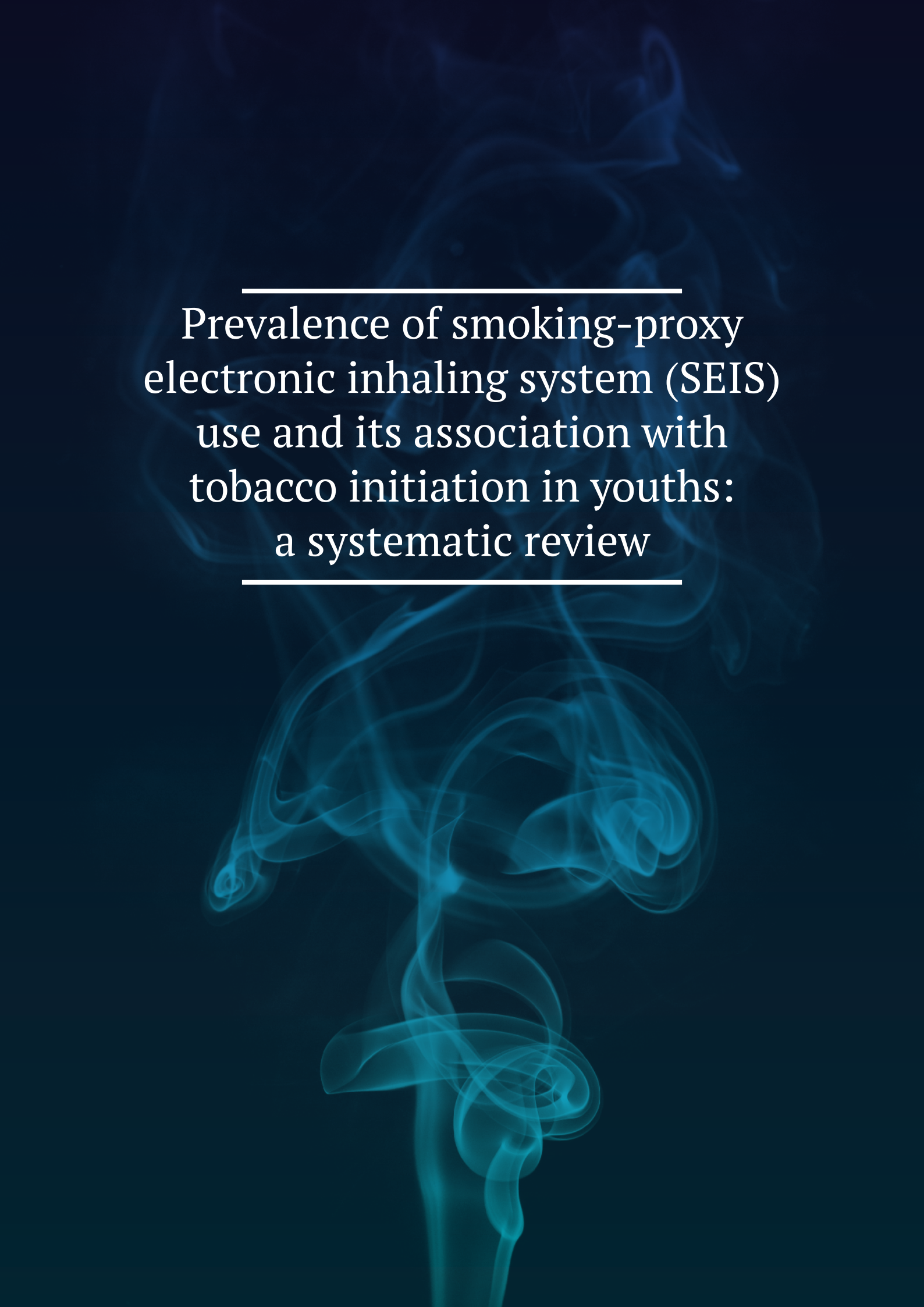
Prevalence of smoking-proxy electronic inhaling system (SEIS) use and its association with tobacco initiation in youths: a systematic review



Prevalence of smoking-proxy electronic inhaling system (SEIS) use and its association with tobacco initiation in youths: a systematic review

Prevalence of smoking-proxy electronic inhaling system (SEIS) use and its association with tobacco initiation in youths: a systematic review

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Declaration of conflict of interest

All authors declare no conflict of interest.

Executive summary

Background

Tobacco smoking remains a leading cause of death and disability worldwide. E-cigarettes (referred to here as smoking-proxy electronic inhaling systems, or SEIS) are marketed as having the potential to aid smoking cessation among current smokers, but may also be associated with increased likelihood of initiating tobacco smoking for non-smokers. A number of studies have suggested an increasing trend in SEIS use among youths, particularly among non-tobacco smokers. A positive association between SEIS use and tobacco use has been consistently reported in cross-sectional studies. To better understand the potential impact of SEIS use by young people, a synthesis of evidence regarding the prevalence and trends of SEIS use among this group is required, as is a synthesis of longitudinal data on the association between SEIS and future tobacco cigarette use.

Objectives

The objectives of the study are as follows:

1. To describe among young people (aged 10–20 years) the population prevalence and trends in prevalence of smoking-proxy electronic inhaling system (SEIS) use overall and among non-smokers and current smokers by country and by sex.

2. To synthesize findings from longitudinal studies of SEIS use by young people (aged ⩽ 20 years) and its association with initiation of tobacco cigarette use.

Methods

A systematic review of the peer-reviewed and grey literature was undertaken in December 2015. Studies were included for objective 1 if they described the prevalence of SEIS use in a general population sample of young people aged ⩽ 20 years in a defined geographical region using census or probability sampling. Studies where participants were recruited based on a specific health condition or as members of particular socioeconomic groups were excluded. There were no restrictions regarding the location of study, peer review status or language. A sensitivity analysis was undertaken including studies that did not include probability sampling but sampled for representativeness.

For objective 2, studies were included if they used a prospective longitudinal cohort design and assessed the association between SEIS use in young people aged ⩽ 20 years at baseline and later use of combustible tobacco products. There were no restrictions on study sampling or recruitment methods, location of the study, peer review status or language of publication.

A single-search strategy for both objectives was employed that encompassed electronic databases of peer-reviewed manuscripts, grey literature Google searches, hand searches of relevant reference lists and consultation with experts in the field. Screening and data extraction were undertaken by three reviewers for peer-reviewed research and one reviewer for grey literature.

For both objectives, data from included studies were combined using random effect meta-analyses. To provide estimates of the prevalence of SEIS use in the previous three years, pooled estimates of "ever use" or "use in last 30 days ('current use')" of SEIS are also reported from studies using data collected between 2013 and 2015. To describe trends in prevalence of SEIS use, changes in prevalence of "ever use" or "use in last 30 days" over time for all studies between 2008 and 2015 were pooled, and described narratively by country where multiple comparable prevalence estimates were available during this time. All analyses were repeated for both current and non-current cigarette smokers. This analysis was repeated in a sensitivity analysis including four additional studies that did not use probability sampling but had sampled to be representative of the population.

Results

Included studies

Objective 1. Overall, 2281 abstracts were screened (2246 electronic databases, 19 reports from the Google search and 16 reports from expert contacts). From these, 135 full texts were obtained for full-text screening, of which 28 publications reporting findings from 35 studies (each study represents a single survey) were included. An additional four publications reporting on findings from six studies were included in the sensitivity analysis. All studies utilized self-reported questionnaires to assess SEIS use. Eight of 32 studies satisfied seven of 10 quality assessment criteria, 17 satisfied five or six criteria, and seven satisfied three or four criteria. None of the studies reported on the reliability of the measures employed.

Objective 2. Overall, 2281 articles were screened and 119 full texts were obtained for further screening, with three studies being included in the final meta-analysis. All studies were undertaken in the United States of America. None of the studies were classified as having a sample representative of the target population and one study had a small sample of SEIS users at baseline (n=16). For all studies it was unclear whether the self-reported methods for collecting data on SEIS use and subgroup characteristics were reliable.

Overall prevalence of SEIS use among overall sample

(a) Ever use. The pooled estimate of the prevalence of SEIS ever use from 20 studies conducted between 2013 and 2015 was 16.4% (95% CI: 12.5–20.6%). Prevalence of ever use was 17.4% (95% CI: 10.9–25%) among males (from 14 studies) and 14.3% (95% CI: 8.7–21%) among females (from 14 studies). In the sensitivity analyses (23 studies), the prevalence of ever use was 16.1% (95% CI: 12.6–20.0%) overall, 19.3% (95% CI: 12.5–27.1%) among males and 15.5% (95% CI: 9.9–22.2%) in females (13 studies).

With one exception (Italy), for all five countries where multiple comparable prevalence estimates were available between 2008 and 2015, the prevalence of ever use increased over time (New Zealand, Poland, Republic of Korea, United States).

(b) Current use. The pooled estimate of the prevalence of current SEIS use from 19 studies conducted between 2013 and 2015 was 5.6% (95% CI: 3.4–8.3%). The prevalence of current use was 6.3% (95% CI: 3.7–9.6%) among males and 4.3% (95% CI: 2.4–6.8%) in females (12 studies). In the sensitivity analyses with an additional five studies (24 studies), the prevalence of SEIS ever use was 5.5% (95% CI: 3.5–7.9%) overall, 7.4 % (95% CI: 4.5–10.8%) among males and 4.9% (95% CI: 2.8–7.4%) in females (13 studies).

In three of the five countries where multiple comparable estimates of prevalence were available between 2008 and 2015, prevalence of current use increased (Poland, United Kingdom, United States). The prevalence of current SEIS use decreased in Hungary between 2012 and 2013, while the prevalence remained stable in Italy.

Prevalence among non-smokers

(a) Ever use. The pooled estimate of the prevalence of ever use among non-smokers from 13 studies conducted between 2013 and 2015 was 7.0% (95% CI: 5.1–9.3%). In the sensitivity analyses with an additional three studies, the prevalence of SEIS ever use was 6.4% (95% CI: 4.6–8.5%) among non-smokers.

Multiple estimates of prevalence over time in the United States indicated that ever use by non-smokers increased. In contrast, the prevalence of such use did not change in Italy.

(b) Current use. The pooled estimate of the prevalence of current SEIS use among non-smokers from nine studies conducted between 2013 and 2015 was 1.5% (95% CI: 0.3–3.5%). In the sensitivity analyses with an additional four studies (15 studies), the prevalence of SEIS ever use among non-smokers was 1.3% (95% CI: 0.4–2.8%).

Comparable estimates of prevalence of current use by non-smokers over time were available between 2008 and 2015 from three countries: Italy, Poland and the United States. In the United States, the prevalence of current use in non-smokers increased in both middle school- and high school-aged students between 2011 and 2014. In Poland, the prevalence of use increased, while in Italy prevalence was 0% across all periods of data collection.

Prevalence among current smokers

(a) Ever use. The pooled estimate of the prevalence of SEIS ever use among current tobacco smokers from 13 studies conducted between 2013 and 2015 was 54.7% (95% CI: 45.9–60.5%). In the sensitivity analyses with an additional two studies (15 studies), the prevalence of SEIS ever use was 53.2% (95% CI: 45.9 –60.5%) among current smokers.

In the United States, the prevalence of SEIS ever use among current tobacco smokers increased, while it remained stable in Italy.

(b) Current use. The pooled estimate of the prevalence of SEIS current use among current tobacco smokers from 10 studies conducted between 2013 and 2015 was 19.4% (95% CI: 8.3–33.5%). In the sensitivity analyses with an additional two studies (14 studies), the prevalence of SEIS ever use was 17.8% (95% CI: 8.8–28.9%).

Multiple comparable estimates of prevalence of SEIS use across 2008–2015 in Poland and the United States showed an increase in current use of SEIS among smokers. In Italy, prevalence remained stable.

Association between SEIS ever use and tobacco cigarette use

Three studies conducted in the United States were included in the analysis, with each study indicating that non-tobacco-smoking young people who were SEIS users were significantly more likely to be tobacco smokers at follow-up. Pooled analysis of the studies indicated that SEIS smokers at baseline had an increased adjusted odds ratio (AOR 2.19; 95% CI: 1.46–3.3%; $I^2 = 59.7\%$) of being a tobacco cigarette user at follow-up.

Conclusions

This systematic review and meta-analysis found substantial differences in prevalence and changes in prevalence of SEIS use by country. More than half of all young tobacco smokers in Canada, Ireland, New Zealand, the United Kingdom and the United States had ever used SEIS. Use of SEIS among young people was reportedly increasing in Poland and the United States but not in some other countries, for example Hungary and Italy. Pooled findings from two longitudinal studies indicated that the use of SEIS by non-smokers more than doubled the odds of tobacco smoking at follow-up.

Despite current low prevalence of SEIS use among non-smoking young people in most jurisdictions, the finding of a longitudinal association between SEIS use and subsequent tobacco use, and the increasing prevalence of SEIS use among non-smoking young people in some countries, supports the need for strategies to discourage SEIS uptake among non-smokers.

1. Background

Internationally, tobacco use is the leading cause of preventable death and disability *(1)*. The 2013 Global Burden of Disease Study reported that tobacco use accounted for 6.1 million deaths and 143.5 million disability-adjusted life-years globally *(2)*. While there is considerable between-country variation in the current prevalence of tobacco use, the global prevalence declined between 1980 and 2012 from 41.2% to 31.1% for men and 10.6% to 6.2% for women *(3)*. Globally, the largest annualized rate of change over this period occurred among those aged 15–19 years, where the rate declined by 1.8% each year *(3)*. Given the significant health and societal burden of tobacco use *(2)*, comprehensive strategies to prevent initiation and assist cessation have been recommended *(4)*.

There has been considerable debate about the potential role of e-cigarettes in addressing tobacco use, particularly among young people *(5, 6)*. Electronic cigarettes (referred to here as smoking-proxy electronic inhaling systems, or SEIS) are battery-operated devices designed to deliver a solution as an aerosol (or "vapour") typically made up of propylene glycol or glycerol (glycerine), nicotine, and flavouring agents, which is inhaled by users *(7)*. The devices are designed to simulate the act of smoking tobacco cigarettes to allow the consumption of nicotine without the burning of tobacco. SEIS has been primarily marketed as an alternative to combustible tobacco, as an aid to reduce or cease tobacco smoking or a means of using nicotine in smoke-free environments *(7)*. To date, the impact of SEIS in aiding smoking cessation is equivocal, with a recent Cochrane review reporting a small positive effect from only two randomized controlled trials *(8)*. Concerns regarding the long-term safety of the use of SEIS however have led to at least 55 countries introducing legislation or bans prohibiting or restricting the sale of SEIS *(9)*.

Since their introduction, the use of SEIS among young people has received considerable attention. A 2014 systematic review reported increasing use of SEIS among young people in countries such as Poland and the United States since 2011 *(10)*. Findings from the review highlighted some differences in patterns of SEIS use among young people compared to older individuals, with a significantly greater proportion of adolescent

SEIS ever users reporting no previous use of tobacco cigarettes. Similarly, a national study in Poland reported that over 20% of adolescent SEIS users were non-tobacco smokers *(11)*; and in some United States jurisdictions, SEIS use among adolescents exceeded traditional tobacco cigarette use *(12)*. While a small proportion of young adults report using SEIS to aid cessation *(13, 14)*, studies suggest that younger adults are more likely to use SEIS primarily for experimentation purposes *(10, 13)*.

The increasing rate of SEIS use among young people generally and among non-smokers in particular has led to concerns that SEIS use and particularly experimentation by young people could lead to nicotine dependence into adulthood and subsequent tobacco initiation *(15)*. The potential mechanisms driving this process are unknown, though a recent review proposed a number of hypothesized pathways that may account for the initial uptake of SEIS and the transition between SEIS experimentation and nicotine dependence *(16)*. To date, however, such concerns that SEIS use may lead to tobacco uptake have primarily been examined via cross-sectional studies. These studies reported positive associations between SEIS use and tobacco smoking behaviour among youths who had not previously used tobacco *(17–19)*. In the absence of longitudinal studies, such findings do not allow for the examination of causality and directionality (i.e. whether SEIS use leads to initiation of tobacco smoking).

A synthesis of the current prevalence and patterns of SEIS use among young smokers and non-smokers is needed to better understand the potential impacts of SEIS use on adolescent tobacco smoking behaviour. Further, a synthesis of longitudinal data regarding the association between SEIS and tobacco smoking by young people is needed to allow examination of the potential impact of SEIS use on subsequent tobacco smoking and other forms of combustible tobacco use. For the purpose of this systematic review, "young people" have been defined as those aged 10–20 years and "adolescents" have been defined as those aged 15–19 years, consistent with WHO definitions.

2. Objectives

The objectives of the study are as follows:

1. To describe among young people (aged ⩽ 20 years) the population prevalence and trends in prevalence of smoking-proxy electronic inhaling system (SEIS) use overall and among non-smokers and current smokers by country, sex and SEIS type.

2. To synthesize findings from longitudinal studies of SEIS use by young people (aged ⩽ 20 years) and initiation of tobacco cigarette use.

3. Methods

A systematic review of the peer-reviewed and grey literature was undertaken between August and December 2015. The review was conducted in accordance with the Cochrane Collaboration review methods and involved searching multiple electronic databases, using two independent reviewers, undertaking formal critical appraisal with the Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data *(20)*, and undertaking meta-analysis where appropriate.

3.1 Inclusion criteria

Objective 1. For this objective, studies were included if they described the prevalence of SEIS use in the general population within a defined geographical region (such as province, state or country). To be eligible studies needed to employ census or probability sampling methods, and report SEIS use in young people with a mean age of between 10 and 20 years. For studies that included those aged over 20 years, the study was included if a subgroup analysis of SEIS use among those aged ⩽ 20 years was reported. Studies reporting any measure of SEIS (e.g. self-reported, secondary (or proxy) reported or biochemical assessments) were included.

Studies using data from specialist panels (such as online research panels) or cohort studies that did not employ probability sampling procedures and recruitment procedures were excluded, regardless of whether population weights were applied to estimates of SEIS use. Probability sampling has been identified as an important requirement of quality prevalence studies *(21)*. Studies where participants were recruited based on a pre-existing disease or condition (e.g. mental health, hospital), or on the basis of specific socioeconomic characteristics (e.g. located in a lower socioeconomic region) and disease characteristics (e.g. patients with cardiovascular disease), were also excluded. Finally, non-databased publications that did not present new data (e.g. commentaries and opinion pieces) were excluded. There were no other restrictions regarding the location of the study, peer review status or language of publication.

Objective 2. For this objective, studies employing prospective longitudinal cohort designs that aimed to assess the association of SEIS use in young people and initiation of combustible tobacco products were included. Cross-sectional, case control and retrospective studies were excluded as they did not allow direct examination of causality, as were non-databased publications that did not present new data. To be eligible, longitudinal cohort studies needed to include non-smokers with a mean age of between 10 and 20 years at baseline and examine tobacco use at follow-up. Studies reporting any measure of SEIS use (e.g. self-reported, secondary (or proxy) reported or biochemical assessments) and that examined tobacco smoking use at follow-up were included. There were no other restrictions on study sampling or recruitment methods, location of the study, peer review status or the language of publication. No restrictions on sampling methods were employed for this objective as the primary aim was to assess association between baseline SEIS use and tobacco cigarette uptake.

3.2 Search strategy

A single-search strategy was employed to identify relevant peer-reviewed and grey literature for both objectives. The search encompassed electronic databases of peer-reviewed manuscripts, Google searches, hand searches and consultation with experts in the field.

