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BMC Public Health

Cost-effectiveness of a complex intervention to reduce children's exposure to second-hand smoke in the home --Manuscript Draft--

Manuscript Number:	PUBH-D-18-01283R2	
Full Title:	Cost-effectiveness of a complex intervention to reduce children's exposure to second-hand smoke in the home	
Article Type:	Research article	
Section/Category:	Health behaviour, health promotion and society	
Funding Information:	UK National Institute for Health Research (RP-PG-0608-10020)	Dr Elena Ratschen
Abstract:	<p>Background Second-hand smoke (SHS) causes numerous health problems in children such as asthma, respiratory tract infections and sudden infant death syndrome. The home is the main source of exposure to SHS for children, particularly for young children. We estimated the cost-effectiveness of a complex intervention designed to reduce SHS exposure of children whose primary caregiver feels unable or unwilling to quit smoking.</p> <p>Methods A cost-effectiveness analysis was carried out alongside an open-label, parallel, randomised controlled trial in deprived communities in Nottingham, England. A complex intervention combining behavioural support, nicotine replacement therapy and personalised feedback on home air quality was compared with usual care. A total number of 205 households were recruited, where the main caregivers were aged 18 and over, with a child aged under five years living in their household reporting smoking inside their home. Analyses for this study were undertaken from the National Health Service/Personal Social Services perspective. All costs were estimated in UK pounds (£) at 2013/14 prices. The primary outcome was the incremental cost-effectiveness of change in air quality in the home, measured as average 16–24 hour levels of particulate matter of <math><2.5\mu\text{m}</math> diameter (PM2.5), between baseline and 12 weeks. Secondary outcomes included incremental cost per quitter, quit attempts and cigarette consumption in the home. A non-parametric bootstrap re-sampling technique was employed to explore uncertainty around the calculated incremental cost-effectiveness ratios.</p> <p>Results The complex intervention achieved reduced PM2.5 by 21.6 ug/m3 (95% CI: 5.4 to 37.9), with an incremental cost of £283 (95% CI: £254-£313), relative to usual care. The incremental cost-effectiveness ratio was £131 (bootstrapped 95% CI: £72-£467) per additional 10ug/m3 reduction in PM2.5, or £71 (bootstrapped 95% CI: -£57-£309) per additional quitter.</p> <p>Conclusions This trial targeted a socio-economically disadvantaged population that has been neglected within the literature. The complex intervention was more costly but more effective in reducing PM2.5 compared with the usual care. It offers huge potential to reduce children's tobacco-related harm by reducing exposure to SHS in the home. The intervention is considered cost-effective if the decision maker is willing to pay £131 per additional 10ug/m3 of PM2.5 reduction.</p>	
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Response to Reviewers:	<p>Associate Editor Comments: Thank you for your prompt and thorough responses to reviewer comments. We are pleased to recommend acceptance of the manuscript.</p> <p>Response: Thank you so much for accepting our manuscript. We would like to thank the editors and reviewers for their comments which have greatly improved our paper. Our responses to editor's new comments are detailed below:</p> <p>Assistant Editor Comments:</p> <p>1. Overlap – We note that the current submission contains some textual overlap with other previously published works, in particular:</p> <p>6% - Ratschen E, Thorley R, Jones L, Breton MO, Cook J, McNeill A, Britton J, Coleman T, Lewis S. A randomised controlled trial of a complex intervention to reduce children's exposure to secondhand smoke in the home. <i>Tobacco control</i>. 2018 Mar 1;27(2):155-62.</p> <p>And</p> <p>2% - Watson J, Toner P, Day DB, Brady LM, Fairhurst C, Renwick C, Templeton L, Akhtar S, Lloyd C, Li J, Cocks K. Youth social behaviour and network therapy (Y-SBNT): adaptation of a family and social network intervention for young people who misuse alcohol and drugs-a randomised controlled feasibility trial. <i>Health technology assessment (Winchester, England)</i>. 2017 Mar;21(15):1.</p> <p>This overlap mainly exists in the Background and Methods sections.</p> <p>While we understand that you may wish to express some of the same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work.</p> <p>If this study uses methodology from a previously published work, please provide a summarizing statement in the methodology together with a citation to the original paper.</p> <p>Please re-phrase these sections to minimise overlap.</p> <p>Response: Thank you for your suggestion. We have now re-phrased those sections (Background & Methods) to minimise overlap. However, it may still have a very small proportion of overlap compared with Ratschen E, 2018, because the current manuscript and that published paper are about the same RCT. Hence, the description of the trial intervention may look very similar as they are the same study.</p> <p>2. Form of consent In your "ethical approval and consent to participate" section, please confirm whether written or verbal consent, was obtained from all participants and clearly state this in your manuscript. If verbal, please state the reason and whether the ethics committee approved this procedure. Response: Written consent was obtained from trial participants prior to them taking part</p>

in the trial.

3. Authors' contributions

We would also like to ask for you to provide more justification for the contributions of RT as currently they do not automatically qualify for authorship. Contribution to day-to-day management of the study alone, does not usually justify authorship.

