Association between population changes in use of e-cigarettes on changes in quit attempts, the success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services: a time-series analysis

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Association between population changes in use of e-cigarettes on changes in quit attempts, the success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services: a time-series analysis

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Abstract (n=294)

Objectives: This paper estimates how far changes in prevalence of e-cigarette use in England have been associated with changes in quit success, quit attempts, and use of licensed medication and behavioural support in quit attempts.

Design: The study involved ARIMAX modelling of data between 2006 and 2015 from the Smoking Toolkit Study, a population survey of adults aged 16+ (quarterly n≅1200 smokers), and monitoring data from the national behavioural support program. Prevalence of e-cigarette use in current smokers and during a quit attempt were used to predict quit success. Prevalence of e-cigarette use in current smokers was used to predict rate of quit attempts. Percentage of quit attempts involving the use of e-cigarettes was also used to predict quit attempts involving use of prescription medications, nicotine replacement therapy (NRT) on prescription and bought over-the-counter, and use of behavioural support. Analyses involved adjustment for a range of potential confounders.

Results: The success rate of quit attempts increased by 0•58% (95%CI 0•38to0•78) and 0•98% (95%CI 0•64to1•32) for every 10% increase in prevalence of use of e-cigarettes by smokers and use during a recent quit attempt, respectively. There was no clear evidence for an association with rate of quit attempts (β 0•025;95%CI -0•035to0•085), use of NRT over-the-counter (β 0•042;95%CI -0•009to0•93), use of prescription medication (β -0.070;95%CI -0•152to0•013) or use of behavioural support (β -0•013 95%CI -0•102to0•077). A negative association was found with prescription NRT use (β -0•098;95%CI -0•189to-0•007).

Conclusion: Changes in prevalence of e-cigarette use in England have been positively associated with the success of quit attempts. No clear association has been found with rate of quit attempts or use of other quitting aids, except for prescription NRT where the association has been negative.

What this paper adds

What is already known on this subject

A recent systematic review raised concerns that the increase in population use of e-cigarettes may be undermining quitting activities. If this is true then e-cigarettes may have a negative impact on public health, even if for an individual smoker who used them in a given quit attempt they may increase the chances of success.

What this study adds

This is the first empirical study to estimate the population impact of e-cigarettes on attempts to quit smoking and their success, the use of smoking cessation pharmacotherapy and the use of stop smoking services, using a time-series approach. The findings conflict with the hypothesis that an increase in population use of e-cigarettes undermines quitting in general, but it may have reduced use of prescription NRT and aided in the success of attempts to stop smoking. These findings are important when considering the possible impact of the Tobacco Products Directive being implemented on the 20th of May 2016, which contains new rules for nicotine-containing e-cigarettes and refill containers.

Introduction

There has been concern that the increase in population use of e-cigarettes may be undermining quitting activities. If this is true then e-cigarettes may have a negative impact on public health, even if for an individual smoker who used them in a given quit attempt they may increase the chances of success [1 2]. England is a country with a relatively liberal regulatory framework for e-cigarettes and has seen a considerable growth in use of e-cigarettes[3 4]. It also has unique time series data to be able to estimate changes over time in key quitting activities as a function of changes in prevalence of e-cigarette use while adjusting for other potential confounding variables [5]. This study used data from England to address the concerns that have been raised.

One source of concern about the potential impact of e-cigarettes on quitting activity arises from a decline in England in the use of licensed stop-smoking medications, and use of stop-smoking behavioural support programs [3 6 7]. It has been suggested that this may be a result of smokers using e-cigarettes instead [8 9]. However, it could also be due to other factors or a secular trend unconnected to the rise in e-cigarette use. In a related study, we found that the increase in population rates of e-cigarette use while smoking was probably not responsible for a decline in use of NRT for smoking reduction [3].

It has also been reported that smokers who currently use, or have used e-cigarettes in the past, are less likely subsequently to quit smoking [10-16]. It has been argued, however, that this association could be due to residual confounding [17]. If the link is causal, then it should be possible to observe an association between changes in prevalence of e-cigarette use over time and changes in quitting activity, adjusting for other potential population level confounding variables such as tobacco control policies.

Time series analysis of population trends allows a direct estimate of population level impact of policies and events. Where associations are found, they cannot unequivocally establish a causal association but can be indicative, as has been the case with estimating the effect of price of cigarettes on population consumption [18], mass media expenditure on use of specialist stop smoking services [19], and introduction of varenicline to the market on prevalence of use of smoking cessation medication [20]. Where associations are not found, or they go in a direction opposite to that expected, this can also be informative.

Thus this study aimed to assess at a population level whether changes in use of e-cigarettes have been associated with changes in key smoking cessation activities and use of licensed medication. More specifically, we were interested in:

1. What is the association between use of e-cigarettes among current smokers and use of e-cigarettes during a quit attempt among those who made a quit attempt, on the success rates of attempts to quit smoking among those who made a quit attempt in the past 12 months?
2. What is the association between use of e-cigarettes among current smokers on attempts to quit smoking in the past year among past-year smokers?
3. What is the association between use of e-cigarettes during a quit attempt among those who made a quit attempt on:
    a. use of prescription medication during a quit attempt among those who made a quit attempt?
    b. use of NRT on prescription during a quit attempt among those who made a quit attempt?
    c. use of NRT over-the-counter during a quit attempt among those who made a quit attempt?
    d. number of smokers setting a quit date at stop smoking services

A range of covariates were added to the models to take account of potential confounding, including tobacco control policies, mass media expenditure and smoking prevalence.

Methods

The dataset consisted of quarterly data on the explanatory, outcome and co-variables. Details of data sources are given below.

Data on explanatory variables

Data on use of e-cigarettes among current smokers and use of e-cigarettes among those who made a quit attempt was obtained from the Smoking Toolkit Study (STS).

The STS involves series of monthly household, face-to-face, computer assisted surveys of representative samples of the population in England aged 16+[5]. It has been collecting data since November 2006. Each survey uses a form of random location sampling design, with initial random selection of grouped output areas (containing 250 households), stratified by ACORN (sociodemographic) characteristics (http://www.caci.co.uk/acron/acornmap.asp) and region. Participants from the STS appear to be representative of the population in England, having similar socio-demographic composition and smoking characteristics to large national surveys based on probability samples such as the Health Survey for England [5].