- **Electronic databases.** A systematic search of the electronic databases MEDLINE, EMBASE, PsycInfo, Cochrane and CINAHL was undertaken by an experienced academic librarian. Search terms for SEIS were based on those used in previous systematic reviews of SEIS use *(8, 22)*. Broadly, the search terms included e-cig*, electronic nicotine*, electronic hookah* and e-hookah* as Medical Subject Headings (MeSH) terms. The full search string for each electronic database is provided in Annex 1.

- **Google search.** Searches were undertaken to identify potentially eligible reports, papers and conference abstracts for inclusion. The terms "electronic cigarette" and "ecigarette" were entered into separate Google.com searches. The results listed on the first 75 pages (750 hits) of each search were examined for relevant grey literature.

- **Hand searches.** Relevant references examining SEIS use in young people identified in the searches above were examined for potentially eligible studies for inclusion. The reference lists of all eligible studies were also screened for any additional studies potentially relevant to the objectives of this review.

- **Experts in the field.** Additional information about SEIS use in young people was sought from experts recommended by the Tobacco Unit of the World Health Organization and from selected authors who had published two or more relevant studies in the SEIS field. Experts were asked to identify any published or unpublished manuscripts (e.g. reports, papers, conference abstracts) or additional data relevant

to the report objectives. An email was sent to 15 experts on 31 August 2015. One respondent suggested an additional two experts be contacted and an email was sent to these experts on 11 September 2015. One respondent also contacted a further 13 experts on 13 September 2015. Given the rapid progress in the SEIS field, this process was repeated by sending another email to these experts on the 16 December 2015 asking whether they had any recent unpublished data that was relevant to this review. The experts were located in Australia, Canada, Germany, Italy, Romania, the United Kingdom and the United States.

3.3 Screening and data extraction

EndNote version X6.0.1 software (Thomson Reuters, PA, United States) was used to manage study inclusion and filter duplicate studies. SLY and LW[1] screened all databased results and FT screened all citations from the grey literature search. The full texts of all potentially eligible studies were obtained and study eligibility was determined based on assessment of the full text. Where eligibility was unclear, authors were contacted to request additional information. "Google translate" was used to assist with assessing the eligibility of non-English language manuscripts (*n*=25), which were all excluded prior to the full-text screening.

SLY, LW or LKC extracted the following information for all included studies in objective 1: author name, publication year, country of study, sample size, participant age range and sex, year of data collection, data collection modality, sampling procedures, measure of SEIS use, type of SEIS used (e.g. e-hookah), prevalence of SEIS use by sex, and prevalence of SEIS use among smokers and non-smokers (including *n*, percentages and 95% confidence intervals, where available) (see Annex 2). A consensus process was used to resolve any differences in extraction. Data for total denominators were also obtained from other sources (e.g. other references or raw datasets) to allow for inclusion in the meta-analysis. For objective 2, author last name, year of publication, participant characteristics (mean age), study design, country, sampling frame, outcomes, data collection modality, analyses, odds ratio and 95% CI, covariates adjusted for and follow-up time points were extracted by SLY. For the included studies, other supporting publications or reports (for example protocols, full descriptions of study methods from government websites) were also sought to obtain relevant information where the data from the primary study were absent or unclear. Data extraction was undertaken using prepiloted data extraction forms developed for the purpose of the study.

3.4 Critical appraisal

Two reviewers (MK and FT) independently undertook critical appraisal using the Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data *(20)*. The instrument contains 10 items examining the following study characteristics: sample representativeness, sampling methods, adequacy of sample size, participant and setting descriptions, coverage of sample, objectivity of criteria, reliability of measurement,

1 Authors' initials: see list of authors.

appropriateness of statistical analysis, confounding factors identified and accounted for, and objective classification of subpopulations (Yes; No; Unclear; and N/A). This tool has been found to have face validity and to be acceptable and easy to use *(23)*.

For objective 2, in addition to completing the Joanna Briggs Institute critical appraisal checklist for studies reporting prevalence data assessment *(20)*, the reviewers also examined the following study characteristics for the longitudinal studies: whether the outcome of interest (tobacco smoking) was absent at baseline, whether known confounders were adjusted for in the analysis, and whether there was appropriate treatment of missing data. For both objectives, where discrepancies in coding emerged between reviewers, inconsistent ratings were discussed between the reviewers until consensus was reached.

3.5 Data synthesis

All analyses were undertaken using Stata version 14 software (StataCorp, College Station, TX, United States) and the Metaprop and Metareg packages. For both objectives, main findings from the individual studies were also described narratively where relevant.

3.5.1 Objective 1

Data from included studies were combined using a random effect meta-analysis, weighted according to the inverse variance method. The Freeman-Tukey double arcsine transformation of prevalences was also used to allow for studies with prevalences that were close to zero. Exact 95% confidence intervals for the individual studies were computed.

Pooled estimates of SEIS ever use, and use in last 30 days ("current use"), were reported as stratified by country and sex (where available). Studies that included occasional users were pooled with ever users; and studies that reported regular use were pooled with last 30 days (or current use). Pooled estimates of ever and current SEIS use among non-smokers and smokers were also reported as stratified by country. Estimates of non-smokers included those not currently smoking (including ex-smokers) where available, and estimates of smokers included those reporting using any tobacco (including experimenters and occasional or current users) where available. Where prevalence of SEIS use by current smokers and non-smokers was not specifically reported, estimates of use were calculated using the following information provided in the original publications: number in total sample, prevalence of SEIS users, prevalence of smokers, and prevalence of concurrent SEIS and tobacco users. Estimates of regular/occasional use were available for four studies *(24–27)*. Where individual studies provided weighted and unweighted measures of SEIS prevalence, weighted estimates were used. Pooled estimates of prevalence are reported as an absolute percentage with 95% confidence intervals. Heterogeneity was assessed using the I-squared statistic and reported for each point estimate, together with the chi-square statistic from the likelihood ratio test comparing the random and fixed effects model, the estimated between-study variance and its test of significance. For pooled estimates of current or ever use, this analysis

was repeated in a sensitivity analysis, including studies that did not use probability sampling but attempted to sample in a way that was representative of the population.

To explore additional potential causes of heterogeneity, an exploratory meta-regression was performed with prevalence of ever and current SEIS use among young people overall and by smokers and non-smokers. Covariates included in this analysis included year of data collection, age, sex and country policies regarding the availability and marketing of SEIS to adolescents (classed as consumer product (no regulation), minimum age of purchase overall or banned overall), and MPOWER scores for 2014. Classification for SEIS regulation was made based on a previously published review examining SEIS policy internationally *(9)*. MPOWER scores (out of 100) for countries included in the review were provided by a representative from the World Health Organization. MPOWER scores were introduced following the WHO Framework Convention on Tobacco Control, and are calculated based on six measures that are considered central to tobacco control policies: taxes and pricing; advertising, promotion and sponsorship; protection against second-hand smoke; public warnings against the dangers of tobacco smoking; providing cessation support to those intending to quit; and monitoring policies *(1)*. The multivariable model that explained the most between-study variance was reported.

3.5.2 Objective 2

To assess whether use of SEIS at baseline was associated with cigarette use at follow-up, a random effects meta-analysis was undertaken with adjusted log odds ratios. The pooled estimates of the odds ratio with 95% confidence intervals were reported.

4. Results

4.1 Eligible studies and study characteristics

4.1.1 Objective 1

Overall, 2281 abstracts were obtained and screened (2246 electronic databases; 19 reports from the Google search and 16 reports from expert contacts). From these, 135 full texts where eligibility was unclear were obtained for full-text screening. Of these, 28 publications that reported findings from 35 studies (each study represents a single survey) were included in the final meta-analyses for at least one of the outcomes. Of those included in the full-text screening, studies were excluded because they examined SEIS use only in individuals aged > 20 (*n*=55), did not report on prevalence of SEIS use (*n*=4), did not use probability sampling (*n*=4), did not sample to be representative of the region (*n*=14), were not empirical studies (*n*=12), or included findings previously reported in other published papers (*n*=18) (Figure A4.1)[2]. The four studies that described population prevalence but did not use probability sampling were included as part of a sensitivity analysis.

The included publications were conducted in 11 high-income countries: the United States (national and subnational) (*n*=11) *(12, 19, 28–36)*, Republic of Korea (*n*=2) *(37, 38)*, New Zealand (*n*=2) *(26, 39)*, United Kingdom (Scotland and Wales) (*n*=2) *(27, 40)*, Poland (*n*=2) *(11, 41)*, Hungary (*n*=1) *(42)*, Canada (*n*=2) *(43, 44)*, Hong Kong Special Administrative Region (*n*=1) *(17)*, France (*n*=1) *(45)*, Ireland (*n*=1) *(24)*, Italy (*n*=1) *(25)*, Iceland (*n*=1) *(46)* and Greece (*n*=1) *(47)*. These studies were conducted between 2008 *(37)* and 2015 *(25)*, and sample size ranged from 99 *(39)* to 75 643 *(38)*. Two studies included both young people and adults as part of their sample but presented findings separately for young people (*n*=99 and *n*=160–163) *(25, 26)*. All studies reported estimates for young people under 20. All studies utilized self-reported questionnaires completed by participants administered via paper and pencil (*n*=23) *(11, 12, 17, 19, 24, 27–33, 36, 37, 39–42, 44–47)*, web (*n*=2) *(38, 48)*, telephone (*n*=1) *(43)* or face to face (*n*=2) *(25, 26)*. Studies either assessed ever use of SEIS (*n*=23) *(11, 24–31, 33, 35–41,*

2 Note: all figures are contained within Annex 4.

43–48) or use in past 30 days ("current use") (*n*=21) *(11, 12, 17, 24–33, 35, 36, 38, 40–43, 47)*. Four publications also reported regular or occasional use (see Annex 3 for measures) *(24–27)*. Dutra and Glantz *(19)* reported on the same dataset as Corey et al. *(31)* (United States National Youth Tobacco Survey 2012 and 2013), but presented findings by smokers and non-smokers. Overall prevalence was included in the meta-analysis only once for these studies. None of the studies examined types of SEIS used. Seventeen publications (reporting on 22 studies) *(11, 17, 19, 24, 25, 27, 30, 33, 37–42, 46, 47)* reported prevalence of SEIS use by current smokers and non-smokers, but none provided these estimates by sex. An additional four studies conducted in Switzerland *(49)* and the United Kingdom *(50–52)* were included in the sensitivity analyses. Study characteristics are reported in Table 1.

4.1.2 Objective 2

For objective 2, 2281 articles were screened and 119 full texts were obtained for further screening, with three studies meeting the eligibility criteria and included in the review (Figure A4.2) *(54–56)*. Studies included in the full-text screening were excluded primarily because they were cross-sectional studies, commentaries or reviews (*n*=79). Other reasons for exclusion included not examining SEIS use (*n*=5), conducted with adults (*n*=5), conference abstract of published data (*n*=1), and did not examine association with tobacco/cigarette smoking (*n*=26) (Figure A4.2). All included studies were undertaken in the United States and quantified participants' SEIS ever use via a single question. The mean age for two studies was 14 years and the other was 20 years. Study characteristics are reported in Table 2.

Table 1. Study characteristics of all included cross-sectional studies examining prevalence of SEIS use among young people (objective 1)

Note: Eastwood, 2015 *(50)*, Ford, 2016 *(52)*, Surís, 2015 *(49)*, and West, 2012 *(53)* (first authors' names) were included in sensitivity analyses and not main analyses.

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Alaska Department of Health and Social Services, 2015 *(35)*	United States (Alaska)	2015	Youth Risk Behaviour Survey	1 418	A nationally representative sample of public high schools in Alaska was scientifically selected	F: 50% M: 50%	grades 9–12	Questionnaire, pen and paper
Anand, 2015 *(28)*	United States (California)	2013	High School Questionnaire modelled after Monitoring the Future	2 769	All three high schools in north California were included in the study	F: 51.1% M: 48.9%	grades 9–12	Questionnaire, pen and paper
Arrazola, 2014 *(29)*	United States	2013	National Youth Tobacco Survey (NYTS)	18 406; 187 schools (74.8%)	A three-stage cluster sampling procedure to generate a cross-sectional, nationally representative sample of students in grades 6–12 from all states and the District of Columbia. A stratified cluster sample, designed to oversample non-Hispanic black and Hispanic students, was employed	F: 49% M: 51%	11–14 years (middle schools), 15–18 years (high schools)	Questionnaire, pen and paper

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Arrazola, 2015 *(12)*	United States	2014	National Youth Tobacco Survey (NYTS)	10 419 middle school students, 11 459 high school students	See Arrazola 2014	Not reported	11–14 years (middle schools), 15–18 years (high schools)	Questionnaire, pen and paper
Babineau, 2015 *(24)*	Ireland	2014	2014 Youth Perception of Plain Packaging Study, a nationally representative school-based survey of 16–17-year olds	821	A representative sample of secondary schools from around the country was selected for participation and stratified based on location, school type and size	F: 50.2% M: 49.8%	16–17 years	Questionnaire, pen and paper
Barnett, 2015 *(30)*	United States (Florida)	2013	2013 Florida Youth Tobacco Survey	12 615 students from 172 schools	The FYTS used a two-stage cluster probability sample design to obtain a random sample of public middle and high schools	F: 49% M: 51%	grades 6–12	Questionnaire, pen and paper
Cho, 2011 *(37)*	Republic of Korea	2008	2008 Health Promotion Fund Project in Republic of Korea	4 341	A cluster probability sample design was used. To distribute the districts evenly, five schools were chosen based on their geographical locations	F: 51.2% M: 48.8%	13–19 years	Questionnaire, pen and paper

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Corey, 2014 *(31)*	United States	2011, 2012	National Youth Tobacco Survey (NYTS)	18 866 (2011),[a] 24 658 (2012)	see Arrazola 2014	(2011) F: 49.4% M: 50.6% (2012) F: 48.9% M: 51.1%	11–14 years (middle schools), 15–18 years (high schools)	Questionnaire, pen and paper
Dautzenberg, 2013 *(45)*	France (Paris)	2012	Annual survey conducted by Paris San Tabac	2 519	Survey was conducted on 2% of students randomly selected by class and provided a representative sample of the 188 000 school children of Paris	F: 49.5% M: 50.5%	12–19 years	Questionnaire, pen and paper
Dutra, 2014 *(19)*	United States	2011, 2012	National Youth Tobacco Survey (NYTS)	17 353 (2011), 22 529 (2012)	See Arrazola 2014	F: 49.4% M: 50.6%	Grades 6–12	Questionnaire, pen and paper

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Eastwood, 2015 *(50)*	United Kingdom (England)	2013, 2014	YouGov 2013/2014	2 177 (2013), 2 068 (2014)	Individuals aged 16–18 were sampled directly from YouGov's online panel of people who had provided consent to be contacted and were sent an email invitation to take part. Individuals aged 11–15 were recruited via an email to parents or legal guardians from the YouGov panel, which asked them to read the information about the survey, and then pass the survey over to their child if they and their child agreed to take part. Those giving consent were asked to follow a link to the survey online	(2013) F: 52.3% M: 47.7% (2014) F: 51.1% M: 48.9%	11–18 years	Web-based questionnaire
Ford, 2016 *(52)*	United Kingdom	2014	Youth Tobacco Policy Survey (YTPS)	1 205	Using random location quota sampling, participants were drawn from 92 electoral wards across the United Kingdom, stratified by Government Office Region and A Classification Of Residential Neighbourhoods (ACORN)[b]	F: 50% M: 50%	11–16 years	Face to face

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Fotiou, 2015 *(47)*	Greece	2014	2014 Health Behaviour in School-aged Children Survey	1 320	A nationwide probability sample of students. Sampling units were school classes drawn by multistage clustered probability sampling from the Ministry of Education's complete listing. Sampling was proportional across school types and regions	F: 51.7% M: 48.3%	15 years	Questionnaire, pen and paper
Gallus, 2013 *(25)*	Italy	2013, 2014, 2015	Unspecified[c]	163 (2013), 153 (2014), 160 (2015)	An overall sample of 3 000 individuals aged ⩾ 15 years representative of the general Italian population aged 15 years and over was surveyed	(2013, 2014) F: 46% M: 54% (2015) F: 48% M: 52%	15–19 years[c]	Face to face
Goniewicz, 2012 *(41)*	Poland	2010–2011	Unspecified	13 787 from 144 schools and 32 universities	A three-stage stratified cluster sampling procedure, whereby schools and universities were treated as the primary unit, was used. Regions with a population of ⩽ 20 000 were excluded	F: 54.8% M: 45.2%	15–19 years	Questionnaire, pen and paper
Goniewicz, 2014 *(11)*	Poland	2013–2014	Unspecified	1 970	See Goniewicz, 2012; only students recruited from 21 schools across two regions in Poland were included in the 2014 comparison	Not reported	15–19 years	Questionnaire, pen and paper

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Hamilton, 2015 *(44)*	Canada (Ontario)	2013	2013 Ontario Student Drug Use and Health Survey	2 832	Stratified two-stage (school, class), two cluster design, students from 42 boards, 198 schools and 671 classrooms. Only half of the sample completed the e-cig part (grades 9–12)	F: 48% M: 52%	grades 9–12	Questionnaire, pen and paper
Hungarian Focal Point for Tobacco Control *(42)*	Hungary	2012, 2013	Global Youth Tobacco Survey	2 325 (2012); 4 108 (2013)	A two-stage stratified cluster sample design that produced samples of students in grades 7, 8 or 9 aged 13–15 years from all Hungarian schools	Not reported	13–15 years	Questionnaire, pen and paper
Johnston, 2015 *(32)*	United States	2014	Monitoring the Future: national survey result on drug use	41 600	A three-stage random sampling procedure used to secure the nationwide sample of students at each grade level from 420 schools	Not reported	13–18 years	Questionnaire, pen and paper
Kristjansson, 2015 *(46)*	Iceland	2015	Youth in Iceland Survey	3 477	Methods similar to the MTF survey and European School Project. The Youth in Iceland surveys are administered to all 10th grade students (ages 15–16 years) in Iceland by the Icelandic Centre for Social Research and Analysis at Reykjavik University	F: 50.8% M: 49.2%	15–16 years	Questionnaire, pen and paper

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Lee, 2014 *(38)*	Republic of Korea	2011	2011 Korean Youth Risk Behaviour Web Survey	75 643	A stratified multistage cluster sampling method was used. The survey was administered to 2 400 classrooms (secondary sampling units) consisting of all students in three classes from each of the 400 middle and 400 high schools (primary sampling units) from 129 strata	F: 47.3% M: 52.7%	13–18 years	Web-based questionnaire
Li, 2015 *(26)*	New Zealand	2014	Health and Lifestyles Survey (HLS)	2 594 but only 3.8% (n=99) were 15–17 years	A multistage, stratified, clustered and random probability sampling method, including an oversample of Māori and Pacific peoples. In 2014, New Zealand 2013 Census mesh blocks (i.e., the smallest geographical units for which the Census data are available) were used	F: 52.1% M: 47.9%	15–17 years	Face to face
Montana Office of Public Instruction, 2015 *(36)*	United States (Montana)	2015	Montana Youth Behavioral Risk Factor	4 486 students from 49 schools (78%)	All public schools in Montana with students in grades 9 through 12 were eligible to be selected for inclusion in the sample. Fifty-four schools were randomly selected with probability proportional to enrolment	F: 51.8% M: 48.2%	grades 9–12	Questionnaire, pen and paper

