciences, Department of Health Policy and Health Economics, Eötvös Loránd University, and Syreon Research Institute, Budapest, Hungary⁷ and CAPHRI Care and Public Health Research Institute, Department of Health Services Research, Maastricht University, Maastricht, the Netherlands⁸

ABSTRACT

Background and aims Modelling return on investment (ROI) from smoking cessation interventions requires estimates of their costs and benefits. This paper describes a standardized method developed to source both economic costs of tobacco smoking and costs of implementing cessation interventions for a Europe-wide ROI model [European study on Quantifying Utility of Investment in Protection from Tobacco model (EQUIPTMOD)]. **Design** Focused search of administrative and published data. A standardized checklist was developed in order to ensure consistency in methods of data collection. **Setting and participants** Adult population (15+ years) in Hungary, Netherlands, Germany, Spain and England. For passive smoking-related costs, child population (0–15 years) was also included. **Measurements** Costs of treating smoking-attributable diseases; productivity losses due to smoking-attributable absenteeism; and costs of implementing smoking cessation interventions. **Findings** Annual costs (per case) of treating smoking attributable lung cancer were between €5074 (Hungary) and €52 106 (Germany); coronary heart disease between €1521 (Spain) and €3955 (Netherlands); chronic obstructive pulmonary disease between €1280 (England) and €4199 (Spain); stroke between €1829 (Hungary) and €14 880 (Netherlands). Costs (per recipient) of smoking cessation medications were estimated to be: for standard duration of varenicline between €225 (England) and €465 (Hungary); for bupropion between €25 (Hungary) and €220 (Germany). Costs (per recipient) of providing behavioural support were also wide-ranging: one-to-one behavioural support between €34 (Hungary) and €474 (Netherlands); and group-based behavioural support between €12 (Hungary) and €257 (Germany). The costs (per recipient) of delivering brief physician advice were: €24 (England); €9 (Germany); €4 (Hungary); €33 (Netherlands); and €27 (Spain). **Conclusions** Costs of treating smoking-attributable diseases as well as the costs of implementing smoking cessation interventions vary substantially across Hungary, Netherlands, Germany, Spain and England. Estimates for the costs of these diseases and interventions can contribute to return on investment estimates in support of national or regional policy decisions.

Keywords Cost, EQUIPT, modelling, return on investment, smoking cessation, tobacco.

Correspondence to: Marta Trapero Bertran, Universitat Internacional de Catalunya (UIC), Faculty of Economics and Social Sciences, c/Immaculada 22, 08017 Barcelona, Spain. E-mail: mtrapero@uic.es

Submitted 20 June 2017; initial review completed 20 July 2017; final version accepted 2 November 2017

INTRODUCTION

Tobacco smoking imposes economic costs on society, as more resources need to be committed to treating smoking-attributable diseases [1]. In addition, smoking

causes people to lose time from their regular activities and results in premature deaths [2]. Determining the economic burden of smoking, both in terms of direct health-care costs and the value of lost time and premature deaths, can help to make the case for investment.

However, further modelling would be required to show how to invest. In model-based economic evaluations, the life-time benefits of tobacco cessation interventions are compared against the total costs (in this case the economic burden/costs plus the cost of implementing services) to show which intervention(s) provide good value for money [3].

Modelling the return on investment (ROI) from tobacco cessation interventions therefore requires estimates of their costs and benefits. The economic costs of smoking have been estimated in several countries [4–6]. Similarly, costs of implementing tobacco cessation services are also available for different countries [7–9]. These costs are often estimates based on the availability of data and resources at the time such studies are conducted, and therefore are likely to vary across studies and between contexts [3]. For a ROI model that works for several countries, a standardized method to source and/or estimate costs (both economic costs of tobacco and costs of implementing interventions) is required. In this paper, we describe the standardized methods used to develop a Europe-wide ROI model for tobacco control [European study on Quantifying Utility of Investment in Protection from Tobacco model (EQUIPTMOD)] and present summary findings [10]. The countries included in this study were: England, Germany, Hungary, Netherlands and Spain.

METHODS

Development of standardized framework

The EQUIPTMOD requires both local population and smoking prevalence data in combination with intervention-related input estimates (i.e. effectiveness, reach and costs) [10]. The National Institute for Health and Care Excellence (NICE) tobacco ROI tool, developed by NICE in the United Kingdom, served as a starting-point to identify different types of costs [11]. To obtain the best available cost estimates, a focused search of administrative and published data was carried out. The available data and their sources were subject to a standardized checklist (Supporting information, Appendix S1) to ensure that all relevant attributes were captured uniformly across the countries in evaluating their relevance to the ROI modelling. Data collection took place in 2014/15 in the five countries. The standardized checklist also ensured that countries reported technical details and sources of the data explicitly and in a transparent manner, including any deviation from the agreed core framework used for data collection. The checklist was informed by best reporting guidelines advocated by major journals for reporting economic evaluation studies [12–14].

Identification of cost estimates

Guided by the methods used in EQUIPTMOD for modelling ROI from tobacco control interventions [10], coupled with data requirements listed in an earlier version of the model [11], it was deemed necessary to collect estimates for the following cost-related model inputs: treatment costs [lung cancer, coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD) and stroke]; cost attributable to passive smoking separately for children [asthma, lower respiratory tract infection (LRTI) and acute otitis media (AOM)] and adults [asthma, lung cancer and ischaemia heart disease]; productivity losses [work days lost per smoker, average hourly wage, employment rates among smokers]; and costs of implementing interventions. This study was restricted to the four major smoking-attributable diseases as per the EQUIPTMOD requirements. The rationale for selecting these diseases has been provided by the model developers elsewhere [10].