The monthly data were aggregated quarterly to improve the accuracy of estimation of each data point, though at the cost of reduced temporal granularity. Participants who reported that they smoked cigarettes (including hand-rolled) every day or that they smoked cigarettes (including hand-rolled) but not every day, were asked the following questions and to select from a list of nicotine products which included use of e-cigarettes as a response option:

1. Which, if any, of the following are you currently using to help you cut down the amount you smoke?

2. Do you regularly use any of the following in situations when you are not allowed to smoke?
3. Can I check, are you using any of the following either to help you stop smoking, to help you cut down or for any other reason at all?

Prevalence of use of an e-cigarette in current smokers was obtained for each quarter by counting the number of respondents who endorsed use of an e-cigarette in response to any of the three questions divided by the number of cigarette smokers. Data were first collected in 2011 and prior to this use was assumed to be stable at 0.1%.

Use of e-cigarettes during a recent quit attempt was also ascertained from the STS by asking past-year smokers who had made a quit attempt in the previous 12 months the following question and to select from a list of cessation aids which include use of e-cigarettes as a response option:

1. Which, if any, of the following did you try to help you stop smoking during the most recent serious quit attempt?

Prevalence of use of an e-cigarette in a quit attempt was obtained for each quarter by counting the number of respondents who reported having used an e-cigarette divided by the number who reported having made a quit attempt. Data were first collected in 2009 and prior to this use was assumed to be stable at 0.1%.

Data on outcome variables

Data on outcome variables also came from the STS. Past-year smokers were asked:

1. How many serious attempts to stop smoking have you made in the last 12 months? By serious attempt I mean you decided that you would try to make sure you never

smoked again. Please include any attempt that you are currently making and please include any successful attempt made within the last year.

The prevalence of quit attempts in each quarter was obtained by counting the number of respondents who reported having made one or more quit attempts in the past 12 months divided by the number of past-year smokers.

2. How long did your most recent serious quit attempt last before you went back to smoking?

The success rate in each quarter was calculated as the number reporting that they were still not smoking divided by the number reporting having made a quit attempt.

3. Which, if any, of the following did you try to help you stop smoking during the most recent serious quit attempt?

The prevalence of use in each quarter of i) NRT over the counter, ii) NRT on prescription, iii) any medication on prescription (NRT, bupropion and/or varenicline) was obtained by counting the number of respondents reporting use of each aid divided by the number reporting that they had tried to quit in the past 12 months.

NHS service usage statistics were obtained from the NHS Information Centre [21]. Data were available up until the first quarter of 2015.

Data on other co-variables

In England, tobacco mass media campaigns have been run as part of a national tobacco control program. Spending was almost completely suspended in 2010 and then re-introduced in 2011 at a much lower level. Previous studies have shown that such cuts were associated with a decreased use of smoking cessation support[19 22]. Thus, advertising expenditure was adjusted for using data obtained from Public Health England.

A number of tobacco control policies were adjusted for in the analyses. These included the move in commissioning of stop smoking services to local authorities in April 2013 [21], introduction of a smoking ban in July 2007 [23] and change in the minimum age of sale of cigarettes October 2007 [24]. Price of cigarettes was correlated 0.99 with time and was thereby taken into account by use of differencing to make the series stationary (see Supplementary Appendix 1).

Smoking prevalence, estimated from the STS, was also included as an additional exogenous variable when assessing the impact on the number of smokers setting a quit date at the stop smoking services. This allows adjustment for the fact that any decline in absolute numbers using the services may reflect the overall decline over time in smoking prevalence.

Analysis

The analysis plan was registered on the Open Science Framework prior to data analysis (https://osf.io/fbgj2/). All data were analysed in R version 3.2.1 using Autoregressive Integrated Moving Average with Exogeneous Input (ARIMAX) modelling. We followed a standard ARIMAX modelling approach[25], which is detailed in eAnalysis and Sample Size. The series were first log-transformed to stabilise the variance, and if required, 'first differenced' and seasonally differenced. The autocorrelation and partial autocorrelation functions were then examined in order to determine the seasonal and non-seasonal moving average (MA) and autoregressive terms (AR). To identify the most appropriate transfer function for the continuous explanatory variables the sample cross-correlation function was checked for each ARIMAX model. Coefficients can be interpreted as estimates of the percentage change in the outcome of interest for every percentage increase in use of e-cigarettes and mass media and absolute impact of tobacco control policies. Strobe guidelines were followed throughout [26].

Role of the funding source

No funders had any involvement in the design of the study, the analysis or interpretation of the data, the writing of the report, or the decision to submit the paper for publication.

Patient involvement

There was no patient involvement in this study.

Results

Sample characteristics

Data were collected on 170,490 adults aged 16+ taking part in the STS who reported their smoking status. Of these, 41,301 (weighted: 23·1%: 95%CI 22·9 to 23·3; unweighted 24·2%: 95%CI 24·0 to 24·4) were past-year smokers and 37,765 (weighted: 21·0%: 95%CI 20·8 to 21·2; unweighted 22·2%: 95%CI 22·0 to 22·3) were current smokers. During the study period, the stop smoking services reported that 8,029,012 smokers set a quit date with their service.

Figure 1 shows that there was a decline followed by an increase then a decline in the proportion of past-year smokers reporting a quit attempt. It changed from 45·4% at the start of the study to 31·2% in the last quarter (mean 37·6%, SD 3·8). There was an increase in the success rate of those who reported a quit attempt (last quarter 2006 10·6% to 18·6% in the 1st quarter of 2015; overall mean 15·2%, SD 2·8). Over the same period, current use of e-cigarettes among smokers increased from negligible use in the last quarter of 2006 to 21·3% at the end of the study (mean 6·4%, SD 8·2). Figure 1 shows that there was also a rise in the use of electronc cigarettes in a quit attempt from negligible levels to 35·0% (mean 8·6%, SD 12·5).