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Moore, 2015 *(27)*	United Kingdom (Wales)	2014	The Child Exposure to Tobacco Smoke (CHETS) survey undertaken in Wales (CHETS Wales 2) and the 2014 Welsh Health Behaviour in School-aged Children (HBSC) Survey (HBSC Wales)	1 495 (CHETS), 8 950 (HBSC Wales)	CHETS Wales 2 sampled from 75 primary schools. State-maintained schools with year 6 students were stratified according to high/low free school meal entitlement, and local education authority HBSC Wales sampled from 82 secondary schools. All maintained and independent secondary schools in Wales were stratified by local authority and eligibility for free school meals	(CHETS) F: 50.2% M: 49.8% (HBSC Wales) F: 50.1% M: 49.9%	10–11 years (CHETS), 11–16 years (HBSC Wales)	Questionnaire, pen and paper
NHS National Services Scotland, 2014 *(40)*	United Kingdom (Scotland)	2013, 2014	Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS)	33 685	The survey sampled pupils in high school (years 2 and 4) in Scotland. All local authority and independently funded schools with pupils in the target age groups were eligible for inclusion in the survey, with the exception of schools for children with special educational needs	F: 50% M: 50%	13, 15 years	Questionnaire, pen and paper

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Pepper, 2013 *(34)*	United States	2011	Knowledge Networks Knowledge Panel	228	A survey company constructed a national panel of United States households by using probability sampling. The survey company then randomly sampled panel members who were parents with sons aged 11–17 years. Parents who consented in 2010 to Wave 1 were recontacted in Wave 2, where their sons were invited to participate	F: 0% M: 100%	12–18 years	Web-based questionnaire
Porter, 2015 *(33)*	United States (Florida)	2011, 2012, 2013, 2014	Data are from the annual 2011–2014 Florida Youth Tobacco Survey (FYTS)	12 208 (2011),[d] 75 428 (2012), 69 923 (2014)	See Barnett 2015	F: 49.6% M: 50.4%	grades 6–12	Questionnaire, pen and paper
Reid, 2015 *(43)*	Canada	2013	Canadian Tobacco, Alcohol and Drugs Survey (CTADS)[e]	2 105	The sample design is a two-phase stratified random sample of telephone numbers. In the first phase, households are selected using random digit dialling. In the second phase, one or two individuals (or none) are selected based upon household composition	F: 49% M: 51%	15–19 years	Questionnaire, telephone

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
Surís, 2015 *(49)*	Switzerland	2014	Data were drawn from ado@internet.ch, a longitudinal study on Internet use based on a representative sample of students in the French-speaking part of Switzerland	621	A random sample of 35 schools were invited to participate in the ado@internet.ch study in 2012. A subsample from the ado@internet.ch study consented to being contacted and were followed up in this wave	F: 50.4% M: 49.6%	16.2 years	Web-based questionnaire
Wang, 2015 *(17)*	China (Hong Kong Special Administrative Region)	2012–2013	Questionnaire adapted from the Global Youth Tobacco Survey (GYTS)	45 128	School sampling was stratified by district, mixed/single sex education, financial support, and school type	F: 48.6% M: 51.4%	12–18 years	Questionnaire, pen and paper
West, 2012; Fidler, 2011 *(53, 51)*	United Kingdom (England)	2014, 2015	Smoking Toolkit Study	1 405 (2014),[f] 1 332 (2015)	Baseline surveys were conducted via monthly cross-sectional household computer-assisted interviews of approximately 1 800 adults aged 16 and over in England, using random location quota sampling, and stratification by A Classification Of Residential Neighbourhoods (ACORN) characteristics	Not provided	16–20 years[f]	Face to face

First author's last name, year	Country of data collection	Year of data collection	Survey name	*n*	Sampling frame	Sex (%)	Age range	Data collection modality
White, 2015 *(39)*	New Zealand	2012, 2014	Youth Insights Survey	3 127 (2012), 2 919 (2014)	A two-stage cluster sample design to obtain a nationally representative sample of New Zealand year 10 students was used	(2012) F: 49% M: 51% (2014) F: 49.8% M: 50.2%	14–15 years	Questionnaire, pen and paper

a. Data obtained from website. Centres for Disease Control and Prevention. Smoking and tobacco use: National Youth Tobacco Survey (NYTS). [Internet]. Centres for Disease Control and Prevention; 2015 [updated 2015 Sep 9; cited 2015 Oct 2]. Available from: http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/.

b. A geodemographic classification system that describes demographic and lifestyle profiles of small geographical areas.

c. Results of subgroup analyses provided by authors. Original publication: Gallus S, Lugo A, Pacifici R, Pichini S, Colombo P, Garattini S et al. E-cigarette awareness, use, and harm perceptions in Italy: a national representative survey. Nicotine and Tobacco Research. 2014;16(12):1541–8.

d. Data obtained from website. Florida Health. 2011 Florida Youth Tobacco Survey reports: Fact Sheet 3: Youth smokeless tobacco use. [Internet]. Florida Department of Health; 2015 [updated 2015 Sep 9; cited 2015 Oct 2]. Available from: http://www.floridahealth.gov/statistics-and-data/survey-data/fl-youth-tobacco-survey/_documents/2011-state/index1.html.

e. Data obtained from website. Government of Canada. Summary of results for 2013: Canadian Tobacco, Alcohol and Drugs Survey (CTADS). [Internet]. Government of Canada; 2015 [updated 2015 Feb 3; cited 2015 Oct 2]. Available from: healthycanadians.gc.ca/science-research-sciences-recherches/data-donnees/ctads-ectad/summary-sommaire-2013-eng.php.

f. Updated results for this subgroup (unpublished data) were provided by corresponding author. Original publication: Fidler JA, Shahab L, West O, Jarvis MJ, McEwen A, Stapleton JA et al. "The smoking toolkit study": a national study of smoking and smoking cessation in England. BMC Public Health. 2011;11(1):1–9.

Table 2. Study characteristics of all included studies for objective 2

First author's last name, year, country of data collection	Study design	*n*	Sampling frame	Sex (%)	Age, mean	Outcomes	Data collection modality	Follow-up time points	Covariates adjusted	Results
Leventhal, 2015, United States *(54)*	Longitudinal, prospective cohort study	2 502	Students in public high schools in the Los Angeles metropolitan area, chosen because of their diverse demographic characteristics and proximity	F: 53.2% M: 46.8%	14.06 years (95% CI: 14.04–14.07)	Use of cigarettes and other combustible nicotine products in the past six months	Surveys either in person, telephone or Internet	Six and 12 months	Sociodemographic (age, sex, race, higher parental education), environmental factors (living situation, peer smoking) and intrapersonal factors (mental health, personality traits, psychological process) associated with smoking, risky behaviour and smoking	SEIS ever users at baseline had significantly increased odds of using any combustible tobacco products (AOR 2.73; 95% CI: 2.00–3.73; $P \leqslant 0.001$) and cigarettes (AOR 1.75; 95% CI: 1.10–2.77; $P = 0.02$).
Primack, 2015, United States *(55)*	Longitudinal, prospective cohort study	694	Data collected from individuals that had been part of a large nationally representative United States study	F: 53.9% M: 46.1%	19.5 years (SD 2.0) for SEIS users; 20 years (SD 2.4) for non-users	Initiation of smoking	Telephone survey	12 months	Sociodemographic, personal and environmental variables including age, sex, race, maternal education, sensation-seeking tendency, parental smoking and peer smoking	Individuals who were non-susceptible non-smokers and SEIS ever users at baseline had significantly higher odds of using cigarettes at 12 months follow-up (AOR 8.3; 95% CI: 1.2–58.6)

First author's last name, year, country of data collection	Study design	*n*	Sampling frame	Sex (%)	Age, mean	Outcomes	Data collection modality	Follow-up time points	Covariates adjusted	Results
Wills, 2016, Hawaii, United States *(56)*	Longitudinal, prospective cohort study	1 302	Schools on the island of Oahu, Hawaii, were selected to be representative of school systems in Hawaii. Six of seven invited schools participated and students were invited to complete the survey	F: 53% M: 47%	14.7 years (SD 0.7)	Onset of smoking	Paper and pencil survey	12 months	The multivariable analyses controlled for demographics, parenting and personality variables and adjusted for clustering within schools	In an imputed analysis, ecigarette users at baseline had significantly increased odds of cigarette use at follow-up (AOR 1.67; 95% CI: 1.17–2.39; $P < 0.001$)

4.2 Risk of bias

4.2.1 Objective 1

Eight of 32 studies satisfied seven of 10 quality assessment criteria, 17 satisfied five or six criteria, and seven satisfied three or four criteria (Figure A4.3). For 22 of the 32 included studies, the study sample was deemed to be representative of the target population. For the majority of these studies, staged cluster sampling and statistical weights were used to ensure the sample was representative of the target population. For the remainder of the studies, sample representativeness was unclear as data weighting was not reported, nor was comparison made between the characteristics of the sample and the target population. Nineteen of the 32 studies described the study setting and the demographics of study subjects in enough detail for comparison to be made to other populations. For all studies apart from four, participant recruitment was rated as appropriate due to random sampling of clusters and participants. In addition, 25 of the 32 studies were deemed to have an adequate sample size. Twenty-two of the 32 studies undertook data weighting to correct for bias due to non-response and ensure sufficient coverage of the sample. For all studies excepted one, the objectivity of the measures was not reported. The reliability of the measures was not reported for all studies. All studies conducted appropriate statistical analysis based on the study aims. The majority (20 of 32) identified and accounted for important confounders and subgroups through regression analysis.

4.2.2 Objective 2

As shown in Figure A4.4, none of the longitudinal studies were classified as having a sample representative of the target population. All three studies described the study setting and the demographics of study subjects in detail. The precision of the prevalence estimates in Primack et al. *(55)* was limited by the small number of participants who reported SEIS use at baseline (n=16). For all studies it was unclear whether the self-reported methods for collecting data on SEIS use and subgroup characteristics were reliable. Also, while Leventhal et al. *(54)* reported that all measures used in the study had adequate psychometric properties, the validity of the measures used in Primack et al. *(55)* and Wills *(56)* was unclear. All studies conducted appropriate statistical analysis, accounting for important confounders associated with cigarette use, such as sex, age, ethnicity and smoking status of family and friends. Appropriately, all studies also used a multiple imputation approach to address attrition bias and examined association only in young people where tobacco smoking was absent at baseline.

4.3 Overall prevalence of SEIS use among young people (objective 1)

Prevalence of SEIS ever use between 2013 and 2015. The pooled estimate of the prevalence of SEIS ever use from 20 studies conducted between 2013 and 2015 was 16.4% (95% CI: 12.5–20.6%) (Figure A4.5). Among the 14 studies that reported data by sex, the prevalence was 17.4% (95% CI: 10.9–25%) among males and 14.3% (95% CI: 8.7–21%) in females (data not shown). In the sensitivity analyses (Figure A4.6), including

an additional three studies *(49, 50, 52)* that did not employ probability sampling (23 studies overall), the prevalence of SEIS ever use was 16.1% (95% CI: 12.6–20.0%) overall, 19.3% (95% CI: 12.5–27.1%) among males (13 studies) and 15.5% (95% CI: 9.9–22.2%) in females (13 studies).

Change in prevalence of ever use between 2008 and 2015. The pooled prevalence of SEIS ever use between 2008 and 2015 by country is shown in Figure A4.7. For four of the five countries where more than one comparable estimate of prevalence was provided over time, prevalence of ever use increased (see Figure A4.7). In the Republic of Korea, prevalence of ever use among 13–19-year-olds increased from 0.5% (95% CI: 0.3–0.8%) in 2008 to 9.4% (95% CI: 9.2–9.6 %) in 2011. In New Zealand, prevalence estimates in 14–15-year-olds increased from 7.0% (95% CI: 6.1–8.0%) to 20.0% (95% CI: 18.6–21.5%) between 2012 and 2014. In Poland, among 15–24-year-olds, prevalence estimates of ever use were 20.9% (95% CI: 20.2–21.6%) in 2010–2011 and 62.1% (95% CI: 59.9–64.2%) in 2013–2014 among 15–19-year-olds. Similarly, in the United States, in nationally representative samples, prevalence of ever use increased from 1.4% (95% CI: 1.2–1.7%) to 3.0% (95% CI: 2.6–3.4%) among middle school children and from 4.7% (95% CI: 4.3–5.1%) to 11.9% (95% CI: 11.3–12.5%) among high school students between 2011 and 2013. Multiple estimates of prevalence over time were also available for Italy, where no difference was observed at the multiple time points (9.2% (95% CI: 5.2–14.7%) in 2013 and 4.4% (95% CI: 1.8–8.8%) in 2015). Different measures however were used for the different data collection years (occasional use in 2014–2015 and ever use for 2013) in Italy.

Prevalence of SEIS current use between 2013 and 2015. The pooled estimate of the prevalence of current SEIS use from 19 studies conducted between 2013 and 2015 was 5.6% (95% CI: 3.4–8.3%) (Figure A4.8). Among the 12 studies that reported data by sex, the prevalence was 6.3% (95% CI: 3.7–9.6%) among males and 4.3% (95% CI: 2.4–6.8%) in females (data not shown). In the sensitivity analyses (Figure A4.9) with an additional five studies *(49–52)* (24 studies overall), the prevalence of SEIS ever use was 5.5% (95% CI: 3.5–7.9%) overall, 7.4 % (95% CI: 4.5–10.8%) among males (13 studies) and 4.9% (95% CI: 2.8–7.4%) in females (13 studies).

Change in prevalence of current use between 2008 and 2015. The pooled prevalence of current SEIS use between 2008 and 2015 by country is shown in Figure A4.10. In three of the four countries where multiple comparable estimates of prevalence were available over time, prevalence of current use increased. In Poland, data collected on 15–24-year-olds in 2010–2011 reported 8.2% (95% CI: 7.8–8.7%) current use, compared with 29.9% (95% CI: 27.9–32.0%) among adolescents aged 15–19 years in 2013–2014. In the United States, data from the National Youth Tobacco Survey reported that prevalence of current use increased from 0.6% (95% CI: 0.4–0.8%) in 2011 to 3.9% (95% CI: 3.5–4.3%) among middle school students and from 1.5% (95% CI: 1.3–1.8%) to 13.4% (95% CI: 12.8–14.0%) among high school students between 2011 and 2014. In Hungary, however, the prevalence of current use decreased from 13% (95% CI:

11.6–14.4%) in 2012 to 9.0% (95% CI: 8.1–9.9%) in 2013 among mainly young people aged 13–15 years. No changes were observed in Italy from 1.8% (95% CI: 0.4–5.3%) in 2013 to 1.3% (95% CI: 0.2–4.4%) in 2015 among adolescents aged 16–19 years.

4.4 Prevalence among non-smokers (objective 1)

Prevalence of SEIS ever use between 2013 and 2015. The pooled estimate of the prevalence of SEIS ever use among non-smokers from 13 studies conducted between 2013 and 2015 was 7.0% (95% CI: 5.1–9.3%) (Figure A4.11). In the sensitivity analyses with an additional three studies *(40, 50)*, the prevalence of SEIS ever use from 15 studies overall was 6.4% (95% CI: 4.6–8.5%) (Figure A4.12).

Change in prevalence of ever use between 2008 and 2015. The pooled prevalence of SEIS ever use among non-smokers between 2008 and 2015 by country is shown in Figure A4.13. National survey data of middle and high school students in the United States reported an increase in prevalence of SEIS ever use from 1.8% (95% CI: 1.6–2.0 %) in 2011 and 4.4% (95% CI: 4.1–4.6%) in 2012. There was no change in prevalence of ever use for Italy, where surveys of 16–19-year-olds reported prevalence of ever use of SEIS by non-smokers of 5.1% (95% CI: 2.1–10.3%) in 2013, 0.7% (95% CI: 0.0–3.9%) in 2014, and 1.4% (95% CI: 0.2–5.0%) in 2015.

Prevalence of SEIS current use between 2013 and 2015. The pooled estimate of the prevalence of current use among non-smokers from 11 studies conducted between 2013 and 2015 was 1.5% (95% CI: 0.3–3.5%) (Figure A4.14). In the sensitivity analyses with an additional four studies *(40, 50)* (15 studies overall), the prevalence of SEIS ever use was 1.3% (95% CI: 0.4–2.8%) (Figure A4.15).

Change in prevalence of current use between 2008 and 2015. The pooled prevalence of current SEIS use among non-smokers between 2008 and 2015 by country is shown in Figure A4.16. Multiple comparable estimates were available from three countries: Italy, Poland and the United States. In the United States, estimates from the state of Florida found prevalence of current use in non-smokers increased from 0.7% (95% CI: 0.5–1.0%) to 2.8% (95% CI: 2.6–3.0%) among middle school students, and from 0.8% (95% CI: 0.6–1.1%) to 6.9% (95% CI: 6.6–7.2%) among high school students between 2011 and 2014. In United States national samples, the prevalence of current SEIS use was 0.6% (95% CI: 0.5–0.7%) for 11–18-year-olds in 2011, and 1.1% (95% CI: 0.9–1.2) in 2012. In Poland, prevalence was 2.4% (95% CI: 2.1–2.7%) in 2010–2011 and 13.0% (95% CI: 11.2–15.0%) in 2013–2014. No changes were observed in Italy (0% (95% CI: 0.0–2.7%) in 2013, 0% (95% CI: 0.0–2.6%) in 2014, and 0% (95% CI: 0.0–2.6%) in 2015.

4.5 Prevalence among current smokers (objective 1)

Prevalence of SEIS ever use between 2013 and 2015. From the 13 studies conducted from 2013, the pooled estimate of SEIS ever use among current tobacco smokers was 54.7% (95% CI: 47.0–62.3%) (Figure A4.17). In the sensitivity analyses with an additional two studies *(50)* (15 studies overall), the prevalence of SEIS ever use was 53.2% (95% CI: 45.9–60.5%) (Figure A4.18).

Change in prevalence of ever use between 2008 and 2015. The pooled prevalence of SEIS ever use among current-smokers between 2008 and 2015 by country is shown in Figure A4.19. In Italy and the United States, multiple estimates of prevalence of SEIS ever use were provided over time. In the United States, among nationally representative samples of 11–18-year-old students, the prevalence increased from 28.1% (95% CI: 25.0–31.5%) in 2011 to 58.1% (95% CI: 54.8–61.4%) in 2012. In Italy no changes in estimates were observed in 2013 (29.6%; 95% CI: 13.8–50.2%), in 2014 (35.7%; 95% CI: 12.8–64.9%), and in 2015 (26.3%; 95% CI: 9.1–51.2%).

Prevalence of SEIS current use between 2013 and 2015. The pooled estimate of the prevalence of current SEIS use among current tobacco smokers from the 10 studies conducted from 2013 was 19.4% (95% CI: 8.3–33.5%) (Figure A4.20). In the sensitivity analyses with an additional two studies *(50)* (14 studies overall), the prevalence of SEIS ever use was 17.8% (95% CI: 8.8–28.9%) (Figure A4.21).

Change in the prevalence of current SEIS use between 2008 and 2015. The pooled prevalence of current SEIS use among current smokers between 2008 and 2015 by country is shown in Figure A4.22. For Poland and the United States, multiple comparable estimates of prevalence available across time showed an increase in current use of SEIS among smokers. In Poland, current use in adolescents increased from 15.3% (95% CI: 14.3–16.4%) in 2010–2011 to 57.4% (95% CI: 53.8–61.0%) in 2013–2014. In the United States, among nationally representative samples of 11–18-year-olds, the prevalence increased from 9.8% (95% CI: 7.8–12.1%) in 2011 to 26.5% (95% CI: 23.6–29.5%) in 2012. No changes in prevalence were observed in Italy between 2013 (11.1%; 95% CI: 2.4–29.2%), 2014 (7.1%; 95% CI: 0.2–33.9%) and 2015 (5.3%; 95% CI: 0.1–26.0%).