Costing perspectives and year

In sourcing the data, a health-care system and a quasi-societal perspective that included exposure to passive smoking and productivity gains in the economy due to reduced smoking were adopted separately. Spain's costs were from the hospital (not the health-care system) perspective, as no data were available from a health-care perspective. This clearly underestimated the true health-care costs of treating smoking-attributable diseases in Spain. We could not ascertain the size of probable underestimation; nor were we able to adjust Spanish estimates using data from the other countries, as the price of health-care goods and services are very different in Spain compared to the other countries. All cost data reported in this article were inflated to 2016/7 prices (in €) using average consumer prices obtained from the World Economic Outlook Database 2015, although they were entered originally in the EQUIPTMOD as 2015/6 prices. To aid the comparative quantitative analysis, the mean unit and annual costs were converted to 2016/7 euros (€) using country-specific or country-group-specific inflation on average consumer prices [15]. The annual costs and mean unit values were adjusted by the interannual inflation rate from the price year to 2017. If required, the unit and annual costs from 2017 were multiplied by the European Central Bank's 2017 exchange rates. For papers not reporting the year in which the costs were calculated, the publication year was used.

Population

The costs included in the model were derived for the adult population older than 15 years until they reach a life expectancy of 100 years in the model. Only passive smoking

costs were considered for a child population younger than age 16 years.

Search strategy and inclusion criteria

Country-specific modellers completed focused searches on respective administrative portals or identified published sources in each country. The technical document on the NICE ROI tool [11] that sourced data following a comprehensive literature review provided guidance on the type of administrative data set or published literature that the countries needed to access first. In addition, countries carried out specific literature reviews and searches in national and international databases, and a generic Google search for completeness reasons using the following keywords: tobacco; smoking; cost*; <input name>. In addition, country-specific stakeholders that were collaborating with this project helped with sourcing data. If multiple data sources were found for a given input value, the specific country-modelling team evaluated those for their robustness and relevance as per the standardized checklist (Supporting information, Appendix S1). The country team's recommendation was considered final. The selected data and their sources were then documented in detail together with reasons for inclusion in a technical annex [16–20].

Consistency checks on included data and internal validation

A single individual (the principal modeller) incorporated all country-specific cost estimates into the model. This process streamlined any inconsistency observed across the countries. The spreadsheet was then sent back to the respective country team to double check. Input data were considered final once both the principal modeller and country teams agreed on the value and source of the cost estimates.

Obtaining cost of treating smoking-attributable diseases

The annual health-care direct costs stemming from using health care resources in patients who suffer from smoking-related diseases were obtained from official reports in Hungary and England [21,22]. In the Netherlands, official data on costs for lung cancer, CHD, stroke and COPD were available [23]. Costs of smoking-related diseases were obtained from the literature in Germany [24–27] and Spain [28–32]. Further details are found in country-specific technical annexes [16–20].

Obtaining costs of treating passive smoking-related diseases

For each country, the population-attributable fraction (PAF) to second-hand smoke, a model input to attribute costs to passive smoking, was sourced for three diseases

in adults: asthma (≥ 15 years), lung cancer (≥ 15 years) and ischaemia heart disease (≥ 15 years) [33] and three diseases in children: LRTI (≤ 4 years), AOM (≤ 3 years) and asthma (0–14 years). The total costs of each of these diseases were sourced from the respective administrative/published data relevant to those age groups, thereby allowing the cost of illness attributable to second-hand smoke exposure to be estimated for each included condition.

In the Netherlands, a cost of illness tool [23] was used to source the cost of respiratory infections and published literature was used to obtain costs of AOM [34]. In Spain, asthma total costs and average prevalence for the adult Spanish population were obtained from a published study [35]. For children, costs from AOM and LRTI were obtained from official diagnosis-related groups (DRG) data, taking into account only hospital costs. Asthma total costs were obtained from the published literature [36]. In Hungary, total costs due to passive smoking were obtained from an official report on Economic Burden of Smoking in Hungary [22]. In Germany, published data [37,38] were used to derive the total cost of passive smoking in adults, whereas passive smoking-related costs among children were sourced from published studies [34,38–42].

Estimating costs of pharmacological interventions

Prices of pharmacological interventions were estimated from drug cost and the cost of one consultation with a general practitioner. Intervention specifications such as medication dosage and duration described elsewhere [43] were utilized to estimate the total amount of medication for a course of smoking cessation treatment. Drug prices for each country were obtained from databases or official documents [42,44–47]. The final drug cost was estimated by multiplying the total amount of medication by the unit price of a medication package. An example of the application of this method using varenicline (standard duration) in England is provided in Supporting information, Appendix S2. Country-specific reports [16–20] explain the estimation for all pharmacological interventions. We assumed that a complete treatment course was given on a single prescription. This was guided by the need to obtain the cost estimate that would reflect full implementation of the intervention. However, it may be typical for general practitioners to prescribe medications on incremental basis (additional medication given only if necessary on repeat prescriptions, to save costs). Therefore, our cost estimates may be an overestimate of the actual costs in practice. However, for the purpose of return on investment modelling here, we assumed that a full course of treatment was necessary in order for the interventions to be as effective as in the original trials [43].

Estimating costs of behavioural interventions

Costs of behavioural interventions were taken from both National Health Service (NHS) reports and statistics in each country and through literature searches. The data obtained in England [48–51] were also used in Spain, as no country-specific evidence was available. In Germany, costs of one-to-one support were obtained based on an Association of Statutory Health Insurance Physicians report [52]; the remaining interventions were obtained from published sources [53,54]. Official databases were available in Hungary, where the costs of behavioural interventions were provided [46]. In the Netherlands, cost estimates of interventions were obtained from the guide for cost studies [55].

Deriving productivity costs

We derived the costs due to lost productivity according to the human capital approach using the following inputs: the percentage of smokers currently employed, the number of days absent from work in a given year and the average hourly wage in each country. In England, Germany, Hungary and Spain data on the number of days lost per smoker came from the published sources [56–59], whereas in the Netherlands, reports on health-care figures were available to derive the number of lost work-days [60]. Average hourly wage was obtained in all cases through search and analysis of national databases [61–64]. In the Netherlands, the hourly wage data were obtained from a guide for health-care cost studies and research [55]. The percentage of smokers who were currently employed were sourced from national statistics for England, Hungary, the Netherlands and Spain [61,65–67] while in Germany these data were sourced from a published study [68].