Table 1 shows the start, end and mean proportion of smokers using various treatments during their most recent quit attempt, and the start, end and mean number of smokers setting a quit date with stop smoking serivices. Figure2 shows that use of prescription medication and stop smoking services rose up to the 4th quarter of 2011, after which there was a decline. In contrast, use of NRT over-the-counter and on prescription declined steadily. Supplementary Appenix 2 shows the changes in smoking prevalence and mass media expenditure over time, and the time points for the introduction of the relevant tobacco control policies.

Association between e-cigarette use i) among current smokers and ii) during a quit attempt among those who made a quit attempt on the success of quit attempts

Table 2 shows the results of the ARIMAX models. In adjusted analyses, use of e-cigarettes by smokers was positively associated with the success of attempts to stop, such that for every 10% increase in use of e-cigarettes the success of quit attempts increased by 0·58%. E-cigarette use in quit attempts was also positively associated with quit success, with every 10% rise in use associated with a 0·98% increase in the success of attempts. There was also evidence for a rise in successful quitting following the increase in age-of-sale and a positive association between mass media spending and successful quitting (Table 2).

Association between use of e-cigarettes among current smokers on quit attempts

Table 3 shows the results of the ARIMAX models. In adjusted and unadjusted analyses, the data were inconclusive as to whether or not an association was present between current use of e-cigarettes by smokers and attempts to quit smoking.

Association between use of e-cigarettes use during a quit attempt among those who made a quit attempt on use of i) prescription medication, ii) prescription NRT iii) over-the-counter NRT and iii) specialist services

Table 4 shows the results of the ARIMAX models. After adjustment, the findings were inconclusive as to whether or not an association was present between e-cigarette use during a quit attempt and the use of stop smoking services, use of NRT over-the-counter and use of prescription medication. However, a significant association was found with use of prescription NRT, such that for every 10% increase in use of e-cigarettes in a quit attempt the use of prescription medication declined by 0·98%. There was evidence that expenditure on mass media was positively associated with use of stop smoking services (Table 4).

Power

Power analyses (based on McLeod and Vingili [27]) indicated that the study had 80% power to detect a 0·087% change in quit attempts predicted from current e-cigarette use; a 0·034% and 0·113% change in the success of quit attempts when predicted from use during a quit attempt and current e-cigarette use respectively; a 0.113% change in use of stop smoking services, 0·131% change in use of any prescription medication, 0·145% change in use of NRT on prescription, and 0·116% change in the use of over-the-counter NRT, as a consequence of a 1% change in e-cigarette use [27].

Discussion

The increase in use of e-cigarettes in England has been positively associated with the success rates of quit attempts after adjusting for a range of confounding variables. No clear association has emerged between use of e-cigarettes and prevalence of quit attempts or use of licensed NRT bought over the counter, prescription medication or behavioural support. However, use of e-cigarettes in quit attempts has been negatively associated with use of NRT on prescription.

To our knowledge, this is the first empirical study to estimate the population impact of e-cigarettes on attempts to quit smoking and their success, the use of smoking cessation pharmacotherapy and the use of stop smoking services, using a time-series approach. A strength of the study is the use of a large representative sample of the English population, in addition to service usage data.

The study had a number of limitations. First, estimates of the impact of some of the tobacco control policies were implausibly large and confidence intervals wide, suggesting caution when drawing conclusions. Interrupted explanatory variables with short time-periods prior to their introduction in ARIMA type models often give inaccurate estimates of the standard errors [28]. Thus, although the increase in age-of-sale has been previously associated with a decline in smoking prevalence[24], the short lead in period may have created a spurious association [27]. Future studies should consider variations in the impact of tobacco control policies, such as more prolonged pulse effects, delayed and sustained effects [29]. Secondly, a better indication of the impact of the move to local authority control may have been the inclusion of a variable reflecting expenditure by stop smoking services. However, such data were not available. Thirdly, the STS required participants to recall use of aids during the previous 12 months which may have introduced scope for bias. Fourthly, the findings may not generalise to other countries. England has a strong tobacco control climate and generally high motivation to quit among smokers, and relatively liberal regulation of e-cigarettes. In countries with weaker tobacco control, or stricter regulation of e-cigarettes, different effects may be observed. Finally, although we are unaware of any other major population level interventions or other events during the study period, we cannot rule out residual confounding.

The findings conflict with the hypothesis that an increase in population use of e-cigarettes undermines quitting in general, but it may have reduced use of prescription NRT. The small positive association with quit success is consistent with an estimated increase in population quitting attributable to e-cigarettes of around 20,000 out of a total smoking population of 8 million) [30]. This would not produce a detectable effect on smoking prevalence in a given year but might be picked up over a period of several years.

In conclusion, the increased prevalence of e-cigarettes in England has not been associated with a detectable change in attempts to stop smoking but has been associated with an increase in success of quit attempts. Growth in the use of e-cigarettes for quitting has been associated with a decline in use of prescription NRT but has not clearly been associated with use of other quitting support.

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Declaration of interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that: RW undertakes consultancy and research for and receives travel funds and hospitality from manufacturers of smoking cessation medications but does not, and will not take funds from e-cigarettes manufacturers or the tobacco industry. RW and SM are honorary co-directors of the National Centre for Smoking Cessation and Training. RW is a Trustee of the stop-smoking charity, QUIT. RW salary is funded by Cancer Research UK. SM salary is funded by Cancer Research UK and by the National Institute for Health Research (NIHR)'s School for Public Health Research (SPHR). EB and JB have received unrestricted research funding from Pfizer. EB and JB are funded by CRUK. EB is also funded by NIHR's SPHR and JB by the Society for the Study of Addiction. RW has received travel funds and hospitality from, and undertaken research and consultancy for pharmaceutical companies that manufacture or research products aimed at helping smokers to stop. These products include nicotine replacement therapies, Champix (varenicline) and Zyban (bupropion). This has led to payments to him personally and to his institution.

Author contributions

EB, JB, SM and RW designed the study. EB wrote the first draft and conducted the analyses. All authors commented on this draft and contributed to the final version.