4.6 Exploring heterogeneity (for objective 1)

To explore reasons for the high observed heterogeneity (> 90%) in the pooled estimates of prevalence (between 2008 and 2015), a meta-regression including year of study, age range, regulation, sex and MPOWER score was undertaken for SEIS ever and current use. For prevalence of ever use, the multivariable model including all five covariates accounted for 44% of the observed heterogeneity, where age range ($P < 0.05$), regulation ($P < 0.05$) and year of data collection ($P < 0.001$) were significant. For current SEIS use, year of data collection ($P < 0.05$) and MPOWER score ($P < 0.05$) were significant, with the multivariable model including all five covariates accounting for 24% of the identified heterogeneity.

Among non-smokers and current smokers, sex was not included in meta-regression modelling due to lack of available data. For ever use among non-smokers, none of the variables were significantly associated with prevalence heterogeneity. For current SEIS use among non-smokers, year ($P < 0.05$), age ($P < 0.05$) and MPOWER score ($P < 0.05$) were significantly associated with prevalence heterogeneity and accounted for 40% of the identified heterogeneity.

Among current smokers, year ($P < 0.05$) and regulation ($P < 0.05$) were significantly associated with the heterogeneity observed in prevalence ever use, and the multivariable model including regulation, year and age accounted for the largest amount (52%) of heterogeneity. For current SEIS use among smokers, only MPOWER score was significant ($P < 0.01$), and the multivariable model including all four covariates (year, age, regulation and MPOWER score) explained 24% of the observed heterogeneity.

4.7 Objective 2

Three studies *(54–56)* conducted in the United States were included (see Table 2 for study characteristics). Leventhal and colleagues undertook a prospective longitudinal cohort study with 2530 14-year-old English-speaking adolescents, recruited from 10 demographically diverse schools in Los Angeles, who had never used any combustible tobacco products *(54)*. In a repeated measure using generalized mixed model analysis, including only non-tobacco users and adjusting for school, time (six and 12 months) and other potential demographic, environmental and personal covariates, those students who had ever used SEIS at baseline were significantly more likely to report using at least one puff of combustible tobacco products (described as use of a few puffs in the past six months) at 12 months follow-up (OR 2.73; 95% CI: 2.00–3.73; $P \leqslant 0.001$). This association was significant across the examined tobacco products: cigarettes (OR 1.75; 95% CI: 1.10–2.77, $P = 0.02$), cigars (OR 2.96; 95% CI: 2.00–4.38; $P \leqslant 0.001$) and hookah (OR 2.26; 95% CI: 1.56–3.29; $P \leqslant 0.001$).

Primack and colleagues *(55)* examined, in a national sample of individuals aged 16–26 years (mean age 19.5 years for SEIS users and 20 years for non-SEIS users), whether being a non-susceptible non-smoker (defined as those reporting that they definitely would not accept a cigarette from a friend and definitely would not smoke in the next year) who used SEIS at baseline (2012/2013) predicted higher experimentation of tobacco cigarette smoking at 12 months follow-up (2013/2014) *(55)*. In the primary analyses imputing for missing data (n=694), a multivariable multinomial logistic regression adjusting for sex, age, race, education level and sensation-seeking tendency found that individuals who smoked SEIS at baseline had significantly higher odds (AOR 8.3; 95% CI: 1.2–58.6%) of progressing from non-susceptible non-smoker to tobacco cigarette smoking one year post baseline. This finding was consistent across multiple sensitivity analyses undertaken by the authors.

Wills and colleagues *(56)* undertook a school-based survey with 9th and 10th grade students in Hawaii, United States, to examine whether, among never smokers, those

who had used e-cigarettes were more likely to have smoked cigarettes at 12-month follow-up. In the adjusted analysis imputing for missing data, individuals who were e-cigarette users at the first time point had an increased odds (AOR 1.67; 95% CI: 1.17–2.39) of smoking at follow-up.

Pooled analysis of the three studies indicated that SEIS smokers at baseline had an increased adjusted odds ratio (AOR 2.19; 95% CI: 1.46–3.3%; $I^2 = 59.7\%$) of being a tobacco cigarette user at follow-up (Figure A4.23).

5. Discussion and conclusion

5.1 Discussion

This review aimed to describe the prevalence and trends of SEIS use by young people aged between 10 and 20 years; and to examine the association between SEIS use and initiation of tobacco smoking in this group. To describe prevalence and trends, 28 eligible studies of SEIS use among youths that utilized probability sampling were identified. Three longitudinal studies were identified that examined associations between SEIS use and initiation of tobacco smoking.

The prevalence of SEIS use varied considerably within and between countries. Most recent estimates (2013 and 2015) show ever use of SEIS among non-smokers of 7% and prevalence of current use of less than 3%. Among smokers, in countries including Canada, Ireland, New Zealand, the United Kingdom and the United States, more than 50% of smokers had ever used SEIS, while in Poland, the Republic of Korea and the United States, over 20% were current users. Use of SEIS among smokers and non-smokers was reportedly increasing in Poland and in the United States but not for countries such as Italy, where current SEIS use remained relatively stable. In the sensitivity analyses, small increases in prevalence of SEIS current use among smokers and non-smokers were observed.

Observed differences between countries in prevalence and trends could potentially be attributed to differences in regulation governing the promotion of SEIS and their sale to young people. For example, the authors of the Polish studies suggested that the greater increase in SEIS use among Polish adolescents may be due to availability of SEIS in the market, more aggressive marketing of SEIS, and lower levels of regulation *(11)*. The increase in SEIS use has also coincided with reduced prevalence of current tobacco use globally *(12, 57)*. This has led to suggestions that smokers who have quit smoking may potentially be substituting tobacco smoking with SEIS. This review however found that a large proportion of young smokers were current SEIS users, suggesting that smokers may continue to use SEIS concurrently with traditional cigarettes. Findings from the meta-regression suggest that a number of factors, including MPOWER scores, time (year) and participant age, may be associated with prevalence heterogeneity of current/

ever e-cigarette use. These findings however need to be interpreted with caution, as there is likely to be other unmeasured confounders that have not been considered in this analysis. Further longitudinal research assessing the potential impact of MPOWER scores or policy regulation on SEIS use is probably needed to ascertain the impact of such strategies on prevalence of use in youths.

Pooled data from three longitudinal studies *(54, 55)* found that the use of SEIS by non-smokers more than doubled the odds of experimentation with tobacco smoking within 12 months. Although a number of design limitations exist, these findings support evidence from previous cross-sectional studies and provide early evidence of a positive association between SEIS use and intentions to try tobacco smoking *(17–19)*. The specific pathway by which SEIS use could lead to uptake of tobacco products is unknown. However, the enjoyment of the sensory tobacco-related cues associated with SEIS use (e.g. inhalation, exhalation) *(58)*, the pharmacological effects of consuming nicotine, and the biological and environmental vulnerability during youth and adolescence have been hypothesized to contribute to an increased inclination of SEIS users to try other nicotine-providing tobacco products *(59)*. Further, other researchers suggest that SEIS may act as catalyst, both in supporting initial initiation of SEIS use and facilitating transition to cigarette uptake *(16)*.

These findings need to be interpreted in light of the limitations of this review. First, all included studies utilized self-reported measures of SEIS use. To our knowledge, the validity of such assessment methods has not been established. Measures such as ever use and use in last 30 days may not provide an appropriate indication of established use behaviours *(60)*. Second, for assessment of current use, this review pooled a variety of measures, primarily "regular use" and "use in the last 30 days", which may have influenced prevalence estimates for some countries. Third, this study also examined tobacco use among non-smokers rather than never smokers. While it is likely that individuals with previous nicotine dependence may have been included, estimates of tobacco use among youths indicates that the majority of non-smoking youths (> 80%) have never smoked *(27, 61)*. Further, there was considerable variability in the definition of smokers in the included studies, which may have resulted in experimenters being classed as current smokers. Fourth, considerable and statistically significant heterogeneity was found among all pooled estimates presented in the review. For prevalence heterogeneity, the I^2 exceeded 70% for each case. None of the covariates examined in the meta-regression significantly accounted for the statistical heterogeneity observed in the meta-analyses of current SEIS use, suggesting that other personal or environmental factors may need to be considered. Finally, only three longitudinal studies were identified to examine associations between SEIS use by non-smokers and later initiation of tobacco. Further research is required to substantiate the findings of such studies.

5.2 Conclusion

Despite SEIS use among non-smoking young people remaining relatively low in most jurisdictions, the finding of a small but significant longitudinal association between SEIS use and tobacco use and of increasing prevalence of SEIS use among non-smoking young people in some countries supports the need for strategies to discourage SEIS use among non-smokers.

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Annex 1: Search terms employed in the electronic databases

CINAHL

#	Searches
S1	e-cig*
S2	electr* cig*
S3	(MH "Electronic Cigarettes")
S4	vaping
S5	"electronic nicotine"
S6	e-hookah*
S7	electronic hookah*
S8	e-nicotine
S9	**S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8**

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#	Searches
1	MeSH descriptor: [Electronic Cigarettes] this term only
2	e-cig*.mp
3	electr* cig*.mp
4	vaping.mp
5	electronic nicotine.mp
6	e-hookah*.mp
7	electronic hookah*.mp
8	e-nicotine.mp
9	**{or #1-#8}**

Database(s): Embase 1974 to 2015 Week 31

#	Searches
1	w-cig*.mp.
2	electr* cig*.mp.
3	vaping.mp.
4	electronic nicotine.mp.
5	e-hookah*.mp.
6	electronic hookah*.mp.
7	e-nicotine.mp.
8	electronic cigarette/
9	**1 or 2 or 3 or 4 or 5 or 6 or 7 or 8**

Database(s): MEDLINE 1946 to Present with Daily Update

#	Searches
1	e-cig*.mp.
2	electr* cig.mp.
3	Electronic Cigarettes/
4	vaping.mp.
5	electronic nicotine.mp.
6	e-hookah*.mp.
7	electronic hookah*.mp.
8	e-nicotine.mp.
9	**1 or 2 or 3 or 4 or 5 or 6 or 7 or 8**

Database(s): MEDLINE In-Process & Other Non-Indexed Citations

#	Searches
1	e-cig*.mp.
2	electr* cig*.mp.
3	vaping.mp.
4	electronic nicotine.mp.
5	e-hookah*.mp.
6	electronic hookah*.mp.
7	e-nicotine.mp.
8	electronic cigarette/
9	**1 or 2 or 3 or 4 or 5 or 6 or 7 or 8**

Database(s): PsycINFO 1806 to July Week 3 2015

#	Searches
1	w-cig*.mp.
2	electr* cig*.mp.
3	vaping.mp.
4	electronic nicotine.mp.
5	e-hookah*.mp.
6	electronic hookah*.mp.
7	e-nicotine.mp.
8	**1 or 2 or 3 or 4 or 5 or 6 or 7**

Annex 2: Data extraction form

(adapted from Cochrane data collection form for intervention reviews)

Citations	Author's name, publication year	
Study design	Country of study	
	Year of Data Collection	
	Type of study	
	Aims	
	Survey name/ database	
Sample (n)	Approached	
	Eligible	
	Consent	
	Analysed	
	Sampling frame, recruitment method (including sampling unit)	
Participants	Inclusion criteria	
	Exclusion criteria	
	Sex (%)	
	Age, mean (SD), range	
	Age range	
	Race/ethnicity	
	Socioeconomic status	
	Other relevant sociodemographic	
	Subgroups analysed by	
Data collection	Data collection modality	
	Measure used	
Measures	Outcomes (e.g. ever used, current use)	
	e-cigarette type (if specified)	
Total (Final sample)	n	
	Prevalence	
	Upper 95% CI	
	Lower 95% CI	

Male (Final sample)	n	
	Prevalence	
	Upper 95% CI	
	Lower 95% CI	
Female (Final sample)	n	
	Prevalence	
	Upper 95% CI	
	Lower 95% CI	
Other	Other results	
	Analysis and statistical adjustments	
	Notes	

Annex 3: Definition of e-cigarette or SEIS use within included studies

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Alaska Department of Health and Social Services 2015 Alaska Youth Risk Behavior Survey Results	Youth Risk Behaviour Survey	Percentage of students who ever used electronic vapor products (e-cigarettes, e-cigars, e-pipes, vape pipes, vaping pens, e-hookahs, and hookah pens such as blu, NJOY, or Starbuzz)	Percentage of students who currently used electronic vapor products (e-cigarettes, e-cigars, e-pipes, vape pipes, vaping pens, e-hookahs, and hookah pens such as blu, NJOY, or Starbuzz on at least 1 day during the 30 days before the survey)
Anand 2015 E-cigarette use and beliefs among urban public high school students in North Carolina	47-item "High School Questionnaire" 2013 modelled after Monitoring the Future with additional information	Have you ever used an e-cigarette? • Yes • No	When was the last time you used an e-cigarette? • Have never used an e-cigarette • Today
Arrazola 2014 Tobacco Use Among Middle and High School Students US 2013	2013 National Youth Tobacco Survey (NYTS)	Ever use of electronic cigarettes was determined by asking, "Which of the following tobacco products have you ever tried, even just one time: bidis, kreteks, hookah, snus, dissolvable tobacco, and electronic cigarettes?"	Current use of electronic cigarettes was determined by asking, "During the past 30 days, which of the following products have you used on at least 1 day- bidis, kreteks, hookah, snus, dissolvable tobacco, and electronic cigarettes?"
Arrazola 2015 Tobacco Use Among Middle and High School Students US 2011-2014	2014 National Youth Tobacco Survey (NYTS)	Not reported	During the past 30 days, on how many days did you use e-cigarettes such as Blu, 21st Century Smoke, or NJOY?

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Babineau 2015 Electronic cigarette use among Irish youth: a cross sectional study of prevalence and associated factors	2014 Youth Perception of Plain Packaging Study, a nationally representative school-based survey of 16-17 year olds	Respondents who selected one of the following as statement that best describes them: • I have tried an e-cigarette once or twice but don't use one regularly • I used to smoke e-cigarettes but have given up	Respondents who selected one of the following as statement that best describes them: • I smoke an e-cigarette at least once a month • I smoke an e-cigarette at least once a week • I smoke an e-cigarette every day.
Barnett 2015 Adolescent electronic cigarette use associations with conventional cigarette and hookah smoking	2013 Florida Youth Tobacco Survey	Have you ever tried, even once, electronic cigarette? • Yes • No	During the past 30 days, have you used an electronic cigarette? • Yes • No
Cho 2011 Electronic Cigarette smoking experience among adolescents	2008 Health Promotion Fund Project in Korea	Have you ever smoked a cigarette, even one or two puffs? • Yes • No	Not reported
Corey 2014 Electronic cigarette use among middle and high school students - United States, 2011-2012	Data are from the annual 2011-2012 National Youth Tobacco Survey (NYTS)	see Arrazola 2014	see Arrazola 2014
Dautzenberg 2013 E-cig : a new tobacco product for school children in Paris	2012 annual survey conducted by Paris San Tabac.	Have you ever used an e-cigarette? • Yes • No	Not assessed
Dutra 2014 Electronic cigarettes and conventional cigarette use among U.S. adolescents: a cross-sectional study	National Youth Tobacco Survey (NYTS)	see Arrazola 2014	see Arrazola 2014

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Eastwood 2015 Electronic cigarette use in young people in Great Britain 2013–2014	YouGov 2013/2014	You said that you have tried an e-cigarette… Which ONE of the following BEST applies to you? • I tried smoking a real cigarette before I first tried using an e-cigarette • I tried using an e-cigarette before I first tried smoking a real cigarette • I have never smoked a real cigarette but have tried an e-cigarette • I don't remember	Those who had heard of e-cigarettes were then asked to describe their experience of e-cigarettes with options range from 'never use' to 'more than once a week'. The following responses were categorised as 'monthly or more users': • I use them sometimes (more than once a month) • I use them often (more than once a week)
Fidler 2011 The smoking toolkit study': a national study of smoking and smoking cessation in England	Smoking Toolkit Study	Not assessed	Other than yourself, does anyone regularly smoke cigarettes or use an e-cigarette in your presence, such as at your home, work, car or other places that you visit regularly? • Yes – cigarettes only • Yes – e-cigarettes only • Yes – both cigarettes and e-cigarettes • No – neither cigarettes nor e-cigarettes

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Ford 2016 Adolescents' responses to the promotion and flavouring of e-cigarettes	Youth Tobacco Policy Survey (YTPS)	Ever smokers included those who indicated being regular smokers (at least one cigarette a week), occasional smokers (less than one a week), those who used to smoke and those who had tried smoking only once. Which of these best describes whether or not you have ever used or tried e-cigarettes? • I have never used e-cigarettes • I have only ever tried e-cigarettes once or twice • I have used e-cigarettes in the past, but I never use them now • I occasionally use e-cigarettes (less than once a month) • I use e-cigarettes at least once a month • I use e-cigarettes at least once a week	Not assessed
Fotiou 2015 Prevalence and correlates of electronic cigarette use among adolescents in Greece: a preliminary cross-sectional analysis of nationwide survey data	2014 Health Behaviour in School-aged Children Survey (HSBC)	Have you ever used an electronic cigarette? • Never • Yes • Only 1-2 times • Yes more than twice • Yes more than twice and I use it now	Have you ever used an electronic cigarette? • Never • Yes • Only 1-2 times • Yes more than twice • Yes more than twice and I use it now

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Gallus 2014 E-Cigarette Awareness, Use, and Harm Perceptions in Italy: A National Representative Survey Additional analyses from author	Structured questionnaire in the context of a computer assisted personal in-house interview in 2013-2015.	Have you ever heard about e-cigarettes, have you ever tried them or do you have the intention to try them? • I heard about e-cigarettes and I tried them. Participants reporting they "have heard about e-cigarettes and have tried them" were labelled as "ever users" of e-cigarettes.	Do you use, occasionally or regularly, the e-cigarette? • Yes, occasionally • Yes, regularly • I used it in the past • No Those who responded yes regularly were classed as current users
Goniewicz 2012 Electronic Cigarette Use Among Teenagers and Young Adults in Poland	The data was collected as part of a national survey on water pipe smoking in 2010-2011, and 2013-2014. Name of survey was unspecified.	Have you ever heard about electronic cigarettes (e-cigarettes)? • Yes • No Have you ever used an e-cigarette? • Yes • No	Have you used an e-cigarette at least once in the previous 30 days? • Yes • No
Goniewicz 2014 Rise in Electronic Cigarette Use Among Adolescents in Poland	The 2012 and 2011 data was subsample of 2 of the regions included as part of a national survey on water pipe smoking. Name of survey was unspecified. Data for 2013-2014 were collected from the same 2 regions.	Students were asked whether they had ever smoked or puffed on e-cigarettes (even a single puff).	Students were asked whether they had currently (in the past 30 days) smoked or puffed on e-cigarettes (even a single puff).