For details of the method used to source or estimate all cost components included in the ROI model, please refer to the country-specific technical annexes [16–20]. Data were presented in five tables: smoking-attributable disease average annual costs; passive smoking-attributable disease total annual costs; pharmacological interventions unit costs; behavioural support intervention unit costs; and

average values of the inputs used to estimate unit productivity costs.

RESULTS

A summary of the estimates of costs and their sources that were evaluated to be the ‘best available evidence’ required to populate the EQUIPTMOD are shown in Tables 1–5. Some country-level variation in the sources of cost data was inevitable.

Table 1 shows the average annual costs (per case) for the treatment of the four smoking-attributable diseases (LC, CHD, COPD and stroke) for England, Germany, Hungary, Netherlands and Spain. Treatment costs in the primary and secondary care settings are included in these estimates. As these conditions require long-term health-care (over several years or the life-time), the respective cost estimates are expressed as ‘annual’. Expressing these costs as annual estimates was also consistent with the EQUIPTMOD, as the model uses a yearly cycle. Annual costs (per case) of treating smoking-attributable lung cancer were between €5074 (Hungary) and €52 106 (Germany); coronary heart disease between €1521 (Spain) and €3955 (Netherlands); chronic obstructive pulmonary disease between €1280 (England) and €4199 (Spain); stroke between €1829 (Hungary); and €14 880 (Netherlands).

Table 2 shows annual total costs of treating diseases that could be related to passive smoking for the five countries. These costs are presented separately for adults and children. These costs are expressed as the ‘total’ annual costs (not average, unlike in Table 1), because EQUIPTMOD applies a fraction (PAF) to the total annual costs to calculate passive smoking-attributable costs [10]. The annual total costs of treating asthma, lung cancer and CHD in adults and AOM, LRTI and asthma in children varied across countries. Total annual costs of treating passive smoking-attributable asthma in children were between €1.3 million (Hungary) and €75.7 million (Germany); and in adults between €28.5 million (Netherlands) and €332 million (Spain).

Table 1 Annual costs (per case) of treating smoking-attributable diseases (€2016/2017).

	<i>England</i>		<i>Germany</i>		<i>Hungary</i>		<i>Netherlands</i>		<i>Spain</i>	
	<i>Average annual cost</i>	<i>source</i>	<i>Average annual cost</i>	<i>source</i>	<i>Average annual cost</i>	<i>source</i>	<i>Average annual cost</i>	<i>source</i>	<i>Average annual cost</i>	<i>source</i>
<i>Smoking attributable diseases</i>										
Lung cancer	8603.06	[21]	52105.74	[25]	5073.87	[22]	22471.87	[23]	16777.23	[28]
Coronary heart disease	1533.02	[21]	1598.64	[24]	1929.69	[22]	3954.69	[23]	1521.20	[29]
Chronic obstructive pulmonary disease	1279.97	[21]	3025.61	[26]	2315.57	[22]	1774.65	[69]	4199.08	[31]
Stroke	7233.57	[21]	9923.14	[27]	1829.00	[22]	14879.51	[23]	8472.68	[32]

Table 2 Annual total costs of treating diseases that are related to passive smoking (€2016/2017).

Diseases	England		Germany		Hungary		Netherlands		Spain	
	Total annual cost	source	Total annual cost	source	Total annual cost	source	Total annual cost	source	Total annual cost	source
Adults										
Asthma	122 508 406	[33]	87 909 503	[33]	78 685 012	[33]	28 539 644	[33]	332 075 581	[33]
Lung cancer	6 335 752	[33]	365 188 609	[33]	2 038 279	[33]	6 682 837	[33]	5 215 915	[33]
CHD	178 239 134	[33]	320 549 524	[33]	9 780 023	[33]	108 650 443	[33]	101 843 582	[33]
Children										
AOM	7 163 684	[33,70,71]	13 515 004	[34,41,42]	211 955	[33,46]	852 306	[33]	454 129	[33,73]
LRTI	24 949 648	[33,70,71]	48 456 735	[39]	1 127 167	[33,46]	4 257 001	[33]	14 160 608	[33,73]
Asthma	11 258 968	[33,70,71]	75,721 929	[37,38,40,42,70]	1 348 729	[33,46]	6 700 683	[33]	49 063 639	[33,36]

AOM = acute otitis media; LRTI = lower respiratory tract infection; CHD = coronary heart disease.

Table 3 shows the unit costs for implementing pharmacological interventions for the five countries included in the study. The unit costs are costs per recipient assuming a complete course of treatment. Costs (per recipient) of smoking cessation medications were estimated to be: for standard duration of varenicline between €225 (England) and €465 (Hungary); for bupropion between €25 (Hungary) and €220 (Germany).

Where an 'NA' (not applicable) appears in the table, the specific intervention did not apply to that particular country [10]. Differences in the unit costs of pharmacological interventions across countries show the different level of prices of medications existing in each of the countries included in this study (Table 3). The cost of over-the-counter mono nicotine replacement therapy (NRT) was assumed to be zero in England, as the EQUIPTMOD considered the NHS perspective in costing for England.

Table 4 shows unit costs (costs per recipient) for behavioural interventions for the five countries included in the study. Costs (per recipient) of providing behavioural support were also wide-ranging: one-to-one behavioural support between €34 (Hungary) and €474 (Netherlands); and group-based behavioural support between €12 (Hungary) and €257 (Germany). The costs (per recipient) of delivering brief physician advice were: €24 (England); €9 (Germany); €4 (Hungary); €33 (Netherlands); €27 (Spain).

In Spain, the unit cost data for behavioural interventions were not available and therefore data from England were assumed to reflect the approximate costs of providing those interventions there (Table 4). Only country-specific data regarding the behavioural interventions (printed self-help materials, one-to-one and group support) were available for Germany.