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Data sharing

For access to the Smoking Toolkit Study (STS) please contact Professor Robert West robertwest100@googlemail.com. R code for this paper is available at https://osf.io/yqaxm/. This code is licensed under a Creative Commons Attribution 4.0 International License. This paper should be acknowledged when used.

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Table 1: Use of treaments during a quit attempt over the study period

Treatment	4th quarter 2006	1st quarter 2015	Mean (SD)
Any medication on prescription (%)	11·0	11·9	16.4 (4·05)
NRT over-the-counter (%)	40·0	20·6	29.0 (5·44)
NRT on prescription (%)	8·5	5·6	8.9 (2·45)
Stop smoking services (n)	119986	122954	171130 (39795)

Note: NRT=nicotine replacement therapy; prescription medication=varenicline, NRT and bupropion; n=number; SD=standard deviation

Table 2: Estimated percentage point changes in the proportion of quitters who meet the criteria for quit success from the last quarter of 2006 until the 1st quarter of 2015, based on Autoregressive Integrated Moving Average with Exogeneous Input (ARIMAX) models

	Unadjusted[a]	Fully adjusted[a]	Unadjusted[b]	Fully adjusted[b]
	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *p*
Use of e-cigarettes by current smokers	0·042 (0·018 to 0·065) <0·001	0·058 (0·038 to 0·078) <0·001	NA	NA
Use of e-cigarettes in a quit attempt	NA	NA	0·076 (-0·002 to 0·155) 0·057	0·098 (0·064 to 0·132) <0·001
Mass media expenditure		0·059 (0·020 to 0·097) 0·003		0·063 (0·025 to 0·101) 0·001
	Total percentage change due to the exposure (95%CI) *p*	Total percentage change due to the exposure (95%CI) *p*		
Smoking ban (Temporary impact in the 3rd quarter of 2007)		0·022 (-0·224 to 0·268) 0·861		0·005 (-0·237 to 0·246) 0·969
Increase in age-of-sale (Temporary impact in the 4th quarter of 2007)		0·328 (0·081 to 0·574) 0·009		0·345 (0·105 to 0·585) 0·005
Move to local authority control (Temporary impact in the 2nd quarter of 2013)		-0·047 (-0·293 to 0·200) 0·712		-0·029 (-0·265 to 0·207) 0·808
Best fitting model	ARIMAX(0,1,1)(0,1,0)[4]	ARIMAX(0,1,1)(0,1,0)[4]	ARIMAX(0,1,1)(0,0,0)[4]	ARIMAX(0,1,1)(0,0,0)[4]
Non-seasonal (p)				
AR	NA	NA	NA	NA
MA	<0·001	<0·001	<0·001	<0·001
Seasonal (p)				
AR	NA	NA	NA	NA
MA	NA	NA	NA	NA
R-squared	0·26	0·55	0·23	0·57

Note: 95%CI=95% confidence interval; MA=moving average; AR=autoregressive; NA=not appropriate. See eTable Footnotes for details of a and b; column's 1 and 2 show the analysis of the impact of current e-cigarette use, while columns 3 and 4 show the impact of use of e-cigarettes during a quit attempt; MA and AR are types of autocorrelation. An AR(1) means that the value of a series at one point in time is the sum of a fraction of the value of the series at the immediately preceding point in time and an error component; while MA(1) means that the value of a series at one point in time is a function of a fraction of the error component of the series at the immediately preceding point in time and an error component at the current point in time.

Table 3: Estimated percentage point changes in the proportion of past-year smokers who attempted to quit from the last quarter of 2006 until the 1st quarter of 2015, based on Autoregressive Integrated Moving Average with Exogeneous Input (ARIMAX) models

	Unadjusted[a]	Fully adjusted[a]
	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *P*
Use of e-cigarettes[1,2]	0·023 (-0·037 to 0·083) 0·455	0·025 (-0·035 to 0·085) 0·409
Mass media expenditure		-0·008 (-0·039 to 0·022) 0·589
	Total percentage change due to the exposure (95%CI) *p*	Total percentage change due to the exposure (95%CI) *p*
Smoking ban (Temporary impact in the 3rd quarter of 2007)		-0·017 (-0·138 to 0·103) 0·777
Increase in age-of-sale (Temporary impact in the 4th quarter of 2007)		-0·037 (-0·159 to 0·083) 0·540
Move to local authority (Temporary impact in the 2nd quarter of 2013)		0·031 (-0·039 to 0·022) 0·565
Best fitting model	ARIMAX(0,1,0)(0,0,0)[4]	ARIMAX(0,1,0)(0,0,0)[4]
Non-seasonal (p)		
AR	NA	NA
MA	NA	NA
Seasonal (p)		
AR	NA	NA
MA	NA	NA
R-squared	0·52	0·53

Note: 95%CI=95% confidence interval; MA=moving average; AR=autoregressive; See eTable Footnotes for details of a; MA and AR are types of autocorrelation. An AR(1) means that the value of a series at one point in time is the sum of a fraction of the value of the series at the immediately preceding point in time and an error component; while MA(1) means that the value of a series at one point in time is a function of a fraction of the error component of the series at the immediately preceding point in time and an error component at the current point in time.

Table 4: Estimated percentage point changes in the proportion of smokers using stop smoking services and pharmacotherapy during a quit attempt from the last quarter of 2006 until the 1st quarter of 2015, based on Autoregressive Integrated Moving Average with Exogeneous Input (ARIMAX) models