An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study. According to the ICMJE guidelines, to qualify as an author one should have:

- a) made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; AND
- b) been involved in drafting the manuscript or revising it critically for important intellectual content; AND
- c) given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; AND
- d) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Anyone listed as an author must be included in this section. If you choose to change your author list you will need to fill out a change in authorship form and send it by email to the Editorial office to be approved by the Editor. The form can be found here: <https://www.biomedcentral.com/getpublished/editorial-policies#authorship>.

Anyone who contributed towards the article who does not meet the criteria for authorship can be acknowledged in the 'Acknowledgements' section.

Response: RT collected and cleaned data used in the economic analysis and have contributed to the revisions of the manuscript. We consider she is qualify for authorship.

4. Additional files – Cheers checklist

Thank you for submitting the completed CHEERS checklist along with the main text. As this is no longer needed for publication, please remove it.

Response: Thanks for your suggestion. We have now removed the Cheers checklist.

5. Figures – we note that you have submitted your Cost Effectiveness Planes as a single figure without labelling them 'a', 'b' or 'c', etc. Please either label them accordingly, or submit them as two separate figures, for clarity.

If reformatting as two separate figures, please upload each figure as separate files, so that each figure fits on a single page in portrait format. Figure files should contain only the image, as well as any associated keys/annotations.

Please also ensure each figure citation in the main text is amended accordingly, for example, Figure 1/Figure 2, or Figure 1a/1b.

Response: We have labelled a & b in the Figure 1 and changed the citation in the text accordingly.

6. Tracked changes

At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Response: Thanks. We have uploaded a clean version of the manuscript and the figure.

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2 **1 Cost-effectiveness of a complex intervention to reduce children's exposure to second-**
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1 **Abstract**

2 **Background** Second-hand smoke (SHS) causes numerous health problems in children such
3 as asthma, respiratory tract infections and sudden infant death syndrome. The home is the
4 main source of exposure to SHS for children, particularly for young children. We estimated
5 the cost-effectiveness of a complex intervention designed to reduce SHS exposure of children
6 whose primary caregiver feels unable or unwilling to quit smoking.

7 **Methods** A cost-effectiveness analysis was carried out alongside an open-label, parallel,
8 randomised controlled trial in deprived communities in Nottingham, England. A complex
9 intervention combining behavioural support, nicotine replacement therapy and personalised
10 feedback on home air quality was compared with usual care. A total number of 205
11 households were recruited, where the main caregivers were aged 18 and over, with a child
12 aged under five years living in their household reporting smoking inside their home. Analyses
13 for this study were undertaken from the National Health Service/Personal Social Services
14 perspective. All costs were estimated in UK pounds (£) at 2013/14 prices. The primary
15 outcome was the incremental cost-effectiveness of change in air quality in the home,
16 measured as average 16–24 hour levels of particulate matter of ≤ 2.5 μm diameter ($\text{PM}_{2.5}$),
17 between baseline and 12 weeks. Secondary outcomes included incremental cost per quitter,
18 quit attempts and cigarette consumption in the home. A non-parametric bootstrap re-sampling
19 technique was employed to explore uncertainty around the calculated incremental cost-
20 effectiveness ratios.

21 **Results** The complex intervention achieved reduced $\text{PM}_{2.5}$ by 21.6 $\mu\text{g}/\text{m}^3$ (95% CI: 5.4 to
22 37.9), with an incremental cost of £283 (95% CI: £254-£313), relative to usual care. The
23 incremental cost-effectiveness ratio was £131 (bootstrapped 95% CI: £72-£467) per
24 additional 10 $\mu\text{g}/\text{m}^3$ reduction in $\text{PM}_{2.5}$, or £71 (bootstrapped 95% CI: -£57-£309) per
25 additional quitter.

1 **Conclusions** This trial targeted a socio-economically disadvantaged population that has been
2 neglected within the literature. The complex intervention was more costly but more effective
3 in reducing PM_{2.5} compared with the usual care. It offers huge potential to reduce children's
4 tobacco-related harm by reducing exposure to SHS in the home. The intervention is
5 considered cost-effective if the decision maker is willing to pay £131 per additional 10ug/m³
6 of PM_{2.5} reduction.

7
8 **Trial Registration** The Smoke Free Homes trial was registered with isrctn.com on 29
9 January 2013 with the identifier ISRCTN81701383

10 **Keywords** Second-hand smoke, smoking cessation, passive smoking, environmental tobacco
11 smoke pollution, cost-effectiveness analysis

1 **Background**

2 The harmful health effects of second-hand smoke (SHS), also known as environmental
3 tobacco smoke, on children are well established [1, 2]. SHS exposure in children is associated
4 with higher risks of various diseases, including asthma and wheeze [3], respiratory tract
5 infections [4], middle ear disease [5], and even sudden infant death syndrome [2]. The home
6 is the main source of exposure to SHS for children, particularly for young children [6]. It is
7 estimated that around 2 million children are regularly exposed to SHS in the home in the UK
8 [7]. As smoking prevalence is generally higher among caregivers from socio-economically
9 disadvantaged groups [8], children from those households face higher exposure to SHS and
10 increased risk of developing SHS-related diseases [9], which can lead to future health
11 inequalities through intergenerational perpetuation of tobacco dependence and harm [10]. In
12 the UK, SHS smoke in children accounts for 165,000 new episodes of diseases, at an
13 estimated cost of about £23.3 million each year [2]. The long-term costs of treating smoking-
14 caused diseases for smokers who take up smoking as a consequence of exposure to SHS has
15 been estimated at £5.7million per year, plus an additional annual £5.6 million in lost
16 productivity [2]. All these costs are potentially avoidable [2]. In addition to improved child
17 health, reducing air pollution in the home will also benefit other family members.