Table 5 shows the input values used to estimate productivity costs for all five countries included in the study. There was a wide variation across countries in terms of the work-days lost, with England reporting the lowest number of days lost (2.74 days) and Germany the highest (8.41 days). As expected, the wage rate also varied throughout the countries. Average numbers of work-days lost due to smoking were: 2.74 (England); 8.41 (Germany); 3.58 (Hungary); 6.60 (Netherlands); and 6.00 (Spain).

DISCUSSION

This paper describes a standardized method developed to source both the economic costs of tobacco and the costs of implementing interventions for a Europe-wide ROI model (EQUIPTMOD). The method helped us to improve consistency in sourcing cost data for a large-scale cross-country economic model. We hope that the detailed description on the standardized method presented in this

Table 3 Unit costs (costs per recipient) of pharmacological interventions (€2016/2017).

Pharmacological interventions	England		Germany		Hungary		Netherlands		Spain	
	Unit cost	Source*	Unit cost	Source*	Unit cost	Source*	Unit cost	Source*	Unit cost	Source*
Rx mono NRT	124.80	[44]	NA	NA	NA	NA	229.48	[55,72]	280.52	[73–75]
Rx combo NRT	230.96	[44]	NA	NA	NA	NA	482.61	[55,72]	562.49	[73–75]
Varenicline (standard duration)	225.06	[44]	300.84	[45]	465.25	[46]	332.11	[55,72]	302.80	[73–75]
Varenicline (extended duration)	417.15	[44]	NA	NA	NA	NA	624.47	[55,72]	617.40	[73–75]
Bupropion	93.78	[44]	220.21	[76]	25.16	[46]	179.24	[55,72]	153.55	[73–75]
Nortriptyline	98.59	[44]	NA	NA	NA	NA	87.53	[55,72]	NA	NA
Cytisine	19.69	[21]	NA	NA	NA	NA	NA	NA	NA	NA
OTC mono NRT	0,00	[77]	326.50	[45]	148.67	[78]	NA	NA	356.26	[75]
OTC combo NRT	n.a.	n.a.	573.20	[42]	NA	NA	NA	NA	NA	NA

*Direct or indirect source. Where indirect, the authors estimated the costs using inputs data available from this source. NRT = nicotine replacement therapy; OTC = over-the-counter; NA = not applicable.

Table 4 Unit costs (costs per recipient) of behavioural support interventions (€2016/2017).

Behavioural support interventions	England		Germany		Hungary		Netherlands		Spain	
	Unit cost	source	Unit cost	source	Unit cost	source	Unit cost	source	Unit cost	source
Specialist behavioural support: one-to-one	148.85	[79]	303.38	[80]	34.28	[46]	474.15	[55]	163.30	[79]
Specialist behavioural support: group-based	45.39	[79]	257.10	[53]	11.67	[46]	42.73	[55]	49.77	[79]
Telephone support: proactive	178.64	[77]	NA	NA	54.48	Expert opinion	121.34	[55]	207.84	[77]
SMS text messaging	20.23	[81]	17.37	[81]	NA	NA	23.92	[81]	23.23	[81]
Printed self-help materials	16.33	[82]	13.47	[54]	0.68	Expert opinion	1.22	[83]	17.86	[82]
Brief physician advice	24.41	[84]	9.42	[85]	4.12	[44]	33.48	[55]	26.84	[84]
Social marketing	1.44	[84]	1.62	[84]	NA	NA	1.62	[84]	1.58	[84]

SMS = short messaging service.

Table 5 Input values used to estimate productivity costs (€2016/2017).

Productivity costs	England		Germany		Hungary		Netherlands		Spain	
	Units	source	Units	source	Units	source	Units	source	Units	source
Work days lost	2.74 days	[56]	8.41 days	[57]	3.58 days	[58–63]	6.60 days	[60]	6.00 days	[59]
Wage per hour (unit costs)	13.78€/h	[61]	18.35€/h	[62]	4.93€/h	[63]	35.90€/h	[55]	14.97€/h	[67]

paper will serve as useful guidance for future similar work in this area.

One notable benefit of the standardized framework is that the checklist developed to critically assess the quality of the cost data has led to improved transparency and sufficiency in reporting of the data included in the economic model. A recently published systematic review [3] has highlighted how important transparency and sufficiency in reporting are for an economic model to be fully transferable to other settings. As noted in the systematic

review, it seemed very important to assess the quality of the cost data in terms of several key attributes: intervention technologies described; monetary reference used; time dimension; cost types; costing methods; perspective; and representativeness. Note that the interventions evaluated in this study have been described elsewhere [43].

Health-care costs were sourced from different studies for some countries (i.e. Germany, Spain). One advantage of the current study has been to identify this methodological heterogeneity between the sources of cost data. It is not

uncommon to estimate cost-of-illness using different approaches [86], but it is only when applying a standardized checklist that one could identify what causes the variation. The wage rates as well as the intensity of support were the cost drivers for the behavioural interventions. However, the most significant variation was observed for the annual average costs of treating the four smoking-attributable diseases. This variation was driven mainly by the differences in the prices of health-care goods and services across the countries. While it is normal for countries to vary in terms of health-care costs, showing this variation explicitly helps policymakers to understand more clearly the ROI estimates that would be produced by using such cost inputs.

Despite taking the NHS perspective, disease costs used in the model for Spain had to rely upon hospitalization costs only. Therefore, the treatment costs predicted by the EQUIPTMOD for Spain are underestimates. This highlights the lack of data related to smoking-attributable health-care costs in some countries in Europe, particularly from an NHS perspective. Future cost-of-illness studies in those countries should focus upon collecting data from the NHS and wider perspectives.