	Stop smoking services		Prescription medication		Over-the-counter NRT		NRT on prescription	
	Adjusted for smoking prevalence[a]	Fully adjusted[a]	Unadjusted[b]	Fully adjusted[b]	Unadjusted[c]	Fully adjusted[c]	Unadjusted[d]	Fully adjusted[d]
	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *P*	Percentage change per percentage increase (95%CI) *P*	Percentage change per 1% change in the exposure (95%CI) *p*	Percentage change per 1% change in the exposure (95%CI) *P*
Use of e-cigarettes in a quit attempt	-0·012(-0·091 to 0·067) 0·765	-0·013 (-0·102 to 0·077) 0·784	-0·069 (-0·161 to 0·022) 0·136	-0·070 (-0·152 to 0·013) 0·097	-0·016 (-0·096 to 0·065) 0·704	-0·006 (-0·088 to 0·077) 0·893	-0·086 (-0·187 to 0·015) 0·097	-0·098 (-0·189 to -0·007) 0·035
Mass media expenditure		0·013 (0·005 to 0·021) 0.001		-0·013 (-0·015 to 0·041) 0·366		-0·008 (-0·053 to 0·037) 0·735		-0·051 (-0·107 to 0·006) 0·081
	Total percentage change due to the exposure (95%CI) *P*	Total percentage change due to the exposure (95%CI) *P*	Total percentage change due to the exposure (95%CI) *P*	Total percentage change due to the exposure (95%CI) *P*	Total percentage change due to the exposure (95%CI) *P*	Total percentage change due to the exposure (95%CI) *P*	Total percentage change due to the exposure (95%CI) *p*	Total percentage change due to the exposure (95%CI) *P*
Smoking ban (Temporary impact in the 3rd quarter of 2007)		-0·019 (-0·294 to 0·257) 0·893		0·173 (-0·097 to 0·442) 0·208		-0·128 (-0·344 to 0·087) 0·243		-0·193 (-0·133 to 0·519) 0.247
Increase in age-of-sale (Temporary impact in the 4th quarter of 2007)		0·011 (-0·219 to 0·238) 0·922		0·077 (-0·190 to 0·343) 0·573		-0·027 (-0·242 to 0·189) 0·809		-0·285 (-0·037 to 0·607) 0.083
Move to local authority (Temporary impact in the 2nd quarter of 2013)		0·034 (-0·162 to 0·230) 0·732		0·056 (-0·225 to 0·337) 0·697		-0·075 (-0·303 to 0·152) 0·516		0·102 (-0·217 to 0·421) 0.529
Best fitting model	ARIMAX(1,1,0)(0,0,1)[4]	ARIMAX(1,1,0)(0,0,1)[4]	ARIMAX(1,1,0)(0,0,0)[4]	ARIMAX(1,1,0)(0,1,1)[4]	ARIMAX(0,1,1)(0,0,0)[4]	ARIMAX(0,1,1)(0,0,0)[4]	ARIMAX(0,1,1)(0,0,0)[4]	ARIMAX(0,1,1)(0,0,1)[4]
Non-seasonal (p)								
AR	0·013	0·001	0·002	0·008	NA	NA	NA	NA
MA	NA	NA	NA	NA	<0·001	0·002	<0·001	<0·001
Seasonal (p)								
AR	NA	NA	NA	NA	NA	NA	NA	NA
MA	0·001	<0·001	NA	NA	NA	NA	NA	NA
R-squared	0·46	0·67	0·64	0·72	0·69	0·71	0·52	0·68

Note: 95%CI=95% confidence interval; MA=moving average; AR=autoregressive; See eTable Footnotes for details of a, b, c and d; ; MA and AR are types of autocorrelation. An AR(1) means that the value of a series at one point in time is the sum of a fraction of the value of the series at the immediately preceding point in time and an error c
MA(1) means that the value of a series at one point in time is a function of a fraction of the error component of the series at the immediately preceding point in time and an error component at the current point in time.

Figure 1: Quarterly prevalence of a) self-reported quit attempts, success of quit attempts and current electronic cigarette use in England and b) success of quit attempts and use of electronic cigarettes during a quit attempt in England.

Note: For a) Quit attempts a function of past year smokers; success of quit attempts a function of adults who smoked and tried to stop or who stopped in the past year; electronic cigarette use a function of current smokers. For b) Success of quit attempts and electronic cigarette use a function of adults who smoked and tried to stop or who stopped in the past year.

Figure 2: Quarterly prevalence of use of electronic cigarettes during a quit attempt and a) prescription medication during a quit attempt, b) NRT over-the-counter during a quit attempt, c) NRT on prescription during a quit attempt, and d) quarterly number of smokers setting a quit attempt at stop smoking services in England.

Figure 3: Changes in smoking prevalence and mass media expenditure over time, and the time points for the introduction of the relevant tobacco control polices.

Supplementary Appendix 1: Analysis and sample size

Analysis

The analysis plan was registered on the Open Science Framework on the 9th of October 2015 prior to data analysis (https://osf.io/fbgj2/). A change to the analysis plan was subsequently registered on the 21st of October 2015 (https://osf.io/7auns/). Use of the auto.arima [1] function in R produced models with higher-order moving average (MA) and autoregressive (AR) terms, which resulted in substantial overfitting; thus the decision was taken to use a non-automated procedure. The original plan had also been to assess the impact of the use of electronic cigarettes during a quit attempt on use of varenicline, buproprion and behavioural support + medication over the study period, but due to low statistical power it was decided to exclude these from the analysis. The mean(SD) use of varenicline was 5.8% (2.80), use of Bupropion was 1.8% (0.83) and use of behavioural support + medication on prescription was 0.9% (1.08) over the study period. On the 21st of Janurary 2016 (https://osf.io/5czbk/) a further amedenment was made to the protocol. Following the publication of a systematic review which suggested a negative impact of eletronic cigarette use on smoking cessation [2]; the decision was made to also assess the effect of electronic cigarette use on the success of quit attempts amongst smokers who reported having made a recent attempt to stop.

All data were analysed in R version 3.2.1 [3]. The analysis proceeded by first aggregating the STS data into quarters to reflect data collection from the stop smoking services. Data were only available on the prevalence of use of electronic cigarettes among smokers from April 2011 and use during a recent quit attempt from July 2009. Thus, prevalence of electronic cigarette use among smokers between July 2009 and April 2011 was estimated from data on use during a quit attempt; use of electronic cigarettes among smokers and as aids to a quit attempt between November 2006 and June 2009 was assumed to be 0.1% of smokers based on previous estimations [4,5].

Descriptive statistics are given for the outcomes of interest. All time series were then plotted to show the prevalence/frequency over time. Autoregressive Integrated Moving Average with Exogeneous Input (ARIMAX) analysis was used to estimate the effect of current electronic cigarette use among smokers on attempts to quit smoking, the success of those attempts, and the effect of electronic cigarette use as an aid to stopping smoking on the success of quit attempts, use of stop smoking services, use of prescription medication, use of NRT over-the-counter and use of NRT on prescription [6-8].