18 Smoking cessation programmes are one of the most cost-effective healthcare interventions
19 available in the UK [11-13]. The majority of smoking cessation interventions are focused on
20 people who are motivated to quit; less attention has been paid to those unwilling to quit. This
21 population, although unwilling to quit, may be amenable to stop smoking within the home,
22 reducing the adverse effects on their children through SHS exposure [14]. Despite the rapidly
23 declining smoking prevalence in the UK, it is important to engage smokers from
24 disadvantaged groups and smokers unwilling to quit, who have yet to respond to existing
25 stimuli to quit [15]. A meta-analysis by Rosen et al. (2015) evaluated seven studies (six in the

1 US and one in Scotland) aimed at reducing SHS exposure [16]. The results suggested that
2 interventions aimed at reducing SHS exposure, with the primary outcome as air pollution,
3 were effective but limited. However, the cost-effectiveness of these interventions was unclear
4 since no analysis of cost-effectiveness was conducted and no costs of intervention reported.

5
6 In this study, we report a cost-effectiveness analysis (CEA) conducted in the context of a
7 randomised controlled trial (RCT) comparing a complex intervention with usual care in
8 reducing children's SHS exposure in the home [17]. The intervention consisted of both
9 pharmacological and behavioural support as well as a personalised indoor air quality
10 feedback. Our objectives were to compare the costs associated with the complex intervention
11 strategies and the usual care, estimate the effectiveness measured using PM_{2.5} levels,
12 consumption of cigarettes in the home, quit attempts and quit rates and assess the cost-
13 effectiveness of the complex intervention compared with the usual care.

14 **Methods**

15 **The Smoke Free Homes Trial**

16 The trial for which the economic evaluation was conducted was the Smoke Free Homes Trial
17 (Trial registration: ISRCTN81701383), as reported in detail elsewhere [17]. In brief, the trial
18 was an open-label, parallel, RCT based in deprived communities in Nottingham City and
19 County in England. Caregivers aged 18 and over, with a child aged under five living in their
20 household, reported smoking tobacco inside their home and were not willing to quit were
21 recruited and randomised to receive either the complex intervention or usual care.
22 Participants were recruited from 81 English 'Sure Start' Children's Centres across
23 Nottinghamshire. A researcher and a smoke-free homes advisor (SFHA) collected data during
24 home visits at baseline, seven and 12 weeks.

1
2 The complex intervention had several components, including behavioural support from a
3 SFHA on how to create a SFH, feedback on the air quality measured in the home, and
4 nicotine replacement therapy (NRT) for temporary abstinence or for reducing number of
5 cigarettes smoked in the home. Participants in the control group received the usual care: a
6 ‘SFH resource pack’ developed by the local Stop Smoking Service. Full details of the study
7 design and intervention have been described in a companion paper presenting the clinical
8 results of the Smoke Free Homes trial [17]. This paper presents a CEA carried out alongside
9 the Smoke Free Homes Trial to assess the value for money of the intervention.

10 11 **Resource use**

12 A micro-costing exercise was conducted following the methods of technology appraisal
13 recommended by the National Institute for Health and Care Excellence (NICE) [18]. The
14 main costing component for the alternative strategies was the costs of inputs for the
15 interventions. No wider health care resource use was collected and all trial-related research
16 costs were excluded. Costs for the intervention group were based on three components: (1) up
17 to four one-hour sessions of behavioural support in the home from a SFHA and a minimum
18 of two proactive phone calls or SMS support; (2) NRT and (3) feedback on the air quality
19 (PM_{2.5}) of the main living area at baseline, seven and 12 weeks, measured using the Sidepak
20 Aerosol Monitor AM510 (TSI Instruments Ltd, High Wycombe, UK) with the *Trakpro*
21 software already installed. Intervention cost for the usual care group was based on one face-
22 to-face home visit and a resource pack provided by Nottingham Smoke-free homes.
23 Intervention costs, therefore, included the staff cost of the SFHAs along with the relevant
24 travel and telephone expenses, the cost of NRT and the air monitors.

1 The household cost for contact with the SFHAs was calculated from the treatment log, which
2 recorded the number of visits per household and the length of appointment for baseline, seven
3 weeks and 12 weeks. Where an appointment time was not given, it was calculated using the
4 estimates of 10 minutes for graphical feedback and 10 minutes for behavioural support. For
5 the intervention group, the 24-hour visit was estimated at 20 minutes and the week three visit
6 at 10 minutes. The advisor wage rate was calculated from the mean of a band 5 and 6
7 smoking advisor wage [19-21]. Travel time and distance from the hospital were recorded in
8 the treatment log. A return trip was calculated based on the mileage, travel time and advisor
9 wage rate.