Some countries lacked specific cost data (e.g. on behavioural support interventions in Spain) required by the ROI model. Upon careful evaluation by the country teams, the available English data were used in those cases, assuming that they would be representative of the population in the country in question. This remains an important limitation of our standardized methods and can only be validated once such data become available in those countries. When countries begin to consider collection of such data in the future, it would be helpful to evaluate different methodological options, e.g. micro-costing in which intervention costs are built up based on cost ingredients or observational costings where actual resource use is tracked alongside a clinical trial. In Spain, for example, there have been some initiatives to develop costing guidelines for different diseases [87,88] and our findings may offer some useful insights to those initiatives as they advance.

CONCLUSION

The costs of treating smoking-attributable diseases as well as the costs of implementing smoking cessation interventions vary substantially across the five study countries. Estimates for the costs of these diseases and interventions can contribute to return on investment estimates in support of national or regional policy decisions.

Ethical approval

None required for this analysis. However, the EQUIPTstudy, on which the current analysis is based, received full

ethical clearance from Brunel University Research Ethics Committee.

Declaration of interests

None.

Acknowledgements

The authors are grateful to the EQUIPT team members for their substantive inputs in validating the cost data reported in this paper. We have received funding from the European Community's Seventh Framework Programme (The EQUIPT Project; grant agreement 602270). The funders had no influence in the conduction of this study or the drafting of this manuscript.

References

1. World Health Organization (WHO). *WHO Report on the Global Tobacco Epidemic*. Spain: Country Profile; 2015 Available at: http://www.who.int/tobacco/surveillance/policy/country_profile/esp.pdf?ua=1 (accessed 15 December 2016).
2. Ekpu V. U., Brown A. K. The economic impact of smoking and of reducing smoking prevalence: review of evidence. *Tob Use Insights* 2015; **14**: 1–35.
3. Berg M. L., Cheung K. L., Hilgsmann M., Evers S., de Kinderen R. J. A., Kulchaitanaroaj P., et al. Model-based economic evaluations in smoking cessation and their transferability to new contexts: a systematic review. *Addiction* 2017; **112**: 946–67.
4. Collins D. J., Lapsley H. M., University of New South Wales *The Costs of Tobacco, Alcohol and Illicit Drug Abuse to Australian Society in 2004/05*. Canberra, Australia: Department of Health and Ageing; 2008.
5. Neubauer S., Welte R., Beiche A., Koenig H. H., Buesch K., Leidl R. Mortality, morbidity and costs attributable to smoking in Germany: update and a 10-year comparison. *Tob Control* 2006; **15**: 464–71.
6. Allender S., Balakrishnan R., Scarborough P., Webster P., Rayner M. The burden of smoking-related ill health in the UK. *Tob Control* 2009; **18**: 262–7.
7. Ayadi M. E., Adams E. K., Melvin C. L., Rivera C. C., Gaffney C. A., Pike J., et al. Costs of a smoking cessation counseling intervention for pregnant women: comparison of three settings. *Public Health Rep* 2006; **121**: 120–6.
8. Cantor S. B., Deshmukh A. A., Luca N. S., Noguera-González G. M., Rajan T., Prokhorov A. V. Cost-effectiveness analysis of smoking-cessation counseling training for physicians and pharmacists. *Addict Behav* 2015; **45**: 79–86.
9. Ekpu V. U., Brown A. K. The economic impact of smoking and of reducing smoking prevalence: review of evidence. *Tobacco Use Insights* 2015; **8**: 1–35.
10. Coyle K., Coyle D., Lester-George A., West R., Trapero-Bertran M., Leidl R., et al. EQUIPTMOD—development and application of an economic model to assess the impact of smoking cessation. *Addiction* 2017; <https://doi.org/10.1111/add.14001>.
11. Pokhrel S., Owen L., Lester-George A., Coyle K., Coyle D., Trapero-Bertran M. *Tobacco Control Return on Investment Tool*. London: National Institute for Health and Clinical Excellence; 2012 Available at: <https://www.nice.org.uk/>