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Hamilton 2015 Waterpipe use among high school students in Ontario: Demographic and substance use correlates	2013 Ontario Student Drug Use and Health Survey	Have you ever smoked at least one puff from an electronic cigarette? • Smoking an e-cigarette with nicotine • Smoking an e-cigarette without nicotine • Never smoked but have heard of e-cigarettes • Never heard of e-cigarettes	Not assessed
Hungarian Focal Point for Tobacco Control. Hungarian and Foreign Data & Statistics: Global Youth Tobacco Survey	Global Youth Tobacco Survey	Not assessed	Those who smoked e-cigarette during the past 30 days
Johnston 2014 Key Findings on Adolescent Drug Use	Monitoring the future: National survey 2014 result on drug use	Not reported	Prevalence of use in the prior 30 days.
Kristjansson 2015 E-cigarette use and relations to tobacco and alcohol use among adolescents	Youth in Iceland Survey	Not reported	Not assessed
Lee 2014 Electronic Cigarette Use Among Korean Adolescents: A Cross-Sectional Study of Market Penetration, Dual Use, and Relationship to Quit Attempts and Former Smoking	2011 Korean Youth Risk Behaviour Web-Survey	Have you ever used an e-cigarette? • Yes • No	Have you used e-cigarettes in the past 30 days? • Yes • No

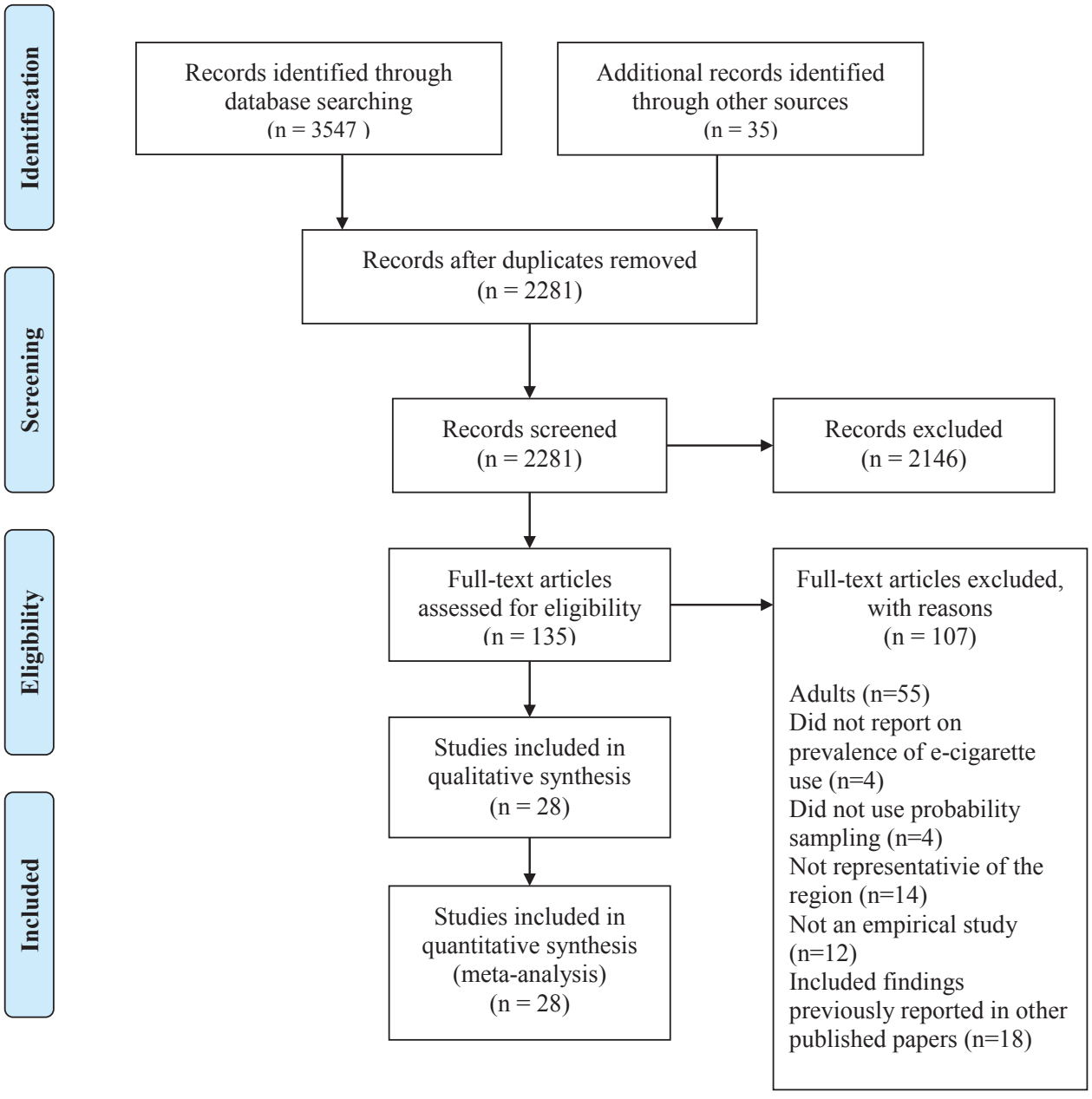
Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Li 2015 The prevalence, correlates and reasons for using electronic cigarettes among New Zealand adults	2014 Health and Lifestyles Survey (HLS)	Have you ever tried an electronic cigarette? • Yes • No	Which best describes how often you use an electronic cigarette now? • At least once a day • At least once a week • At least once a month • Less often than once a month • Do not use one now Current use was defined as at least once a month.
Montana Office of Public Instruction 2015 Montana Youth Risk Behaviour Survey High School Results	Montana Youth Behavioural Risk Factor	Electronic vapor products, such as blu, NJOY, or Starbuzz, include e-cigarettes, e-cigars, e-pipes, vape pipes, vaping pens, e-hookahs, and hookah pens. Have you ever used an electronic vapor product? • Yes • No	Electronic vapor products, such as blu, NJOY, or Starbuzz, include e-cigarettes, e-cigars, e-pipes, vape pipes, vaping pens, e-hookahs, and hookah pens. During the past 30 days, on how many days did you use an electronic vapor product? • 0 days • 1 or 2 days • 3 to 5 days • 6 to 9 days • 10 to 19 days • 20 to 29 days • All 30 days

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Moore 2015 Electronic-cigarette use among young people in Wales: evidence from two cross-sectional surveys	Data from two data sets: the CHild Exposure to Tobacco Smoke (CHETS) survey undertaken in Wales ('CHETS Wales 2') in 2014; and 2014 Welsh Health Behaviour in School-aged Children (HBSC) Survey ('HBSC Wales').	In CHETS Wales 2, children were asked if they had ever used an e-cigarette, with response options of: • 'no'; 'yes, once'; or • 'yes more than once'. In HBSC Wales, young people were asked if they had ever used an e-cigarette, with at least once a month response options of: 'I have never used or tried e-cigarettes'; 'I have used e-cigarettes on a few occasions (1–5 times)'; or 'I regularly use e-cigarettes (at least once a month)'	Those who selected using cigarettes at least once a month were classed as regular users
National Services Scotland 2014 Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS): SMOKING Among 13 and 15 year olds in Scotland 2013	2013/2014 Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS)	An electronic cigarette (sometimes called an 'e-cigarette') is a tube that can look like a normal cigarette, can have a glowing tip and puffs a vapour that looks like smoke but unlike normal cigarettes, they don't burn tobacco. Now read the following statements carefully and cross the box next to the ONE which best describes you • I have never used an e-cigarette • I used to use e-cigarettes but don't use them anymore • I have tried an e-cigarette once • I have tried e-cigarettes a few times	An electronic cigarette (sometimes called an 'e-cigarette') is a tube that can look like a normal cigarette, can have a glowing tip and puffs a vapour that looks like smoke but unlike normal cigarettes, they don't burn tobacco. Now read the following statements carefully and cross the box next to the ONE which best describes you • I use e-cigarettes sometimes, but no more than once a month • I use e-cigarettes more than once a month, but less than once a week • I use e-cigarettes once a week or more

Citation	Survey name/ Database	Ever e-cigarettes user measure	Current e-cigarettes user measure
Pepper 2013 Adolescent males' awareness of and willingness to try electronic cigarettes	Knowledge Networks' Knowledge Panel	Have you ever used an e-cigarette? • Yes • No	Not assessed
Porter 2015 Electronic cigarette and traditional cigarette use among middle and high school students in Florida, 2011-2014	Data are from the annual 2011–2014 Florida Youth Tobacco Survey (FYTS)	Have you ever tried once using electronic cigarettes? • Yes • No	During the past 30 days have you used an electronic cigarette? • Yes • No
Reid 2015 Tobacco Use in Canada: Patterns and Trends, 2015 Edition.	2015 Canadian Tobacco, Alcohol and Drugs Survey (CTADS)	Have you ever tried an electronic cigarette, also known as an e-cigarette? • Yes • No	In the past 30 days did you use an electronic cigarette, also known as an e-cigarette? • Yes • No
Surís 2015 Reasons to use e-cigarettes and associations with other substances among adolescents in Switzerland	Data were drawn from ado @ internet.ch, a longitudinal study on Internet use based on a representative sample of students in the French- speaking part of Switzerland.	Have you ever tried electronic cigarettes? • Never • Only once • Several times • Regularly Those who selected 'only once' were classed as experimenters.	Have you ever tried electronic cigarettes? • Never • Only once • Several times • Regularly Those who selected 'several times' and 'regularly' were classed as users.
Wang 2015 Electronic cigarette use and its association with smoking in Hong Kong Chinese adolescents	A 2012-2013, anonymous, self-administered questionnaire in Chinese adapted from the Global Youth Tobacco Survey (GYTS) (The GTSS Collaborative Group, 2006)	Not assessed	Only one questions on e-cigarettes use in the past 30 days (yes vs no) was used. No levels of use were specified and students were expected to report any use including even 1 puff.
White 2015 Tripling Use of Electronic Cigarettes Among New Zealand Adolescents Between 2012 and 2014	2012 & 2014 The Youth Insights Survey	Have you ever tried electronic cigarettes? • Yes • No	Not assessed

Annex 4: List of Figures

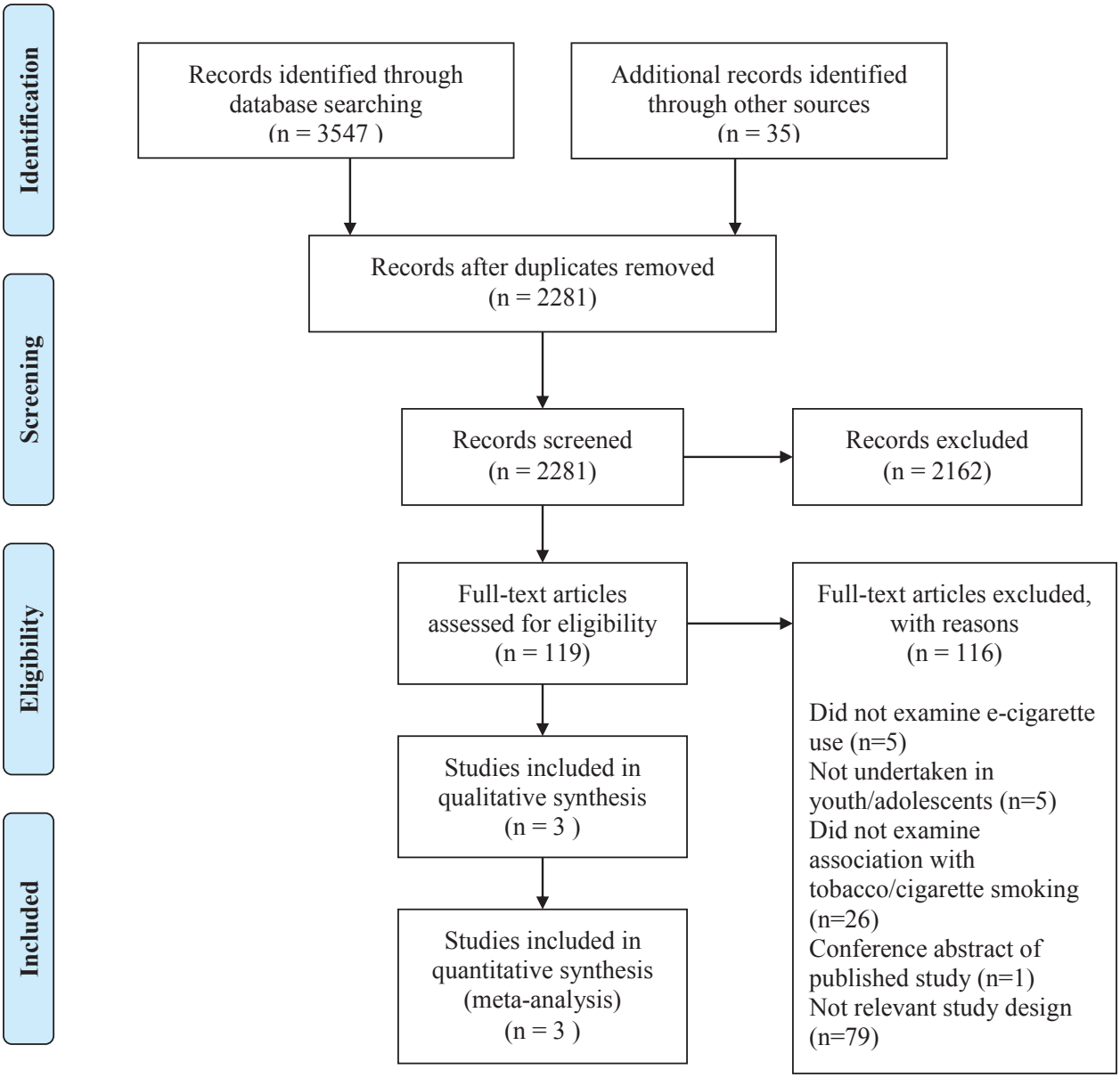
Figure 1: PRISMA diagram outlining study selection for prevalence of e-cigarette use (Objective 1)



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

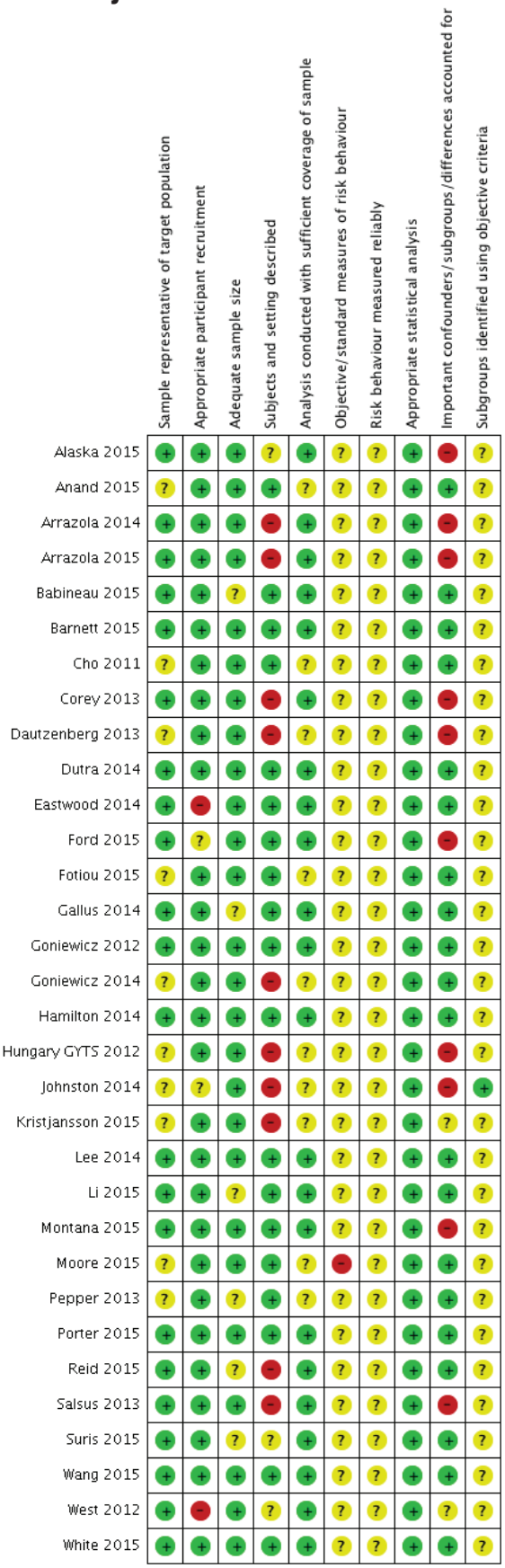
Figure 2: PRISMA diagram outlining study selection for association of e-cigarette use and tobacco uptake (Objective 2)



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Figure 3: Quality assessment for individual cross-sectional studies included for Objective 1



*Eastwood 2014, Ford 2015, Suris 2015, West 2012 were included in the sensitivity analyses.

Figure 4: Quality assessment for individual longitudinal studies included for Objective 2

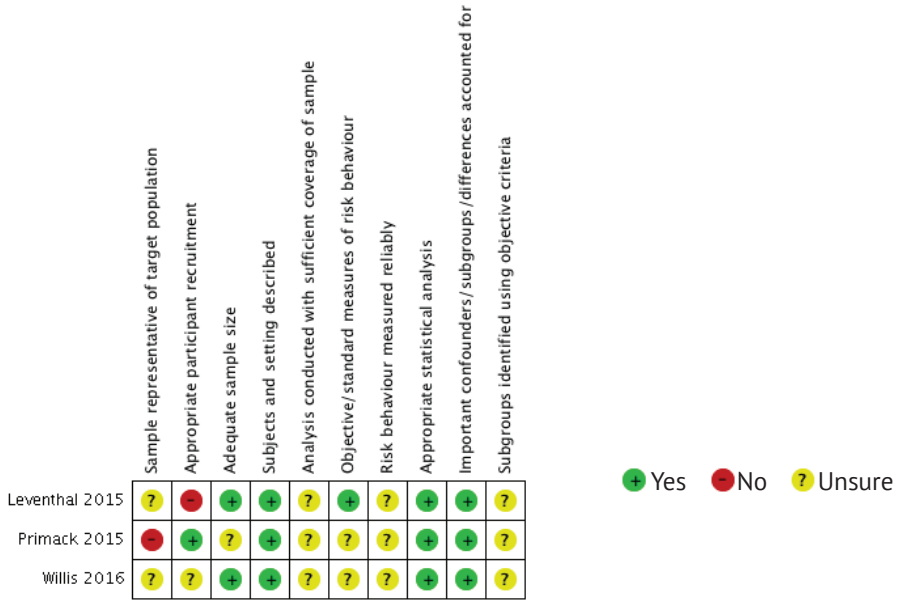


Figure 5: Pooled analysis of ever e-cigarette use among youth from 2013-2015

Author	Country	Data collection	Age range	N	Outcome (n)	ES (95% CI)
Reid	Canada	2013	15-19	16586	3284	19.8 (19.2, 20.4)
Gallus	Italy	2013	16-19	163	15	9.2 (5.2, 14.7)
Anand	US (California)	2013	15-18	2769	421	15.2 (13.9, 16.6)
Barnett	US (Florida)	2013	11-18	12615	1098	8.7 (8.2, 9.2)
Arrazola	US NYTS	2013	11-14	8111	243	3.0 (2.6, 3.4)
Arrazola	US NYTS	2013	15-18	10190	1213	11.9 (11.3, 12.5)
Goniewicz	Poland	2013-2014	15-19	1970	1223	62.1 (59.9, 64.2)
SALSUS	UK (Scotland)	2013-2014	13-15	32051	3487	10.9 (10.5, 11.2)
Fotiou	Greece	2014	15	1320	219	16.6 (14.6, 18.7)
Babineau	Ireland	2014	16-17	821	196	23.9 (21.0, 26.9)
Gallus	Italy	2014	16-19	153	7	4.6 (1.9, 9.2)
White	New Zealand	2014	14-15	2919	584	20.0 (18.6, 21.5)
Li	New Zealand	2014	15-17	99	20	20.2 (12.8, 29.5)
Moore	UK (Wales)	2014	10-11	1601	87	5.4 (4.4, 6.7)
Moore	UK (Wales)	2014	11-16	9055	1018	11.2 (10.6, 11.9)
Porter	US (Florida)	2014	11-14	36979	3143	8.5 (8.2, 8.8)
Porter	US (Florida)	2014	15-18	32921	6749	20.5 (20.1, 20.9)
Hamilton	Canada (Ontario)	2015	14-18	2892	422	14.6 (13.3, 15.9)
Kristjansson	Iceland	2015	15-16	3477	587	16.9 (15.7, 18.2)
Gallus	Italy	2015	16-19	160	7	4.4 (1.8, 8.8)
Alaska	US (Alaska)	2015	14-18	1418	512	36.1 (33.6, 38.7)
Montana	US (Montana)	2015	14-18	4486	2292	51.1 (49.6, 52.6)
Overall (I^2 = 99.8%, p = 0.0)						16.4 (12.5, 20.6)