10 Within the treatment log telephone calls were recorded at 10 minutes per call. Before each
11 visit an additional courtesy call was made to the caregiver. NRT dispensed per person was
12 recorded within the treatment log and costed according to the quantity given per household.

13 The cost of the air monitor was calculated for one year of its 10 life-years (estimated by the
14 manufacturer) and then a cost per use was derived by dividing the annual cost by the number
15 of uses, based on the assumption that the device could be used every other day. Included in
16 the annual cost were the yearly calibration and other fixed costs such as the flow meter.
17 Graphical feedback was costed as 10 minutes of the appointment time with the associated
18 printing costs.

19 **Valuation of Costs**

20 All resource use was valued in monetary terms, and unit costs were reported in pounds
21 sterling for the financial year 2013/14. All costs were inflated to 2013/14 prices levels where
22 necessary, using the Hospital and Community Health Services pay and price inflation index
23 [22]. The follow-up for the analysis was 12 weeks from randomisation, so no discounting was
24 needed. Table 1 reports the unit costs used in order to cost the intervention. For the support

1 pack, Public Health England provided information on the Smokefree Homes and Cars kit, last
 2 distributed in 2012 and the unit cost of £1.45 was given, which was defined as covering
 3 production costs only (printing and postage but not fulfilment costs) [23].

4 **Table 1: Unit costs and their sources**

Resource	Unit cost	Sources
Smoking advisor	£31/hour	Smoking Cessation Services (NICE) [19]
Travel	£0.45/mile	Estimated from Smoke Free Homes trial
Telephone call	£0.63/minute	Estimated from Smoke Free Homes trial
SMS	£0.04/text	Estimated from Smoke Free Homes trial
Air monitor	£0.60/use	Calculated using manufacturer's lifetime estimates
Support pack	£1.45/pack	Public Health England (PHE) [23]
Medication (Quantity per pack)		
1.00mg Nicorette Mouth Spray QuickMist - Double Pack (26)	£19.43	Estimated from Smoke Free Homes trial
1.00mg Nicorette Mouth Spray QuickMist - Individual Pack (13)	£12.05	
2.00mg Nicorette Lozenge Nicorette Cool (20)	£4.25	
2.00mg Nicorette Chewing Gum (30)	£3.41	
2.00mg Nicorette Chewing Gum Icy White (30)	£3.58	
2.00mg Nicorette Chewing Gum Icy White (105)	£10.25	
4.00mg Nicorette Chewing Gum Icy White (105)	£12.05	
15.00mg Nicorette Inhalator Inhalator (4)	£4.35	
15.00mg Nicorette Inhalator	£15.40	

Inhalator (20)		
10.00mg Nicorette Inhalator (starter pack) (6)	£4.68	
10.00mg Nicorette Inhalator (refill pack) (42)	£15.39	
1.50mg Niquitin CQ Lozenge Mint Mini Lozenge (20)	£3.34	
1.50mg Niquitin CQ Lozenge Mini Lozenge (60)	£9.37	
4.00mg Niquitin CQ Lozenge Mint Mini Lozenge (20)	£3.18	
4.00mg Niquitin CQ Lozenge Mini Lozenge (60)	£9.37	
21.00mg Nicotinell TTS 30 Patch (7)	£8.73	
14.00mg Nicotinell TTS 20 Patch (7)	£8.24	

Outcome measures

The primary outcome measure of the trial was the difference in average 16–24 hours PM_{2.5} between baseline and 12 weeks. Secondary outcome measures included number of quitters (those who self-reported they had “quit smoking altogether” at 12 weeks), number of quit attempts (lasting longer than 24-hours) and difference in cigarette consumption (cigarettes smoked per day in the home) between baseline and 12 weeks.

Cost-effectiveness analysis

A CEA was undertaken to combine the costs of the trial intervention with PM_{2.5} level and the number of quitters. The primary analysis was conducted on an intent-to-treat (ITT) basis, whereby all randomised households were included and analysed in the groups to which they were randomised. Following NICE guidelines, the analysis was conducted from the NHS/Personal Social Services perspective (including only costs that fall within the healthcare and social services system).

1
2 This article's companion paper used statistical models to adjust for baseline covariates; since
3 there was little difference between those adjusted and those unadjusted, we utilised raw
4 adjustments for our analysis [17]. This allowed us to present all results in the original units
5 (PM_{2.5}, quitters, quit attempts, consumption of cigarettes), which was more meaningful for
6 an economic evaluation than log-transforming PM_{2.5}. The results may differ slightly from
7 the main paper because our multiple imputation model contained cost variables. The
8 incremental cost-effectiveness ratio (ICER), in terms of cost per additional 10ug/m³ reduction
9 in PM_{2.5}, was calculated using the mean difference in cost between two trial groups divided
10 by the mean difference in effectiveness [24]. The ICER was calculated using 10ug/m³
11 reduction, as this change in PM_{2.5} is utilised by the World Health Organisation (WHO) for
12 mortality risk and therefore considered a meaningful reduction [25]. An additional ICER was
13 calculated for cost per additional quitter. The ICER is calculated using the formula below; Δ
14 represents difference, E represents effects, C represents the cost of the intervention, while
15 subscripts 'I' and 'UC' refer to intervention and usual care, respectively [24].