ARIMAX is an extension of autoregressive integrated moving average analysis (ARIMA), which produces forecasts based upon prior values in the time series (AR terms) and the errors made by previous predictions (MA terms). Such models have been used to explore the impact of tobacco price and mass media campaigns on smoking prevalence [7,9]. Standard recommended procedures were used to select the ARIMAX models [6,10]. The analysis proceeded by first assessing each time series for outlying values which may have biased the results, and then assessing the presence of exogeneity using the Granger Causality test. If the time-series were non-stationary, they were then differenced (i.e. the value of the series at each point in time was replaced by the value of the difference between that point and the value of the time series in the previous quarter) and log-transformed [11]. If there was significant autocorrelation at seasonal lags, the time series were also seasonally differenced. First differences' are the change between one observation and the next, while seasonal differences are the change between one year and the next. Plots of the differenced data and unit root tests (i.e. Osborn-Chui-Smith-Birchenhall test and Kwiatkowski, Phillips, Schmidt, and Shin (KPSS) test) were used to determine the number of differences required for the time series to be made stationary [12,13]. Price of cigarettes was correlated 0.99 with time and so was taken into account by use of differencing.

To identify the most appropriate transfer function for the continuous explanatory variables (i.e. to identify the manner in which past values of the electronic cigarette time series are used to forecast future values of the outcome) the sample cross-correlation function was checked for each ARIMAX model, with pre-whitened data [8]. Pre-whitening removes autocorrelation in the input series that may causes spurious cross-correlation effects and therefore aids interpretation. Additional checks were also run by comparing univariate ARIMAX models with variations for the transfer function.

First, models were run with the exogenous variable current electronic cigarette use or electronic cigarette use during a quit attempt. Smoking prevalence, estimated from the STS, was also included as an additional exogenous variable when assessing the impact on the number of smokers setting a quit date at the stop smoking services. This allows adjustment for the fact that any decline in frequency may reflect the overall decline over time in smoking prevalence. Following this, adjusted models were run with mass media expenditure as an exogenous variable and the various tobacco control policies as covariates.

To determine the initial values of the AR and MA terms for the baseline models, the autocorrelation function (ACF) and partial autocorrelation function (PACF) were assessed. Additional models with various fitted AR and MA terms were then compared to this baseline model using the Akaike information criterion (AIC). According to the Box-Jenkins method, in ARIMA (p, d, q) the value of p and q should be 2 or less or the total number of parameters should be less than 3 [6]. Therefore, we only checked ARIMAX models for p and q values of 3 or less. The models with lower AIC values were selected. Next the ACF for the residuals of the best fitting models were checked for additional correlation (thus the need for additional MA/AR seasonal or non-seasonal terms) and the coefficients of the correlation terms assessed for significance and whether they fell within the bounds of stationarity and invertibility [11,14].

The Ljung-Box test for white noise and plot of the ACF for model residuals were used to statistically evaluate the degree to which the residuals were free of serial correlation [15], and the final models residuals were assessed for normality. Coefficients are reported along with their 95% confidence intervals (95% CIs), and a pseudo-R-squared calculated as the squared correlation of fitted to actual values. STROBE guidelines were followed throughout [16].

Sample size

ARIMAX-based models assessing the association between two time-series are suitable for short-time series data so long as there are more observation periods than parameters [17]. Given our data are aggregated quarterly, even if we required 2 AR and 1 MA terms for the model and seasonality components, we would only need 12 quarters of data collection. Thus our 34 quarters from the STS and from the NHS SSS leaves enough degrees of freedom to include exogenous variables. These assumptions seem appropriate given that time series in the literature rarely contain AR or MA terms of an order higher than two [18,19].However, for interrupted time-series analyses the recommendation is that at least 50 time points of data are available [11]. Simulation studies predict that, on the basis of a 36 period time-series with one-third post-intervention and a small amount of autocorrelation [20], there would be 80% power to detect only a moderate effect size [21]. Thus caution should be taken when interpreting the findings for the dummy covariates reflecting the introduction of tobacco control policies.

Power analyses were carried out to compute a retrospective indication of the power of the study to detect a significant change, using the variance observed in the sample to calculate the minimum effect size that could be detected with statistical power of 80% [22].

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Supplementary Appendix 2: Footnotes for tables

Table 2

[a] Unit root tests and plots of the differenced time-series identified that first ordering non-seasonal differencing was required. Additional seasonal differencing resulted in an over-differenced series (negative lag-1 correlation greater than 0.5). The cross-correlation function suggested a (1,0) transfer function for mass media and (0,0) for e-cigarettes. Granger causality test was not violated. Plots of the ACF and PCAF cut off abruptly at lag 1, with both lag 1's being negative. Thus the baseline model was chosen to include 1 MA term [ARIMAX(0,1,1)(0,0,0)]. A number of additional models with non-seasonal AR and MA terms (a maximum of 3 terms in total) were also run. None of these models had lower AIC values. The plot of the residuals ACF and the Ljung-Box test for the models showed that there was no additional seasonal or non-seasonal autocorrelation. The model residuals were normally distributed. MA coefficients fell within bounds of stationarity and invertibility. i.e -1<coefficient<1. In sensitivity analyses, a significant positive association with mass media and e-cigarette use remained with (0,0) transfer functions in adjusted analyses.

[b] Unit root tests and plots of the differenced time-series identified that first ordering non-seasonal differencing was required. Additional seasonal differencing resulted in an over-differenced series (negative lag-1 correlation greater than 0.5). The cross-correlation function suggested a (1,0) transfer function for mass media and (1,0) for e-cigarettes. Granger causality test was not violated. Plots of the ACF and PCAF cut off abruptly at lag 1, with both lag 1's being negative. Thus the baseline model was chosen to include 1 MA term [ARIMAX(0,1,1)(0,0,0)]. A number of additional models with non-seasonal AR and MA terms (a maximum of 3 terms in total) were also run. None of these models had lower AIC values. The plot of the residuals ACF and the Ljung-Box test for the models showed that there was no additional seasonal or non-seasonal autocorrelation.