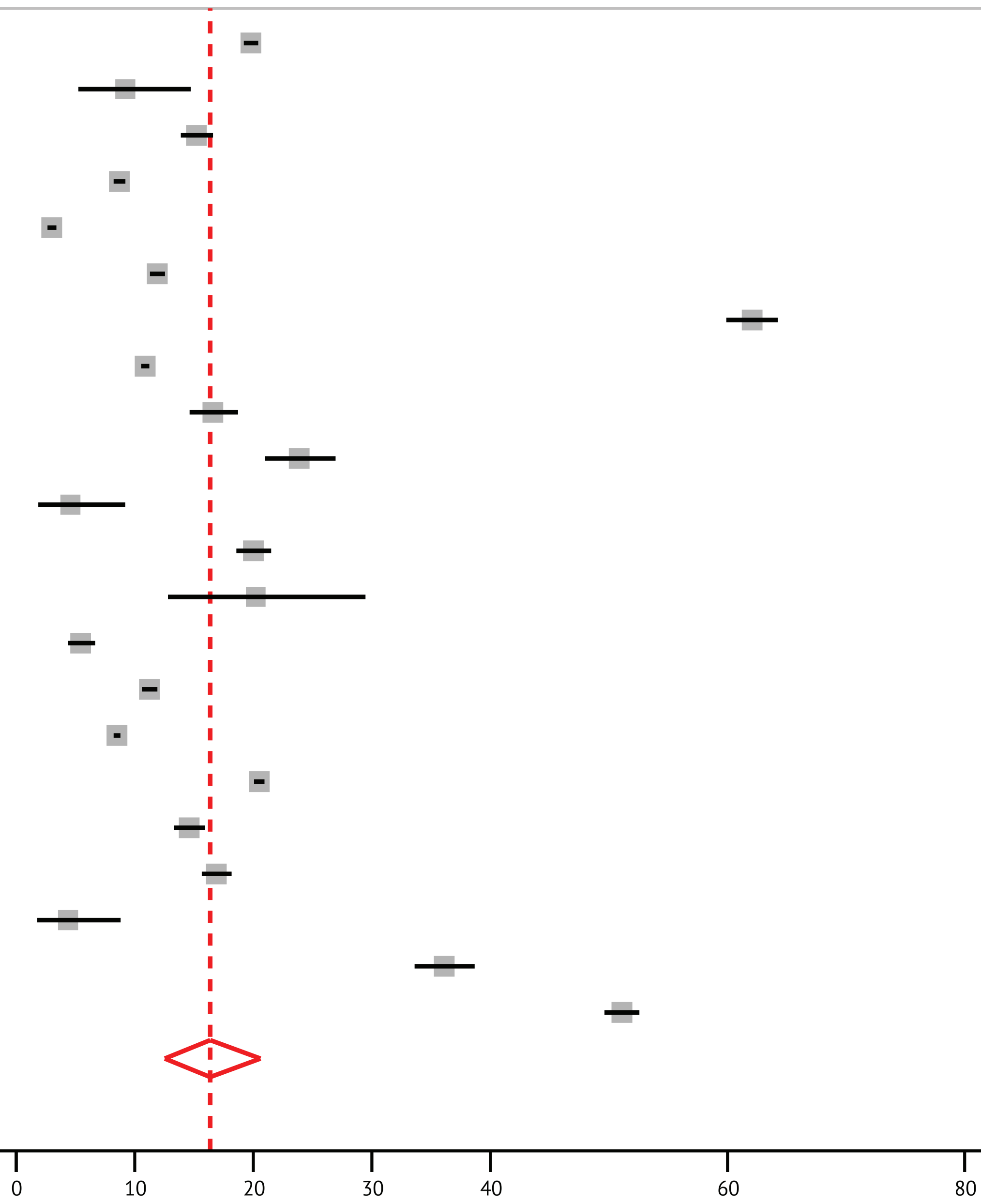


Figure 6: Sensitivity analysis of ever e-cigarette use among youth from 2013-2015

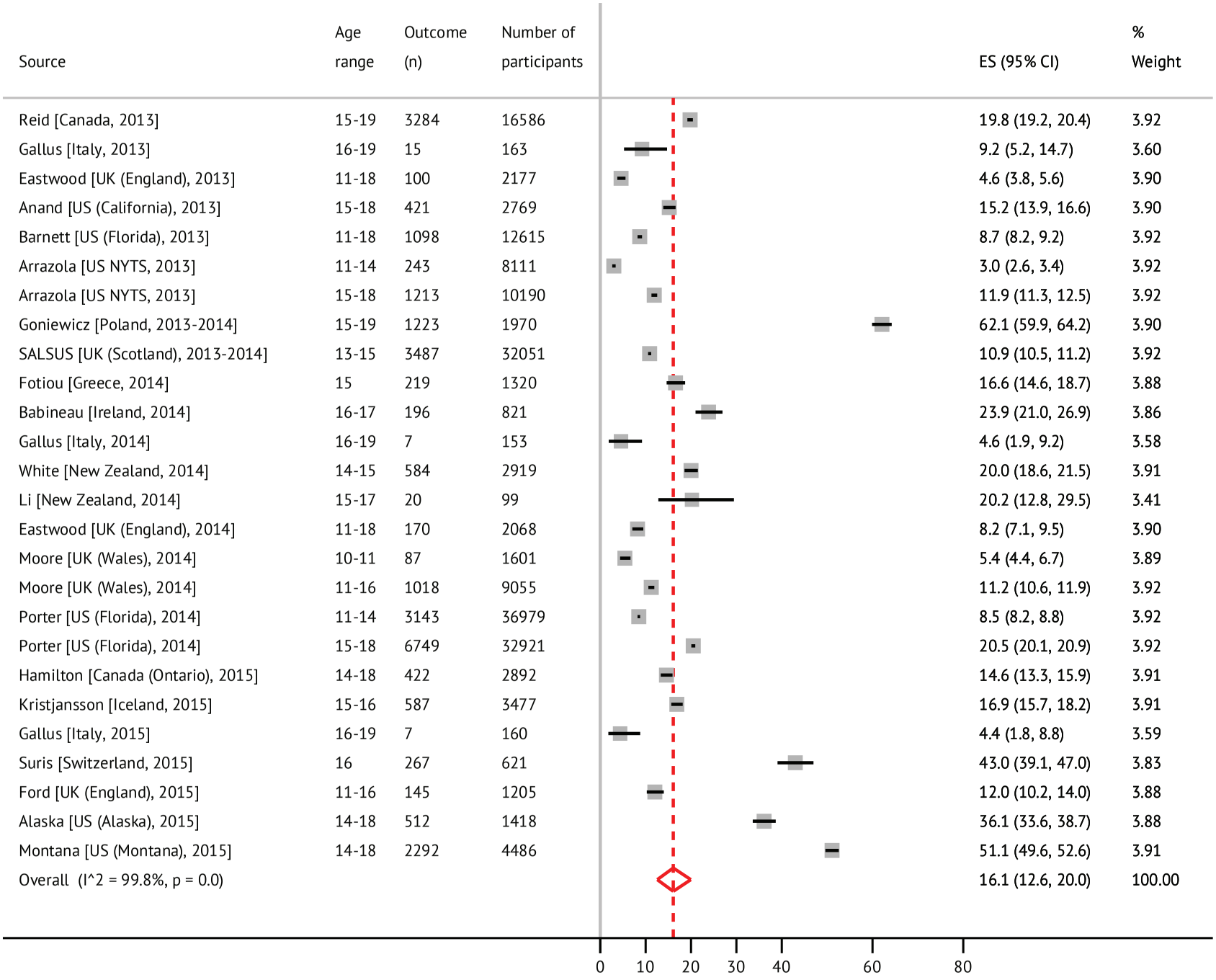


Figure 7: Pooled analysis of ever e-cigarette use among youth by country (2008-2015)

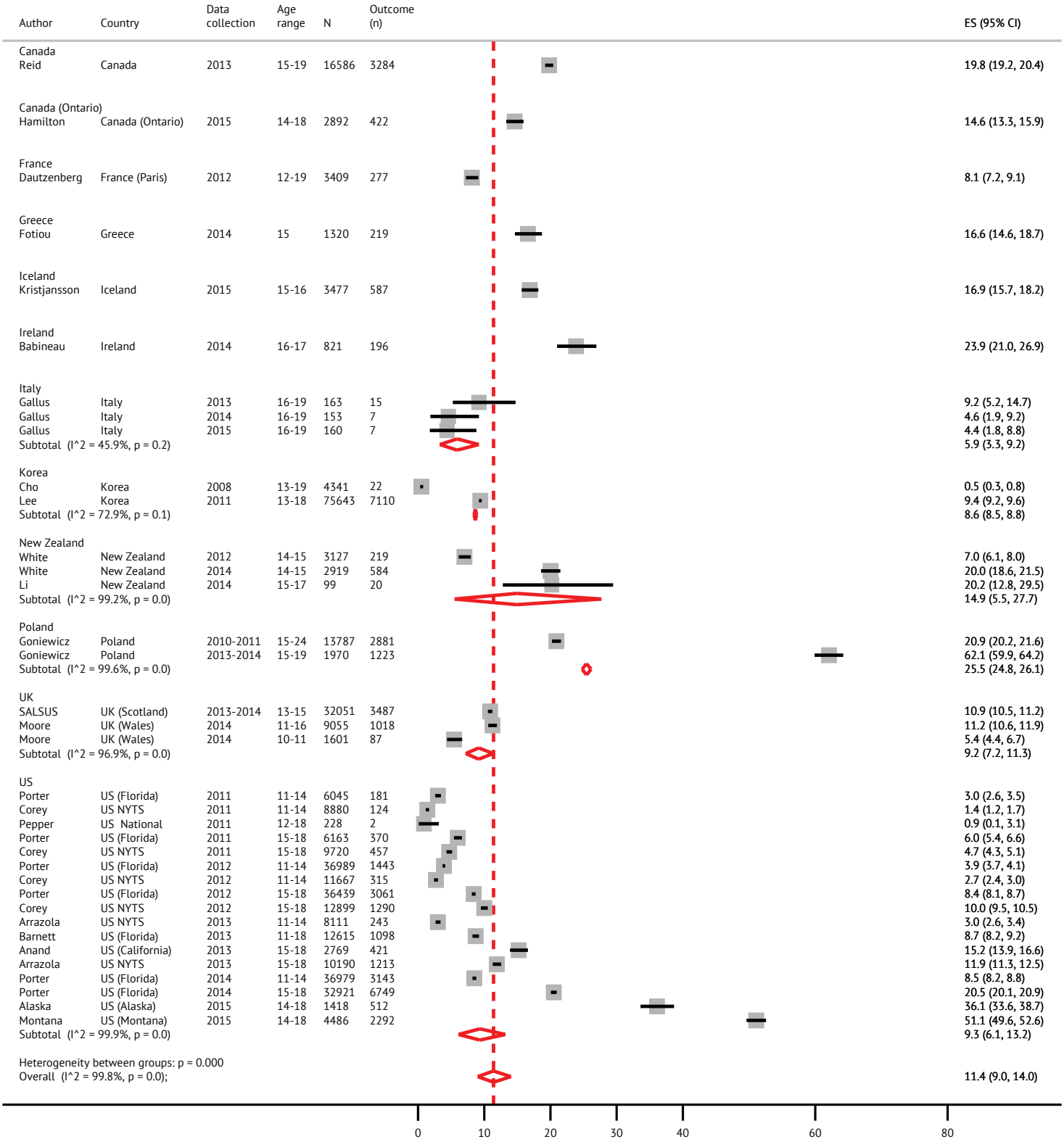


Figure 8: Pooled analysis of current e-cigarette use among youth from 2013-2015

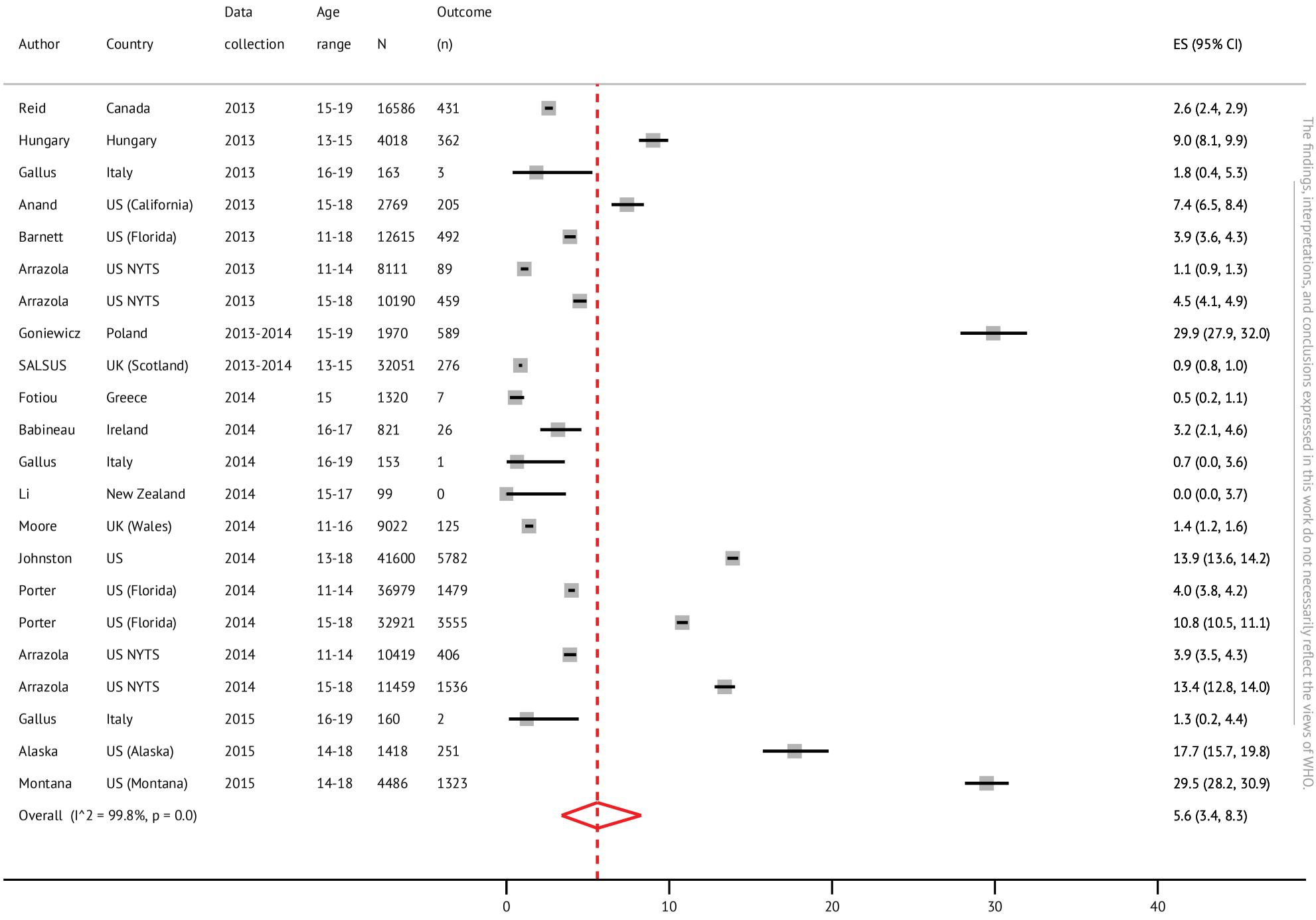


Figure 9: Sensitivity analysis of current e-cigarette use among youth from 2013-2015

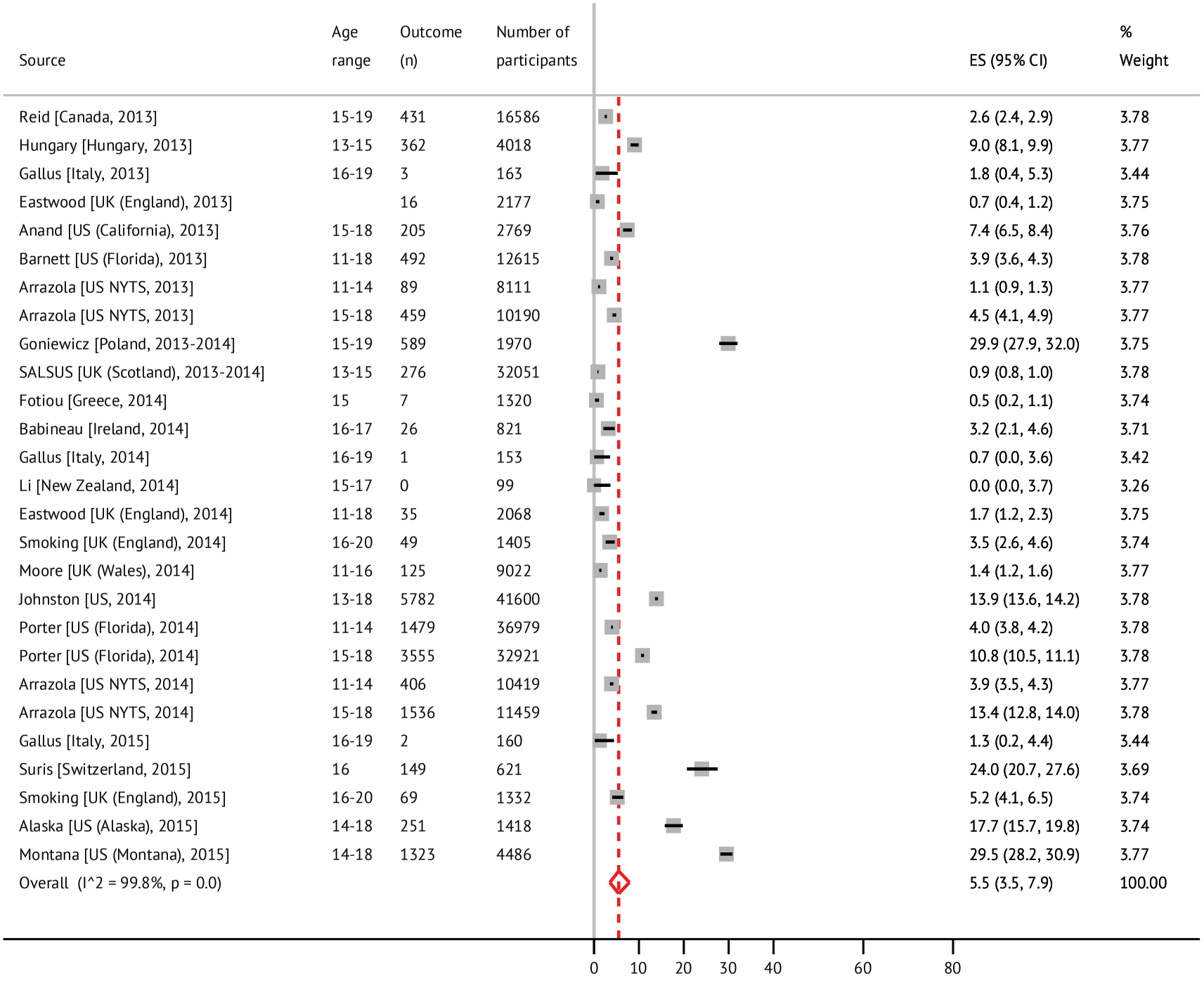


Figure 10: Pooled analysis of current e-cigarette use among youth by country (2008-2015)