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{C_I - C_{UC}}{E_I - E_{UC}}$$

17 Missing data for outcomes (16% for PM_{2.5}) costs (7%) resulted from lost-to-follow-up were
18 imputed using Rubin's multiple imputation (MI) method [24, 26, 27]. As the data were not
19 normally distributed, we used a non-parametric bootstrap re-sampling method to test the
20 sensitivity of calculated ICERs [28-31]. 5000 estimates of mean costs and mean QALYs were
21 generated for each intervention group and the results were then displayed graphically using a
22 cost-effectiveness plane (CEP) to depict the uncertainty surrounding the mean estimates. To
23 assess the uncertainty surrounding the ICER, bootstrapped 95% confidence intervals (CIs)
24 were generated.

In addition to the primary analysis based on the multiple imputed dataset, a sensitivity analysis was undertaken to repeat the CEA using the 172 out of 204 households who had complete data for the primary outcome and the 188 households who had complete data for number of quitters. All analyses were conducted with Stata version 14.0 and Excel (version 2013). Statistical significance was accepted at $P < 0.05$ in each of the analyses.

Results

A total number of 205 households were recruited to the trial, but one withdrew from the intervention group, resulting in 204 households (102 in each group) included in the analysis.

The majority of primary carers recruited to the trial were female, with just 9% male; the mean age was 28, and 94% were white-British. Full details of trial participants and clinical outcomes are given elsewhere [17].

Table 2 presents a breakdown of the mean cost per household for each element of the intervention. The intervention group had a greater mean total intervention cost than the usual care group (£328 (SD=£151) compared to £45 (SD=£20)). The biggest drivers in this difference were the use of NRT, travel cost and staff time also categorised as feedback time. Greater travel cost was attributable to the extra visits required for the intervention group, since the air monitor drop off/picks ups and the week seven and week 12 follow ups were not included in the costing of the usual care group, as these were considered research costs only (maximum number of visits costed for the intervention group was seven compared to one for the usual care group).

Table 2: Mean total cost per household

	Intervention (SD) (n=102)	Usual Care (SD) (n=102)	Difference (95% CI)

Staff	£29 (£8)	£11 (£3)	£18 (£16 to £19)
Feedback	£15 (£2.70)	-	£15 (£14.65 to £15.70)
Telephone	£10 (£4)	£0.10 (£0)	£10 (£8.80 to £10.40)
Travel	£216 (£143)	£32 (£20)	£184 (£156 to £213)
NRT	£56 (£47)	-	£56 (£47 to £65)
Air monitor	£1.68 (£0.32)	-	£1.68 (£1.62 to £1.74)
Support pack	-	£1.45 (£0)	£1.45 (£1.45 to £1.45)
Total	£328 (£151)	£45 (£20)	£283* (£254 to £313)

* Statistically significant (p-value<0.001)

Table 3 reports the base-case results with a decrease of 22.1ug/m³ in average 16-24 hour PM_{2.5} in the intervention group, compared to just 0.5ug/m³ for the usual care group (this is also presented in table 3 by 10ug/m³ decrease, as was used for the ICER). This translated into a 41% mean reduction in the average 16-24-hour average PM_{2.5} between baseline and 12 weeks for the intervention group, compared with a 1% mean reduction in the usual care group. The quit rate was higher in the intervention group versus the usual care group (8.0% compared to 4.3%, p-value=0.2614), but did not reach statistical significance in either analysis. Table 4 shows the intervention group experienced a mean reduction of 11 (SD=10.7) cigarettes smoked in the home per day compared with the usual care's reduction of 4 (SD=10.8) fewer cigarettes smoked (p-value<0.001). The quit attempt rate was significantly higher in the intervention group (29.4% compared to 8.6%, p-value<0.001).

Table 3: Results of PM_{2.5} and quit rate

	Base-case analysis (with imputed data)				Complete case analysis			
	Intervention	Usual Care	Difference (95% CI)	P-value	Intervention	Usual care	Difference (95% CI)	P-value

No. of households	n=102	n=102	n=204		n=90	n=82	n=172	
Cost (SD)	£328 (£151)	£45 (£20)	£283 (£254 to £313)	<0.00 1	£331 (£149)	£46 (£21)	£285 (£252 to £318)	<0.00 1
Reduction in PM _{2.5} (ug/m ³) (SD)	22.1 (65.2)	0.5 (52.0)	21.6 (5.4 to 37.9)	0.009 6	24.0 (58.9)	0.9 (52.4)	23.2(6.3 to 40.0)	0.007
Reduction in PM _{2.5} (10ug/m ³) (SD)	2.21 (6.52)	0.05 (5.20)	2.16 (0.54 to 3.79)	0.009 6	2.40 (5.89)	0.09 (5.24)	2.32 (0.63 to 4.0)	0.007
ICER (bootstrapped 95% CI)	£131 (£72 to £467)				£121 (£70 to £471)			
No. of households	n=102	n=102	n=204		n=95	n=93	n=188	
Cost (SD)	£328 (£151)	£45 (£20)	£283 (£254 to £313)	<0.00 1	£331 (£148)	£44 (£21)	£286 (£256 to £317)	<0.00 1
Quit rate (%) (SD)	8.0% (27.0%)	4.3% (19.6%)	3.7% (-2.8% to 10.2%)	0.261 4	8.4% (27.9%)	4.3% (20.4%)	4.1% (-2.9% to 11.2%)	0.248
ICER (bootstrapped 95% CI)	£71 (-£57 to £309)				£72 (-£22 to £313)			

1

2 Tables 3 and 4 report the results of the complete case analysis, although there was little
3 variation. The results only differed slightly between the base-case analysis and the complete
4 case analysis with the average 16-24 hour PM_{2.5} results generally better for the intervention
5 group in the base-case.