The model residuals were normally distributed. MA coefficients fell within bounds of stationarity and invertibility. i.e -1<coefficient<1. In sensitivity analyses, a significant positive association with mass media and e-cigarette use remained with (0,0) transfer functions in adjusted analyses.

Table 3

[a] Unit root tests and plots of the differenced time-series identified that first ordering non-seasonal differencing was required. Additional seasonal differencing resulted in an over-differenced series (negative lag-1 correlation greater than 0.5). The cross-correlation function suggested a (1,0) transfer function for mass media and (0,0) for e-cigarettes. Granger causality test was not violated. Plots of the ACF and PACF did not identify any significant lags. Thus the baseline model chosen was an [ARIMAX(0,1,0)(0,0,0)]. A number of additional models with non-seasonal AR and MA terms (a maximum of 3 terms in total) were also run. None of these models had lower AIC values. The plot of the residuals ACF and the Ljung-Box test for the models showed that there was no additional seasonal or non-seasonal autocorrelation. The model residuals were normally distributed.

Table 4

[a] Unit root tests and plots of the differenced time-series identified that 1^{st} ordering non-seasonal differencing was required. Additional seasonal differencing resulted in an over-differenced series (negative lag-1 correlation greater than 0.5). The cross-correlation function suggested a (3,0) transfer function for mass media, (0,0) for smoking, and (0,0) for e-cigarettes. Granger causality test was not violated. Plot of the ACF showed an exponential decline, while the PCAF cut off abruptly at lag 4 (with lag 2 non-significant). Thus the baseline model was chosen to include 1 AR term [ARIMAX(1,1,0)(0,0,0)]. A number of additional models with non-seasonal AR and MA terms (a maximum of 3 terms in total) were also run. Two models had lower AIC values: (1,1,2)(0,0,0) and (3,1,0)(0,0,0). The MA and AR terms all contributed significantly to these. However, these models were discarded as those with lower order terms did not provide a better fit and the AIC has a tendency to select overparameterized models. The plot of the residuals ACF and the Ljung-Box test for the models showed that there was some additional seasonal correlation. As the autocorrelation of the differenced series was positive at lags 4, 8 and 12, an SAR term was considered and contributed significantly to the models. However, this had the effect of knocking out the AR term and resulted in overfitting. Thus, a number of additional models with seasonal AR and MA terms (a maximum of 3 terms in total) were also run. Those models with lower AIC values and whose correlation terms were significant were considered as alternative models. A SMA term contributed significantly and was added to the final model. The MA and AR coefficients fell within bounds of stationarity and invertibility. i.e -1<coefficient<1 and the model residuals were normally distributed. In sensitivity analyses, smoking prevalence was included as an offset variable rather (coefficient fixed to 1) to ensure that there was a one-to-one relation between population size and stop smoking service use. This did not affect the findings for e-cigarette use: β-0.002, 95%CI -0.073 to 0.070 =0.962

[b] Unit root tests and plots of the differenced time-series identified that first ordering non-seasonal differencing was required. Additional seasonal differencing resulted in an over-differenced series (negative lag-1 correlation greater than 0.5). The cross-correlation function suggested a (3,0) transfer function for mass media and (0,0) for e-cigarettes. Granger causality test was not violated. Plots of the ACF declined exponentially, while the PCAF cut off abruptly at lag 1. Thus the baseline model was chosen to include 1 AR term [ARIMAX(1,1,0)(0,0,0)]. A number of additional models with non-seasonal AR and MA terms (a maximum of 3 terms in total) were also run. One model had a lower AIC value: (0,1,3)(0,0,0). The MA and AR terms all contributed significantly to this model. However, the model was discarded as those with lower order MA terms did not provide a better fit and the AIC has a tendency to select overparameterized models. The plot of the residuals ACF and the Ljung-Box test for the models showed that there was no additional seasonal or non-seasonal autocorrelation. The model residuals were normally distributed. AR coefficients fell within bounds of stationarity and invertibility. i.e -1<coefficient<1.

[c] Unit root tests and plots of the differenced time-series identified that first ordering non-seasonal differencing was required. Additional seasonal differencing resulted in an over-differenced series (negative lag-1 correlation greater than 0.5). The cross-correlation function suggested a (1,0) transfer function for mass media and (0,0) for e-cigarettes. Granger causality test was not violated. Plots of the ACF and PCAF cut off abruptly at lag 1, with both lag 1's being negative. Thus the baseline model was chosen to include 1 MA term

[ARIMAX(0,1,1)(0,0,0)]. A number of additional models with non-seasonal AR and MA terms (a maximum of 3 terms in total) were also run. None of these models had lower AIC values. The plot of the residuals ACF and the Ljung-Box test for the models showed that there was no additional seasonal or no-seasonal correlation The MA coefficients fell within bounds of stationarity and invertibility. i.e -1<coefficient<1 and the model residuals were normally distributed.

[d] Unit root tests and plots of the differenced time-series identified that first ordering non-seasonal differencing was required. Additional seasonal differencing resulted in an over-differenced series (negative lag-1 correlation greater than 0.5). The cross-correlation function suggested a (3,0) transfer function for mass media and (0,0) for e-cigarettes. Granger causality test was not violated. Plots of the ACF and PCAF cut off abruptly at lag 1, with both lag 1'sbeing negative. Thus the baseline model was chosen to include 1 MA term [ARIMAX(0,1,1)(0,0,0)]. A number of additional models with non-seasonal AR and MA terms (a maximum of 3 terms in total) were also run. None of these models had lower AIC values. The plot of the residuals ACF and the Ljung-Box test for the models showed that there was no additional seasonal or non-seasonal autocorrelation. The model residuals were normally distributed. MA coefficients fell within bounds of stationarity and invertibility. i.e -1<coefficient<1. In sensitivity analyses, a close to significant positive association with e-cigarette use remained with a (2,0) and (1,0) transfer function for mass media in adjusted analyses.