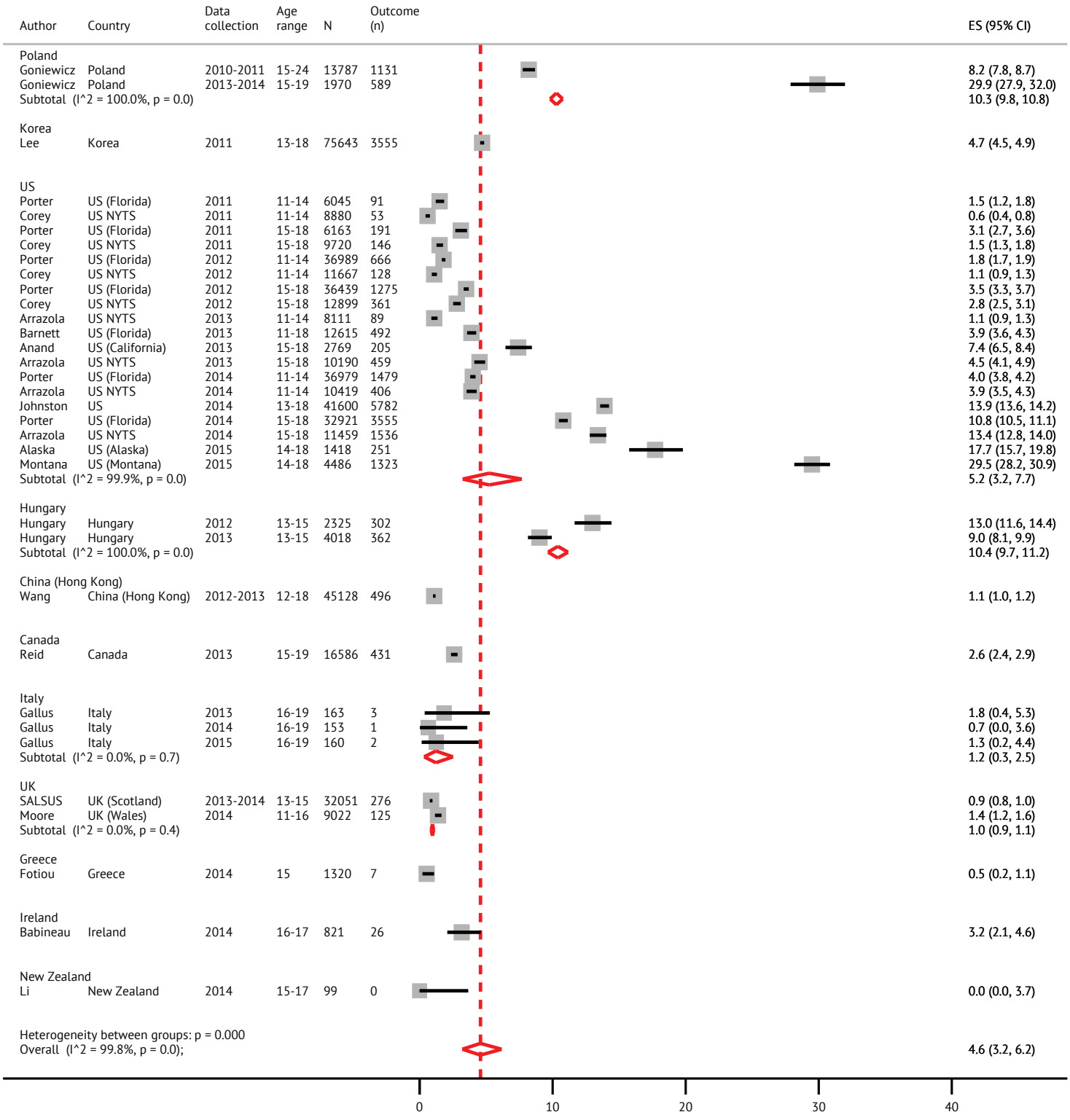


Figure 11: Pooled analysis of ever e-cigarette use among non-smoking youth from 2013-2015

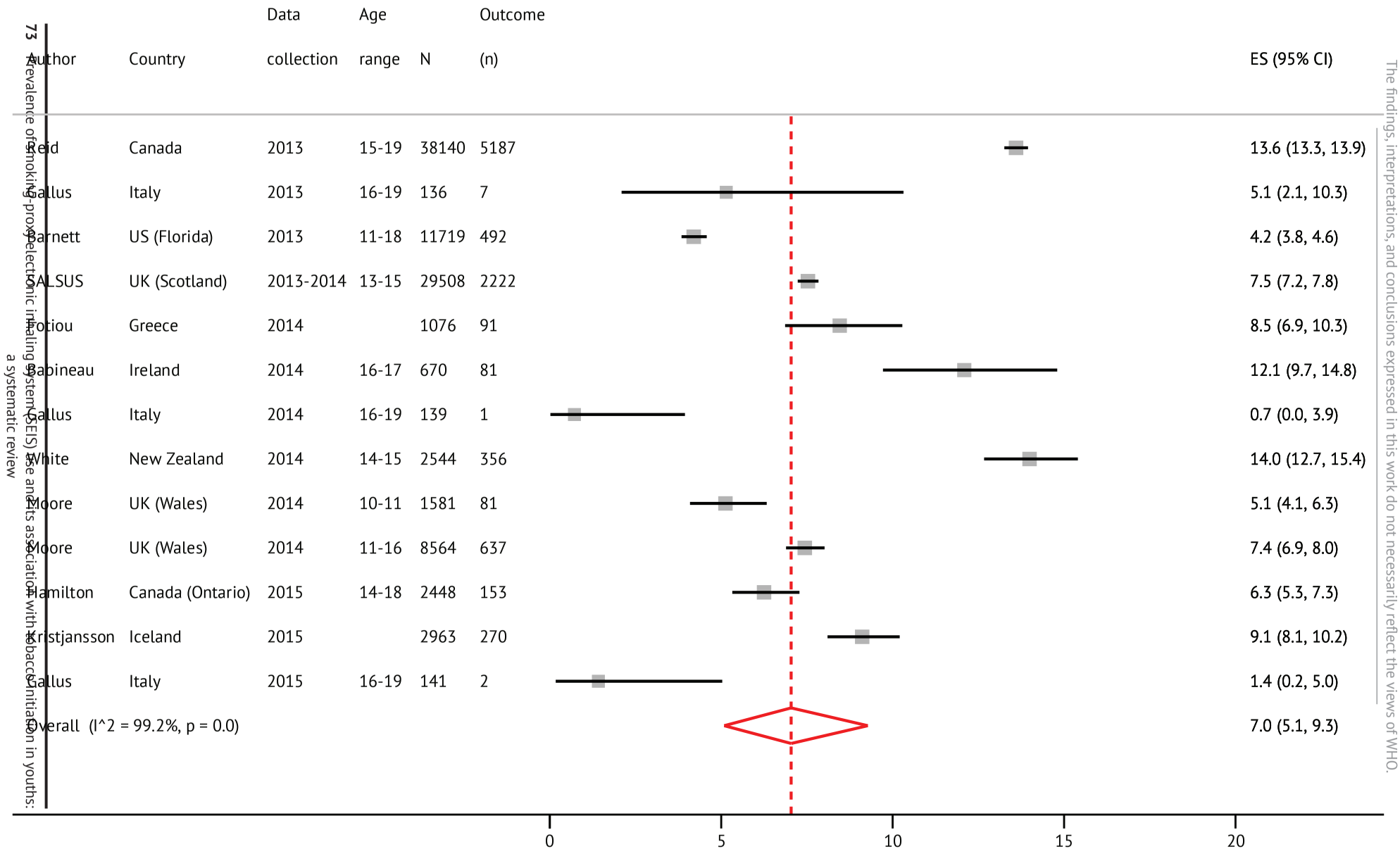


Figure 12: Sensitivity analysis of ever e-cigarette use among non-smoking youth from 2013-2015

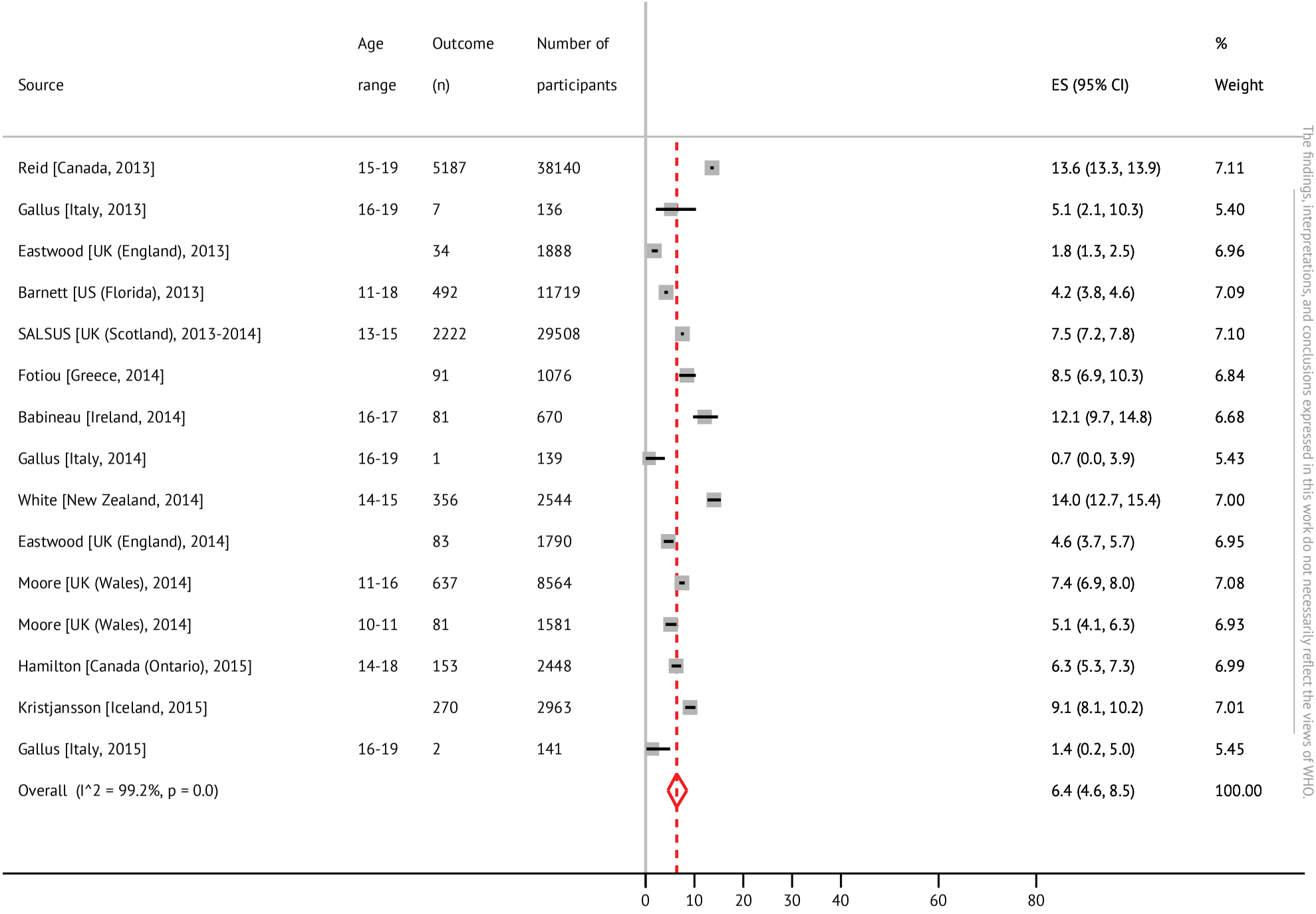


Figure 13: Pooled analysis of ever e-cigarette use among non-smoking youth by country (2008-2015)

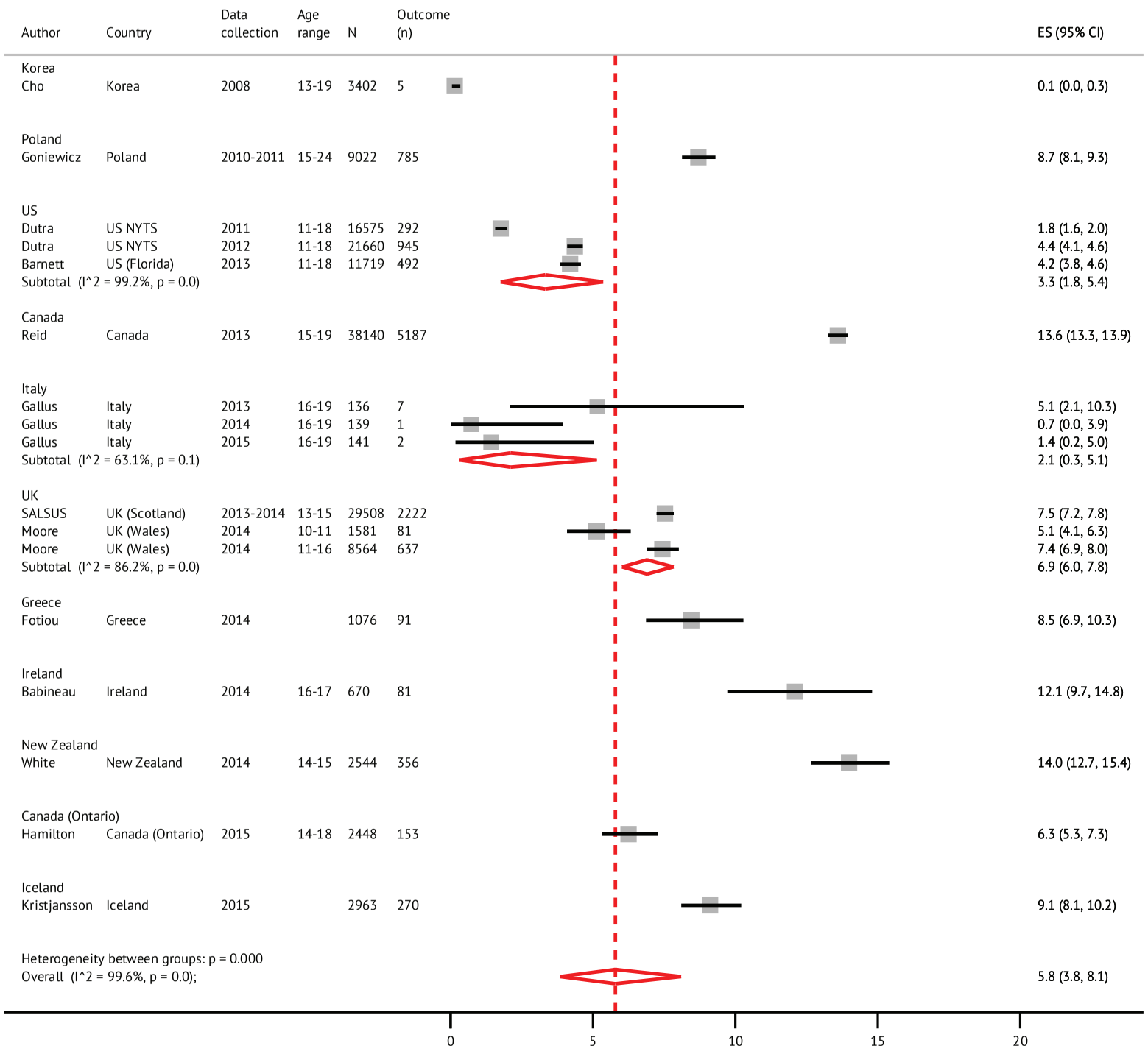


Figure 14: Pooled analysis of current e-cigarette use among non-smoking youth from 2013-2015

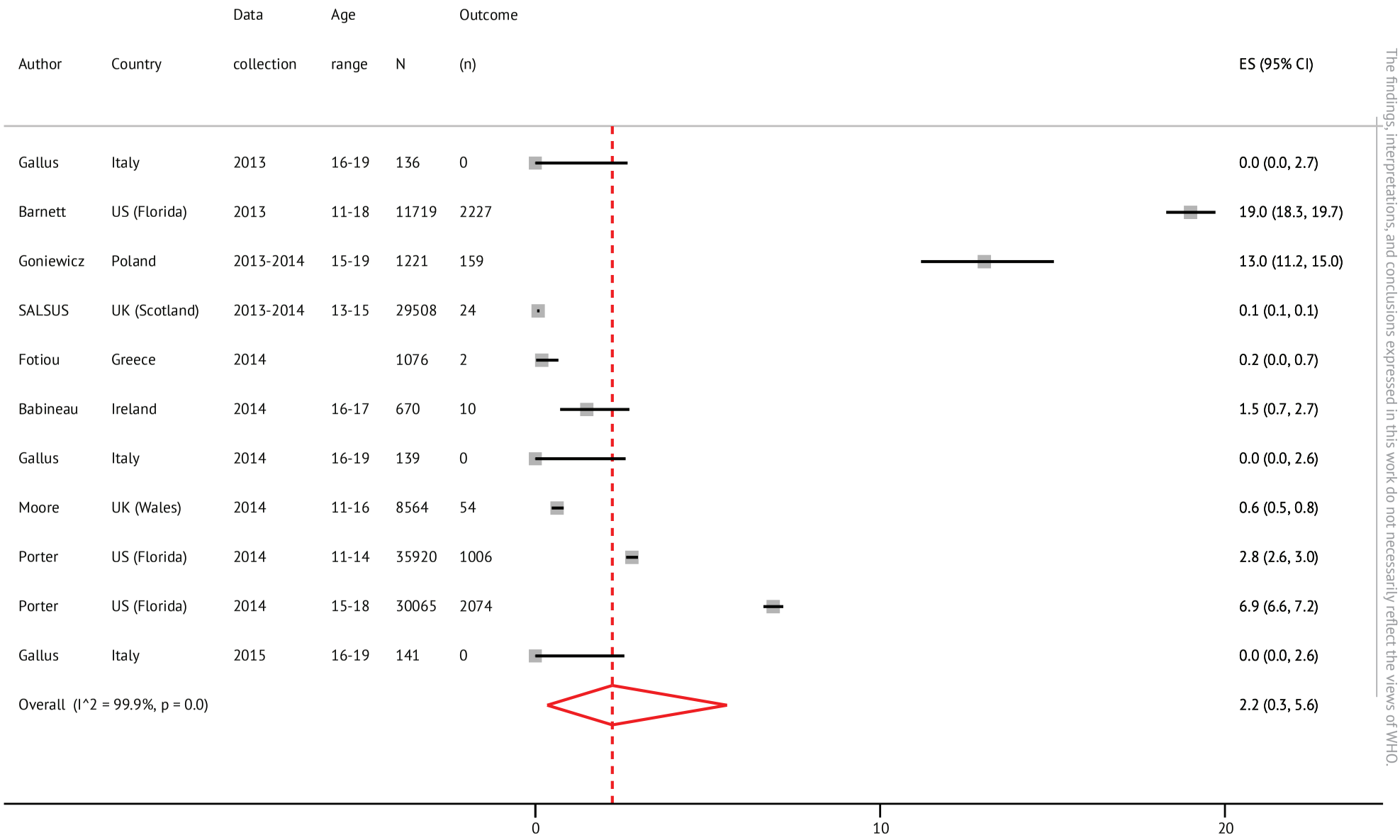


Figure 15: Sensitivity analysis of current e-cigarette use among non-smoking youth from 2013-2015