1 The primary outcome, average 16 to 24-hour PM2.5, was selected for the CEA along with
 2 quitters. Table 3 presents the ICERs which combine the differential costs of the two groups
 3 with the differential outcome measures. The intervention group was more costly than the
 4 usual care group, but had a greater decrease in the PM2.5 level. This resulted in an ICER of
 5 £131 (bootstrapped 95% CI: £72-£467) per additional 10ug/m³ reduction of 16 to 24-hour
 6 PM2.5. Analyses of the quitters resulted in an ICER of £71 (-£57 to £309) per additional
 7 quitter. The uncertainty surrounding this ICER was reflected by the bootstrapped CIs for both
 8 analyses. The complete case analysis showed very similar results.

9 **Table 4: Results of consumption of cigarettes in the home and quit attempts**

	Base-case analysis (with imputed data)				Complete case analysis			
	Intervention	Usual Care	Difference (95% CI)	P-value	Intervention	Usual care	Difference (95% CI)	P-value
No. of households	n=102	n=102	n=204		n=95	n=93	n=188	
Cost (SD)	£328 (£151)	£45 (£20)	£283 (£254 to £313)	<0.001	£330 (£148)	£44 (£21)	£286 (£256 to £317)	<0.001
Reduction of consumption in the home (no. of cigarettes per day) (SD)	11 (10.7)	4 (10.8)	7 (9.8 to 3.9 to 9.8)	<0.001	11 (10.8)	4 (10.5)	7.5 (4.4 to 10.6)	<0.001
No. of households	n=102	n=102	n=204		n=93	n=93	n=186	

Cost (SD)	£328 (£151)	£45 (£20)	£283 (£254 to £313)	<0.00 1	£331 (£149)	£44 (£21)	£286 (£256 to £318))	<0.00 1
Quit attempt rate (%)(SD)	29.4% (43.6%)	8.6% (27.1 %)	20.7% (10.8% to 30.8%)	<0.00 1	29% (45.6%)	8.6% (28.2%)	20.4% (7.3% to 32.0%)	<0.00 1

The bootstrapping results of the 5000 re-samples for each outcome were plotted on a CEP (Figure 1), visually displaying any uncertainty surrounding the mean differences in costs and benefits between the intervention and usual care groups. Figure 1 shows this uncertainty for the primary outcome (PM_{2.5} difference). The majority of the plots fall in the south-east quadrant, this indicates although the intervention is always more costly, it is more likely to be effective at reducing PM_{2.5} levels, compared with usual care. The quit rate is more uncertain as shown by some of the plots falling in the south-east region of the CEP (Figure 1b) therefore there is a lack of evidence to show the intervention was more effective at helping people to quit. This is unsurprising, as this was not the main aim of the trial.

Discussion

To our knowledge, the present study is the first full economic evaluation alongside an RCT to assess the cost-effectiveness of a complex intervention designed to reduce children's exposure to SHS in the home. The study has shown the complex intervention significantly reduced SHS exposure in the home among families in which parents had expressed no interest in quitting smoking previously. Decision makers must be willing to pay £131 (bootstrapped 95% CI: £72-£467) per additional 10ug/m³ reduction of PM_{2.5} in order to reduce SHS in the home and limit harm to children. It was presented per additional 10ug/m as

1 this was seen as a meaningful reduction and is used by WHO when presenting mortality risk
2 [25]. The results revealed the intervention was more costly (mean cost: £328 (SD=£151) vs
3 £45 (SD=£20)) than usual care, but produced better outcomes. Total mean costs were £283
4 (95% CI: £254 to £313) higher in the intervention group, this was mostly attributable to the
5 cost of travel with a mean difference of £184 (95% CI: £156 to £213) and the cost of NRT
6 with a mean difference of £56 (95% CI: £47 to £65). Based on WHO recommendations, the
7 safe level of PM_{2.5} <25 ug/m³ (24-hour mean), however children are recognised as
8 particularly vulnerable and there is no threshold below which adverse health effects do not
9 occur [25, 32]. Neither the usual care nor intervention group met the WHO threshold at 12
10 weeks (usual care= 47 ug/m³, intervention=32 ug/m³), but the intervention group did
11 experience an overall reduction of 41% from baseline to 12 weeks.