- about/what-we-do/into-practice/return-on-investment-tools/tobacco-return-on-investment-tool (accessed 12 October 2015).
12. Drummond M. E., Jefferson T. O. Guidelines for authors and peer reviewers of economic submissions to the BMJ. *BMJ* 1996; **313**: –283.
 13. Husereau D., Drummond M., Petrou S., Carswell C., Greenberg D., Augustovski E., *et al.* Consolidated health economic evaluation reporting standards (CHEERS) statement. *BMJ* 2013; **16**: 231–50.
 14. Husereau D., Drummond M., Petrou S., Carswell C., Moher D., Greenberg D., *et al.* Consolidated health economic evaluation reporting standards (CHEERS)—explanation and elaboration: a report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. *Value Health* 2013; **16**: 231–50.
 15. International Monetary Fund. World economic outlook database [internet]. Washington: International Monetary Fund; 2017 [cited 2017 June]. Available at: <https://www.imf.org/> (accessed 10 January 2017).
 16. The EQUIPT Study Group. EQUIPTMOD Technical Manual Appendix—England. 2016. Available at: <http://equipt.eu/deliverables> (accessed 10 October 2016).
 17. The EQUIPT Study Group. EQUIPTMOD Technical Manual Appendix—Germany. 2016. Available at: <http://equipt.eu/deliverables> (accessed 10 October 2016).
 18. The EQUIPT Study Group. EQUIPTMOD Technical Manual Appendix—Hungary. 2016. Available at: <http://equipt.eu/deliverables> (accessed 10 October 2016).
 19. The EQUIPT Study Group. EQUIPTMOD Technical Manual Appendix—Netherlands. 2016. Available at: <http://equipt.eu/deliverables> (accessed 10 October 2016).
 20. The EQUIPT Study Group. EQUIPTMOD Technical Manual Appendix—Spain. 2016. Available at: <http://equipt.eu/deliverables> (accessed 10 October 2016).
 21. Leaviss J., Sullivan W., Ren S., Everson-Hock E., Stevenson M., Stevens J. W., *et al.* What is the clinical effectiveness and cost-effectiveness of cytisine compared with varenicline for smoking cessation? A systematic review and economic evaluation. *Health Technol Assess* 2014; **18**: 1–120.
 22. The Hungarian National Institute for Health Development. (Országos Egészségfejlesztési Intézetként). The economic burden of smoking in Hungary. 2010. Edited by Országos Egészségfejlesztési Intézetként, Hungary. Available at: http://www.egeszseg.hu/szakmai_oldalok/ (accessed 15 October 2015).
 23. Rijksinstituut voor Volksgezondheid en Milieu (RIVM). *Kosten van Ziekten [Cost of Diseases]*. [internet]. Amsterdam: RIVM; 2011. Available at: <https://www.volksgezondheidenzorg.info/kosten-van-ziekten> (accessed 16 December 2016).
 24. Leal J., Luengo-Fernandez R., Gray A. Economic costs. Pages 116–123. In: Nichols M., Townsend N., Luengo-Fernandez R., Leal J., Gray A., Scarborough P., Rayner M. (2012). *European Cardiovascular Disease Statistics* 2012. European Heart Network, Brussels, European Society of Cardiology, Sophia Antipolis.
 25. Luengo-Fernandez R., Leal J., Gray A., Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol* 2013; **14**: 1165–74.
 26. Nowak D., Dietrich E. S., Oberender P., Uberla K., Reitberger U., Schlegel C., *et al.* Cost-of-illness study for the treatment of COPD in Germany. *Pneumologie* 2004; **58**: 837–44.
 27. Kolominsky-Rabas P. L., Heuschmann P. U., Marschall D., Emmert M., Baltzer N., Neundorfer B., *et al.* Life-time cost of ischemic stroke in Germany: results and national projections from a population-based stroke registry: the Erlangen stroke project. *Stroke* 2006; **37**: 1179–83.
 28. Corral J., Espinàs J. A., Cots F., Pareja L., Solà J., Font R., *et al.* Estimation of lung cancer diagnosis and treatment costs based on a patient-level analysis in Catalonia (Spain). *BMC Health Serv Res* 2015; **15**: 70.
 29. Ramirez de Arellano A., Coca A., de la Figuera M., Rubio-Terrés C., Rubio-Rodríguez D., Gracia A., *et al.* Economic evaluation of cardio inCode, a clinical-genetic function for coronary heart disease risk assessment. *Appl Health Econ Health Policy* 2013; **11**: 531–42.
 30. Sicras-Mainar A., Velasco-Velasco S., González-Rojas Guix N., Rodríguez-Cid J. L. Clinical and economic evaluation in accordance with the level of cardiovascular risk in subjects appertaining to Spanish population setting. *Med Clin (Barc)* 2008; **131**: 158–9.
 31. Izquierdo J. L. The burden of COPD in Spain: results from the confronting COPD survey. *Respir Med* 2003; **97**: S61–S69.
 32. Álvarez-Sabin J. Spanish: *Los cuidados del paciente tras el ictus: Estudio CONOCES [Oral communication]*. English: *Patient care after stroke: CONOCES study*. [Oral communication]. Pamplona: Health Economics Association Conference; 2014 (accessed 15 October 2015).
 33. Öberg M., Jaakkola M. S., Prüss-Üstün A., Schweizer C., Woodward A. *Second-hand Smoke: Assessing the Environmental Burden of Disease at National and Local Levels*, WHO Environmental Burden of Disease Series, no. 18. Geneva: World Health Organization; 2010.
 34. Wolleswinkel-van den Bosch J. H., Stolk E. A., Francois M., Gasparini R., Brosa M. The health care burden and societal impact of acute otitis media in seven European countries: results of an internet survey. *Vaccine* 2010; **28**: G39–G52.
 35. Martínez-Moragon E., Serra-Batlles J., De Diego A., Palop M., Casan P., Rubio-Terres C., *et al.* Economic cost of treating the patient with asthma in Spain: the AsmaCost study. *Arch Bronconeumol* 2009; **45**: 481–6.
 36. Blasco Bravo A. J., Perez-Yarza E. G., Lazaro y de Mercado P., Bonillo Perales A., Diaz Vazquez C. A., Moreno Galdo A. Cost of childhood asthma in Spain: a cost evaluation model based on the prevalence. *Anales de pediatria* 2011; **74**: 145–53.
 37. Stock S., Redaelli M., Luengen M., Wendland G., Civallo D., Lauterbach K. W. Asthma: prevalence and cost of illness. *Eur Respir J* 2005; **25**: 47–53.
 38. Kirsch F., Teuner C. M., Menn P., Leidl R. Costs of illness for asthma and COPD in adults in Germany. *Gesundheitswesen* 2013; **75**: 413–23.
 39. Ehlken B., Ihorst G., Lippert B., Rohwedder A., Petersen G., Schumacher M., *et al.* Economic impact of community-acquired and nosocomial lower respiratory tract infections in young children in Germany. *Eur J Pediatr* 2005; **164**: 607–15.
 40. Aumann I., Prenzler A., Welte T., Gillissen A. Epidemiology and costs of asthma in Germany—a systematic literature review. *Pneumologie* 2014; **68**: 557–67.
 41. Liese J. G., Silfverdal S. A., Giaquinto C., Carmona A., Larcombe J. H., Garcia-Sicilia J., *et al.* Incidence and clinical presentation of acute otitis media in children aged <6 years in European medical practices. *Epidemiol Infect* 2014; **142**: 1778–88.
 42. Federal Statistical Office. Available at: <https://www.destatis.de/EN/Homepage.html> (accessed 15 October 2015).