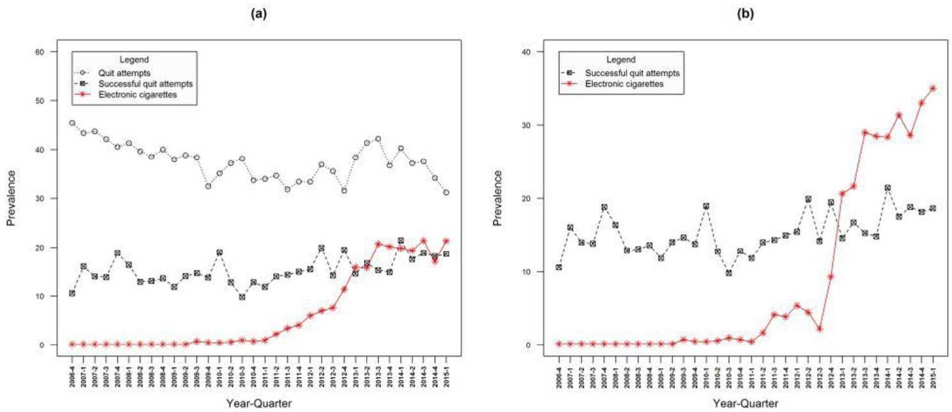

Figure 1: Quarterly prevalence of a) self-reported quit attempts, success of quit attempts and current electronic cigarette use in England and b) success of quit attempts and use of electronic cigarettes during a quit attempt in England.

Note: For a) Quit attempts a function of past year smokers; success of quit attempts a function of adults who smoked and tried to stop or who stopped in the past year; electronic cigarette use a function of current smokers. For b) Success of quit attempts and electronic cigarette use a function of adults who smoked and tried to stop or who stopped in the past year.

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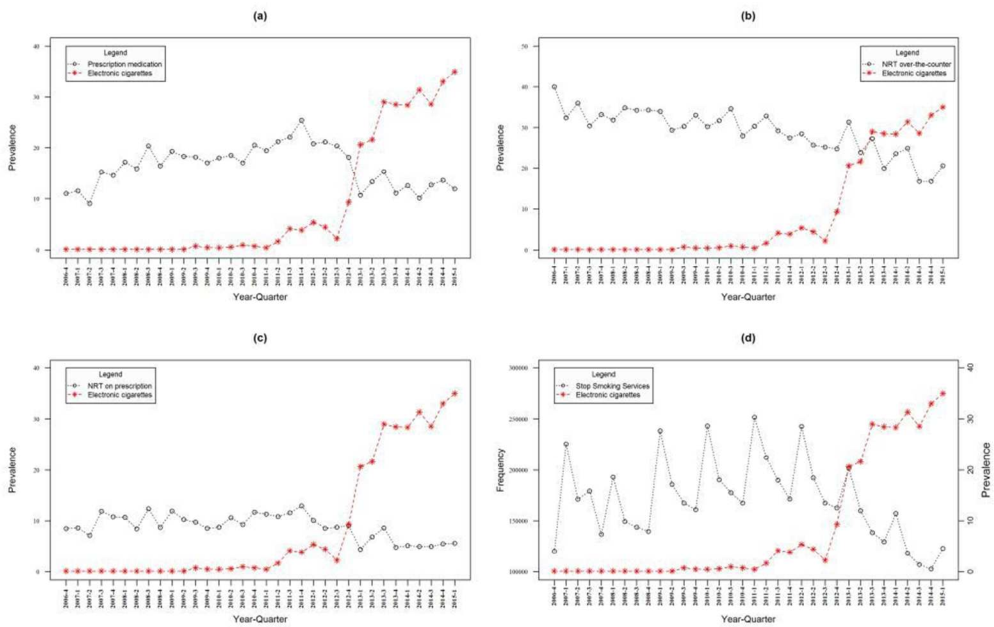

Figure 2: Quarterly prevalence of use of electronic cigarettes during a quit attempt and a) prescription medication during a quit attempt, b) NRT over-the-counter during a quit attempt, c) NRT on prescription during a quit attempt, and d) quarterly number of smokers setting a quit attempt at stop smoking services in England.

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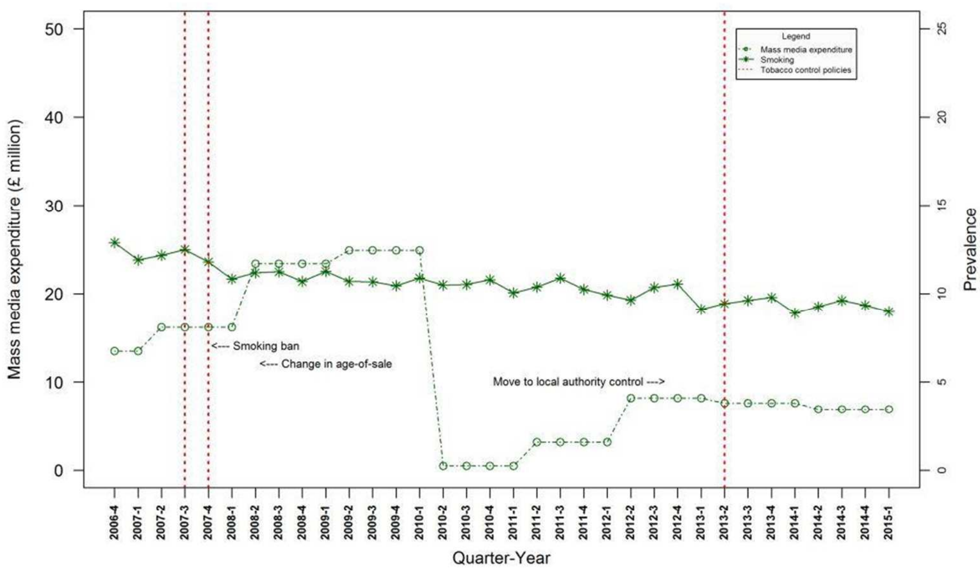

Figure 3: Changes in smoking prevalence and mass media expenditure over time, and the time points for the introduction of the relevant tobacco control polices.

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