12 The strength of the economic analysis has been impacted by a few limitations of the study.
13 Firstly, wider health care resource use beyond the trial interventions was not collected and
14 this plays an important role in the drive behind reducing SHS exposure. This cost dimension
15 would have strengthened the economic analysis and brought it more in line with NICE
16 guidelines. Secondly, the trial follow-up period was only 12 weeks, and it may not be long
17 enough to capture the full impact of the intervention. Further research with longer-term
18 follow-up is needed to explore any potential long-term benefits from the intervention.

19 This longer follow-up would also allow the use of the EQ-5D and the subsequent calculation
20 of Quality Adjusted Life-Years (QALYs), a generic health measure [33-35]. QALYs can be
21 used and easily compared across interventions with a willingness to pay thresholds range of
22 £20,000 to £30,000 per additional QALY gained to decide cost-effectiveness [18]. However,
23 QALYs can be insensitive to disease-specific conditions, in particular those concerning
24 mental health [37]. Thirdly, no definitive conclusion about cost-effectiveness can be made

1 due to the absence of decision-making thresholds for any of the outcomes collected alongside
2 the trial.

3 These limitations aside, this trial targeted a socio-economically disadvantaged population that
4 has been neglected within the literature. Previous research showed great success with
5 sophisticated methods for interventions aimed at smokers who are serious about and willing
6 to quit [38, 39]. Despite the rapidly declining smoking prevalence, it is important to engage
7 with smokers who have not yet responded to existing stimuli to quit [15]. New and
8 innovative approaches are needed to target those who are not willing to quit, but may be
9 willing to reduce consumption in the home, thereby limiting the impact of SHS on children.
10 Our results showed a reduced number of cigarettes being smoked inside the home and lower
11 PM_{2.5} level, indicating some success in the trial aims. Although not statistically significant,
12 this intervention group had a 3.7% higher quit rate than usual care, suggesting even those
13 who are seemingly not willing to quit are still able to and should not be ignored, but this
14 result should be taken with caution due to the high level of uncertainty. The results showed a
15 higher number of quit attempts in the intervention group (20.8% higher quit attempt rate).
16 Chaiton et al. (2016) argue when taking into account those smokers who are less willing to
17 quit, it may take 30 or more quit attempts before being successful [40]. Therefore, these
18 increased quit attempts may indicate a likelihood of longer term success.

19 More high quality research such as larger RCTs with longer follow-up periods, generic health
20 outcome measures and collection of wider healthcare resource use is needed to explore the
21 impact of complex interventions on reducing children's SHS exposure. Furthermore, studies
22 exploring interventions that help those who are not willing to quit smoking are needed. These
23 interventions may have short term objectives of reduced consumption, but with the potential
24 of long term success of quitting.

1 **Conclusions**

2 This trial targeted a socio-economically disadvantaged population that has been neglected
3 within the literature. The complex intervention was more costly but more effective in
4 reducing PM_{2.5} compared with the usual care. It offers huge potential to reduce children's
5 tobacco-related harm by reducing exposure to secondhand tobacco smoke in the home. The
6 intervention is considered cost-effective if the decision maker is willing to pay £131 per
7 additional 10ug/m³ of PM_{2.5} reduction.

9 **List of abbreviations**

- 10 **CEA:** Cost-effectiveness analysis
11 **CEP:** Cost-effectiveness plane
12 **CI:** Confidence interval
13 **ICER:** Incremental cost-effectiveness ratio
14 **MI:** Multiple imputation
15 **NICE:** National Institute for Health and Care Excellence
16 **NRT:** Nicotine replacement therapy
17 **QALY:** Quality adjusted life years
18 **RCT:** Randomised controlled trial
19 **SFHA:** Smoke free homes advisor
20 **SHS:** Second-hand smoke
21 **WHO:** World Health Organisation

1 **Declarations**

2
3 **2 Ethics approval and consent to participate** Ethics approved by National Research Ethics
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5 **3** Service West Midlands, Solihull (REC, 25/09/2012, ref: 12/WM/0286). Informed consent
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8 **4** was obtained by all human subjects before the research began.
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11 **5 Consent for publication** Not applicable
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14 **6 Availability of data and material** The datasets used and/or analysed during the current
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17 **7** study are available from the corresponding author on reasonable request
18

19
20 **8 Competing interests** The authors declare that they have no competing interests
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23
24 **9 Funding** This trial was funded by the UK National Institute for Health Research (NIHR):
25
26 **10** RP-PG-0608-10020. The funding bodies played no role in the design of the study, nor in the
27
28
29 **11** collection, analysis, or interpretation of data.
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32 **12 Authors' contributions** CR carried out the economic evaluation and write-up, QW
33
34
35 **13** contributed to the analysis and write-up, MOB was the statistician and contributed to the
36
37 **14** analysis, supervised by SL who provided strategic and statistical senior support, RT was the
38
39
40 **15** trial manager, responsible for the day-to-day management of the study, collected and cleaned
41
42 **16** data used in the economic analysis, JB and SL designed the programme of work which led to
43
44 **17** development and economic evaluation of the intervention, SP contributed to early evaluation
45
46
47 **18** design and provided economic senior support throughout, ER was the Chief Investigator
48
49
50 **19** responsible for the main trial paper, managing the team throughout. All authors contributed
51
52 **20** to the production of the paper. All authors read and approved the final manuscript.
53