43. West R., Coyle K., Owen L., Coyle D., Pokhrel S., on behalf of the EQUIPT Study Group Estimates of effectiveness and reach for 'return on investment' modelling of smoking cessation interventions using data from England. *Addiction* 2017; <https://doi.org/10.1111/add.14006>.
44. British National Formulary (BNF). London: National Health Service; 2015. Available at: <http://www.evidence.nhs.uk/formulary/bnf/current/4-central-nervous-system/410-drugs-used-in-substance-dependence/4102-nicotine-dependence/nicotine-replacement-therapy/nicotine> (accessed 15 October 2015).
45. Doc Morris. *Nicotine Replacement Therapy products [internet]*. Doc Morris. Online Pharmacy: Heerlen; 2015 Available at: <https://www.docmorris.de> (accessed 15 November 2015).
46. National Health Insurance Fund Hungary (NHIF). *Drug Database [internet]*. Budapest: NHIF; 2014. Available at: <http://www.oep.hu/> (accessed 17 December 2016).
47. Spanish: Colegio Oficial de Farmacéuticos de Pontevedra (COFPO). Listado de Precios de los medicamentos (October 2015). English: Official College of Pharmacists of Pontevedra (COFPO). Price list of medicines (October 2015). Available at: <http://www.cofpo.org/index.php/medic-es.html> (accessed 20 February 2015).
48. Lancaster T., Stead L. F. Individual behavioural counselling for smoking cessation. *Cochrane Database Syst Rev* 20052; CD001292.
49. Stead L. E., Lancaster T. Group behaviour therapy programmes for smoking cessation. *Cochrane Database Syst Rev* 2005; 2: CD001007.
50. Whittaker R., McRobbie H., Bullen C., Borland R., Rodgers A., Gu Y. Mobile phone-based interventions for smoking cessation. *Cochrane Database Syst Rev* 2012; 11: CD006611.
51. Hartmann-Boyce J., Lancaster T., Stead L. F. Print-based self-help interventions for smoking cessation. *Cochrane Database Syst Rev* 2014; 6: CD001118.
52. Association of Statutory Health Insurance Physicians. Available at: https://www.kvberlin.de/20praxis/30abrechnung_honorar/10ebm/ (accessed 10 October 2015).
53. Wenig J. R., Erfurt L., Kroger C. B., Nowak D. Smoking cessation in groups—who benefits in the long term? *Health Educ Res* 2013; 28: 869–78.
54. Kröger CB, Piontek D. German: Tabakentwöhnung in Deutschland. Grundlagen und kommentierte Übersicht. 3. Erweiterte und überarbeitete Auflage 2011. English: Tobacco cessation in Germany. Basics and annotated overview. 3. Extended and revised edition 2011. Bundeszentrale für gesundheitliche Aufklärung (BZgA) 2011.
55. Hakkaart-van Roijen L, Van der Linden N, Bouwmans CAM, Kanters TA, Tan SS. Dutch: Kostenhandleiding. Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg. Geactualiseerde versie 2015. English: Methodology of cost research and reference prices for economic evaluations in health care. Updated version 2015. Diemen, the Netherlands; Zorginstituut Nederland; 2015.
56. Weng S. E., Ali S., Leonardi-Bee J. Smoking and absence from work: systematic review and meta-analysis of occupational studies. *Addiction* 2013; 108: 307–19.
57. Wacker M., Holle R., Heinrich J., Ladwig K. H., Peters A., Leidl R., et al. The association of smoking status with health-care utilisation, productivity loss and resulting costs: results from the population-based KORA F4 study. *BMC Health Serv Res* 2013; 13: 278.
58. Gresz M., Nagy J., Freyler P. Health related costs of smoking from the viewpoint of the health Insurance Fund in Hungary. *Orv Hetil* 2012; 153: 344–50.
59. National Committee for Smoking Prevention (CNPT). Spanish: *Evaluación del Control del Tabaquismo sobre los costes empresariales y sanitarios*. English: Evaluation of Smoking Control on business and health costs. Madrid: Comité Nacional para la Prevención del Tabaquismo; 2009.
60. Gezondheid en zorg in cijfers. Dutch: Centraal Bureau voor de Statistiek (CBS) English: Central Bureau of Statistics (CBS), 2007. Available at: http://www.loketgezondleven.nl/object_binary/o12346_factsheet-stoppen-met-roken.pdf (accessed 15 November 2015).
61. Office of National Statistics (ONS). *Annual Survey of Hours and Earnings [internet]*. London: Office for National Statistics; 2014. Available at: <https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2014-11-19> (accessed 18 December 2016).
62. Dutch: Durchschnittlicher Stundenlohn von Beschäftigten (DESTATIS) English: Federal Statistical Office in Germany. Average hourly wage of employees (DESTATIS). Berlin: Statistisches Bundesamt; 2010. Available at: https://www.destatis.de/DE/ZahlenFakten/Indikatoren/QualitaetArbeit/Dimension2/2_5_Stundenlohn.html (accessed 18 December 2016).
63. Hungarian Central Statistical Office (KSH) *Quick Report on Gross Earnings*. Budapest: Hungarian Central Statistical Office; 2014.
64. National Statistics Institute (INE). Spanish National Health Survey (SNHS) 2011–2012. Available at: <http://www.ine.es/>
65. European Health Interview Survey (EHIS). 2009. Own calculated value. Available at: <http://ec.europa.eu/eurostat/web/microdata/european-health-interview-survey> (accessed 15 October 2015).
66. Centraal Bureau voor de Statistiek (CBS) *Gezondheid en zorg in cijfers*. Voorburg: CBS; 2015 Available at: <https://www.cbs.nl/en-gb/labour-and-income/labour-and-social-security> (accessed 7 November 2015).
67. INE *Wage Structure Survey [internet]*. Madrid: National Statistics Institute; 2012. Available at: http://www.ine.es/dyngs/INEbase/es/operacion.htm?c=Estadistica_C&cid=1254736177025&menu=ultiDatos&idp=1254735976596 (accessed 23 December 2014).
68. Schunck R., Rogge B. G. Unemployment and smoking: causation, selection, or common cause? Evidence from longitudinal data. SOEP papers on Multidisciplinary Panel Data Research (DIW Berlin). Available at: http://www.diw.de/documents/publikationen/73/diw_01.c.409934.de/diw_sp0491.pdf (accessed 15 October 2015).
69. Suijkerbuijk A. W. M., Hoogeveen R. T., de Wit G. A., Wijga A. H., Hoogendoorn E. J. I., Rutten-van Molken M. P. M. H., et al. Dutch: *Maatschappelijke kosten voor astma, COPD en respiratoire allergie*. Rijksinstituut voor Volksgezondheid en Milieu: English: *Social costs for asthma, COPD and respiratory allergy*. National Institute for Health and Environment Bilthoven; 2013.
70. Royal College of Physicians (RCP). Passive smoking and children. A report by the Tobacco Advisory Group. London: RCP; 2010.
71. Office of National Statistics (ONS) *Population data [internet]*. London: Office for National Statistics; 2014. Available at: <https://www.ons.gov.uk> (accessed 18 December 2016).

72. Zorginstituut Nederland (National Health Care Institute). Pharmacotherapeutic compass. Quicker access to information about medication. Available at: <https://www.farmacotherapeutischkompas.nl/>. Edited by Zorginstituut Nederland. (accessed 15 September 2015).
73. Spanish: Centro de Información online de Medicamentos de la AEMPS—CIMA. English: Online Medicine Information Center of the Spanish Agency of Medicines and Health Products (AEMPS—CIMA). Agencia Española de Medicamentos y Productos Sanitarios. Ministerio de Sanidad, Servicios Sociales e Igualdad. Available at: <http://www.aemps.gob.es/cima/fichasTecnicas.do?metodo=detalleForm> (accessed 8 February 2016).
74. Spanish: Documento de Consenso para la Atención Clínica del Tabaquismo en España. Madrid: Comité Nacional para la Prevención del Tabaquismo; 2013. English: National Committee for Smoking Prevention (CNPT). Consensus Document for the Clinical Care of Smoking in Spain. Madrid: National Committee for Smoking Prevention; 2013.
75. Spanish: Listado de Precios de los medicamentos (Octubre 2015). Colegio Oficial de Farmacéuticos de Pontevedra. Available at: <http://www.cofpo.org/index.php/medic-es.html> (accessed 20 February 2015). English: Official College of Pharmacists of Pontevedra. Price list of medicines. October 2015. Available at: <http://www.cofpo.org/index.php/medic-es.html> (accessed 20 February 2015).
76. The information service around the personal health on HYPERLINK <https://www.onmeda.de>. Own calculations, based on packages of the supplier Glaxo Smith Cline. Available at: <https://www.onmeda.de/> (accessed 10 October 2015).
77. West R., Owen L. Estimates of 52-week continuous abstinence rates following selected smoking cessation interventions in England. Smoking in England 2012 Report. Info version 2. 2012. Available at: <http://www.smokinginengland.info/reports/>.
78. Digital online data center. Leading center on health related data. Data on drugs or OTC treatments on smoking. Available at: <http://www.HáziPatika.com> (accessed 15 October 2015).
79. National Institute for Health and Care Excellence (NICE). Stop smoking services. Guidance PH10 (NICE 2008). Last updated 2013. London: NICE; 2008.
80. Association of Statutory Health Insurance Physicians. Available at: https://www.kvberlin.de/20praxis/30abrechnung_honorar/10ebm/ (accessed 12 October 2015).
81. Guerrierra C., Cairns J., Roberts I., *et al.* The cost effectiveness of smoking cessation support delivered by mobile phone text messaging: Txt2stop. *Eur J Health Econ* 2013; **14**: 789–97.
82. Blyth A., Maskrey V., Notley C., Barton G. R., Brown T. J., Aveyard P., *et al.* Effectiveness and economic evaluation of self-help educational materials for the prevention of smoking relapse: randomised controlled trial. *Health Technol Assess* 2015; **19**; Available at: https://ueaeprints.uea.ac.uk/54168/3/FullReport_hta19590.pdf
83. Feenstra T. L., Hamberg-van Reenen H. H., Hoogenveen R. T., Rutten-van Mölken M. P. Cost-effectiveness of face-to-face smoking cessation interventions: a dynamic modeling study. *Value Health* 2005; **8**: 178–90.
84. Curtis L. Unit Costs of Health and Social Care 2014. Personal Social Services Research Unit. 2014. Canterbury: University of Kent; 2014.
85. Kassenärztliche Federal Association. Drug prices. Germany. Available at: <http://www.kbv.de/html/> (accessed 3 November 2015).
86. Akobundu E., Ju J., Blatt L., Mullins C. D. Cost-of-illness studies—a review of current methods. *Pharmacoeconomics* 2006; **24**: 869–90.
87. Trapero-Bertran M., Oliva Moreno J y Grupo de Expertos GECA. Spanish: Guía Metodológica para la estimación de costes en asma (GECA). Methodological Guide for Estimating Costs in Asthma (GECA). 2017. Editorial Mundipharma. Depósito legal: M-1617-2017. Madrid Spain.
88. Zozaya N., Villoro R., Hidalgo A., Betolaza San Miguel J. I., García Pérez S., Mata Cases M. *et al.* Spanish: Guía metodológica para estimar los costes asociados a la diabetes. Mayo 2015. English: Methodological guide to estimate the costs associated with diabetes. May 2015. Edita Instituto Max Weber. Madrid Spain.
89. Weinmann S., Kamtsiuris P., Henke K. D., Wickman M., Jenner A., Wahn U. The costs of atopy and asthma in children: assessment of direct costs and their determinants in a birth cohort. *Pediatr Allergy Immunol* 2003; **14**: 18–26.
90. Ministerio de Sanidad Política Social e Igualdad. Hospital records (CMBD-H). 2012. Available at: <http://pestadistico.msc.es/PEMSC25/ArbolNodos.aspx> (accessed 9 December 2014).

Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article.

Appendix S1 Standardized checklist used for each model input including costs.

Appendix S2 An example of standardized method adopted to cost pharmacotherapy (varenicline standard duration, England, £).