54
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56
57
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59
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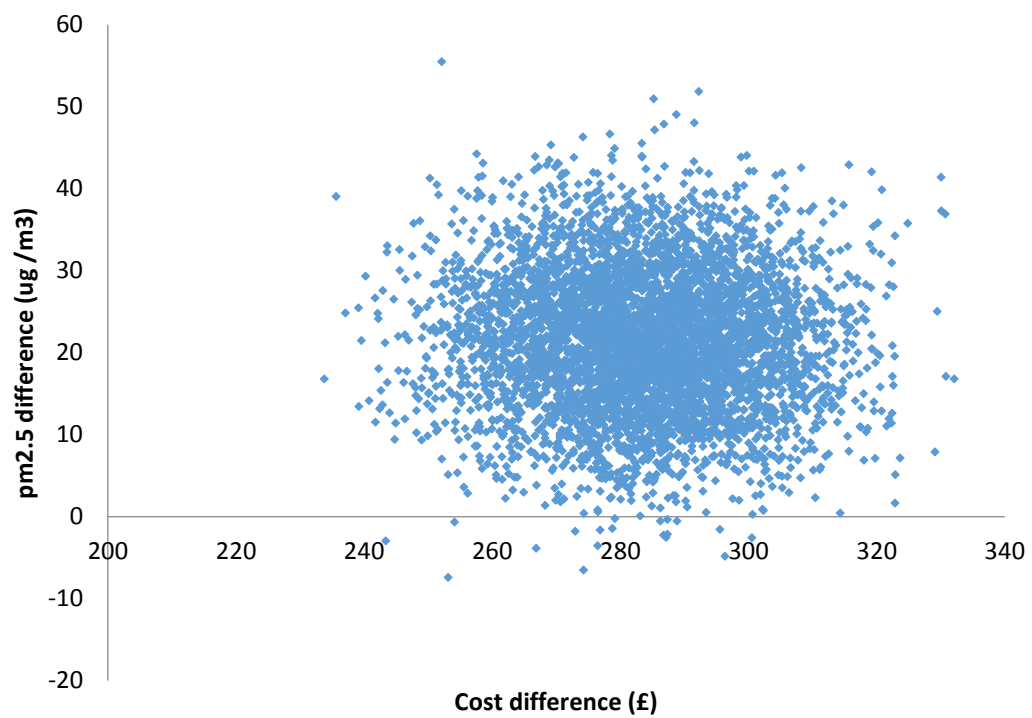
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1 **Figures legend**

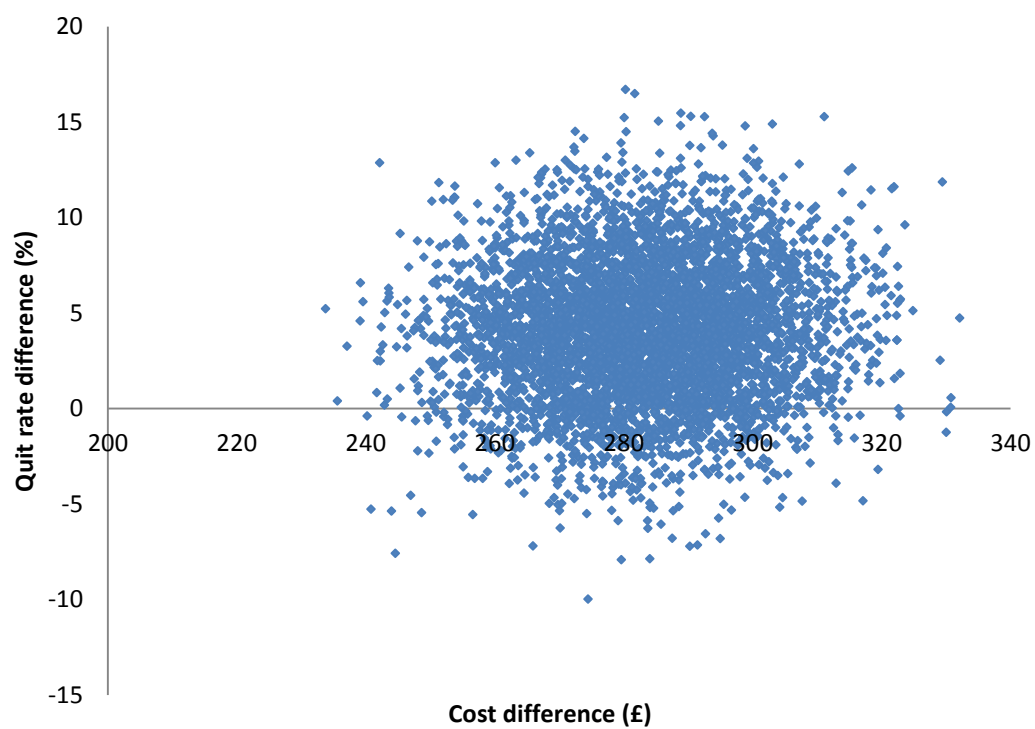
2 -Figure 1: Cost-effectiveness planes (CEPs)

3 -The bootstrapping results of the 5000 re-samples for each outcome

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(b)