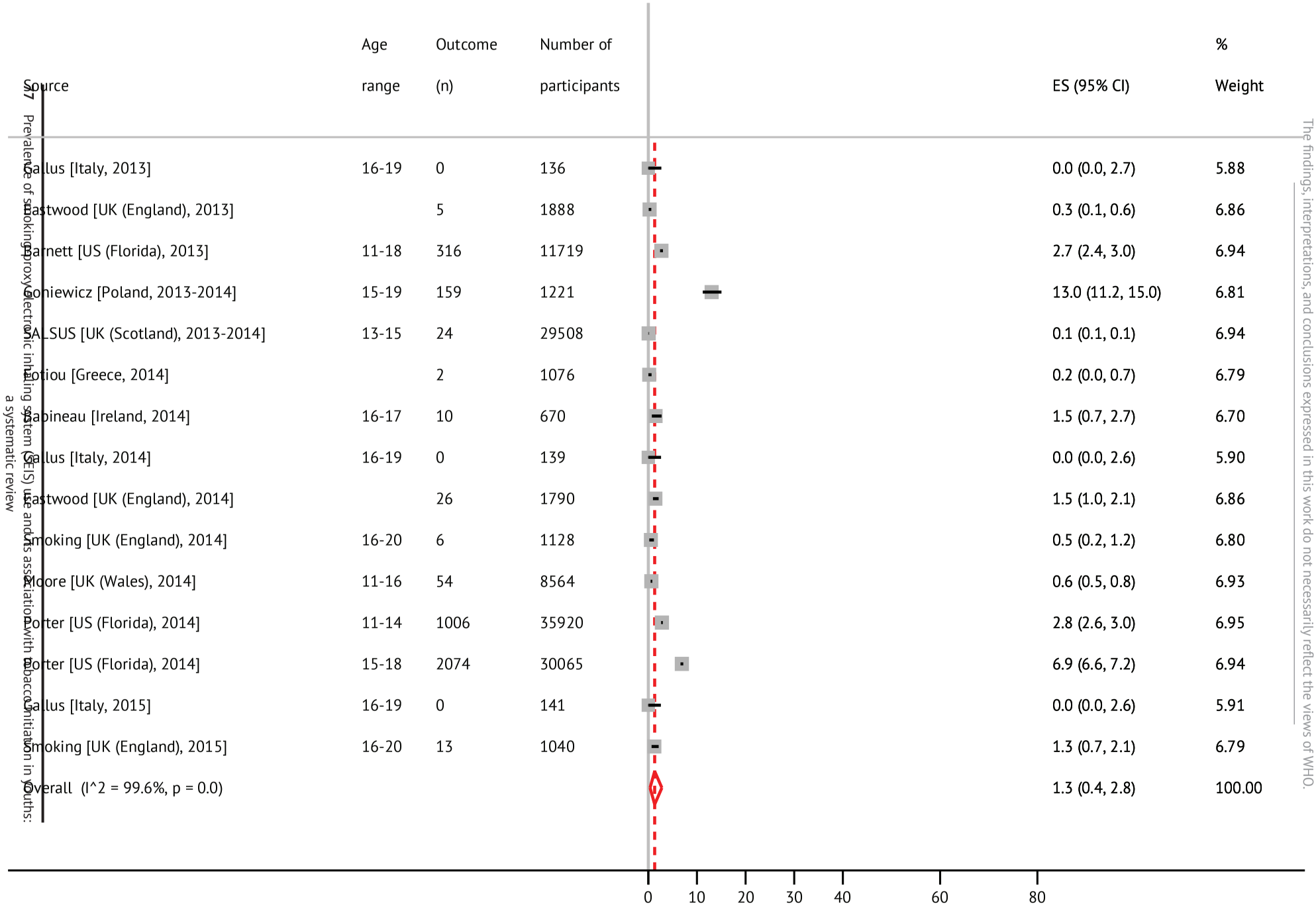


Figure 16: Pooled analysis of current e-cigarette use among non-smoking youth by country (2010-2015)

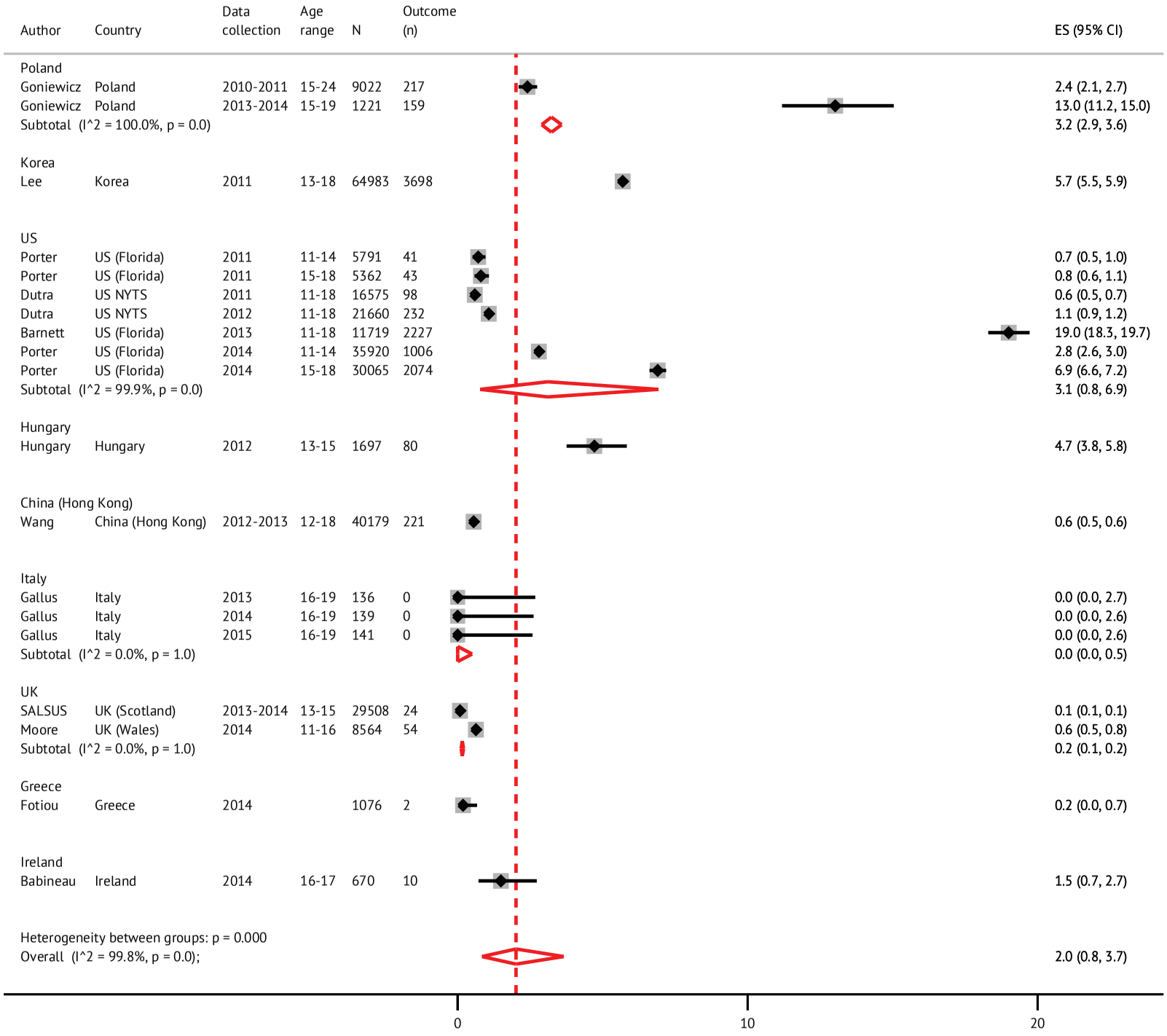


Figure 17: Pooled analysis of ever e-cigarette use among smoking youth from 2013-2015

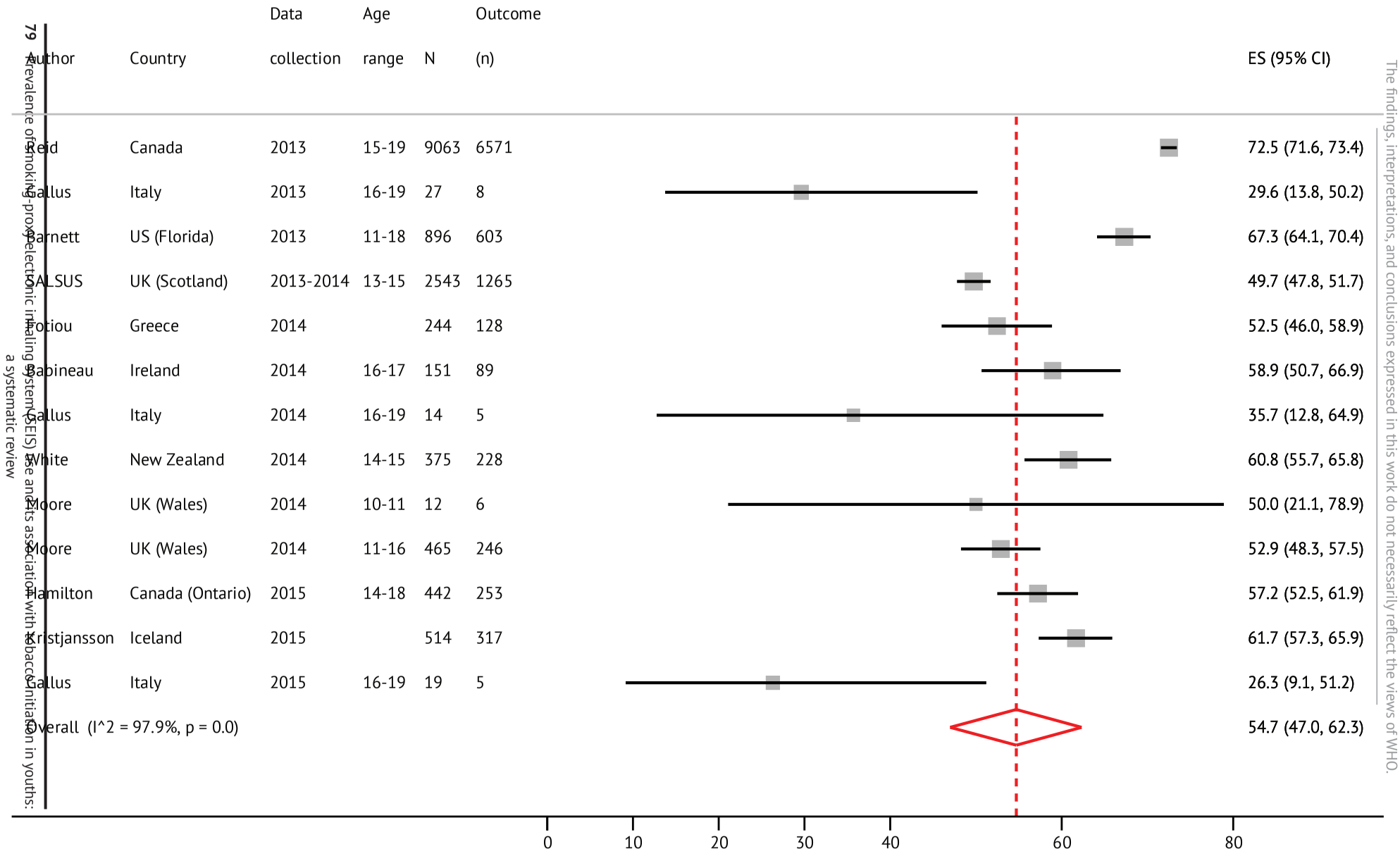


Figure 18: Sensitivity analysis of ever e-cigarette use among smoking youth from 2013-2015

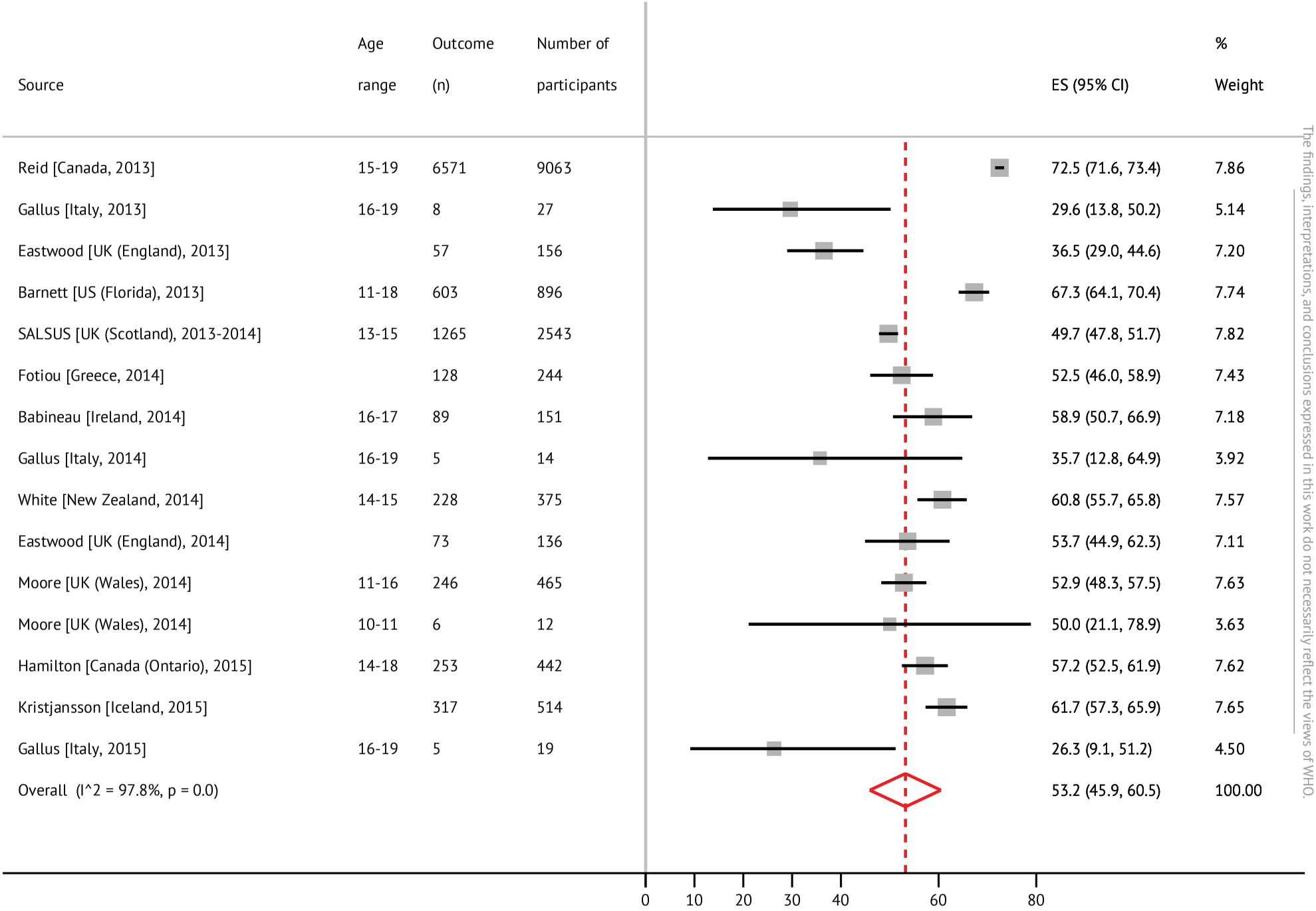


Figure 19: Pooled analysis of ever e-cigarette use among smoking youth by country (2008-2015)

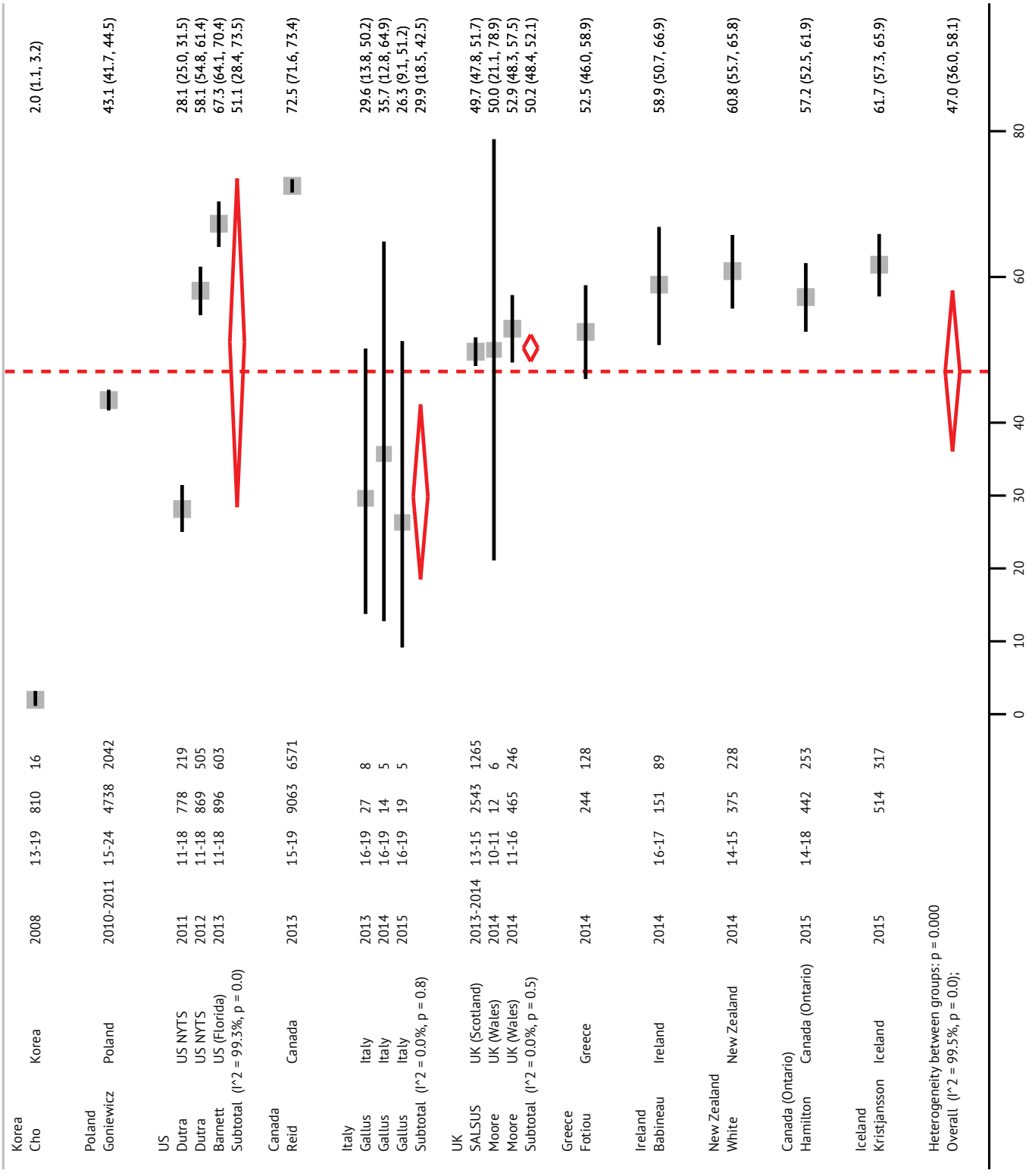


Figure 20: Pooled analysis of current e-cigarette use among smoking youth from 2013-2015

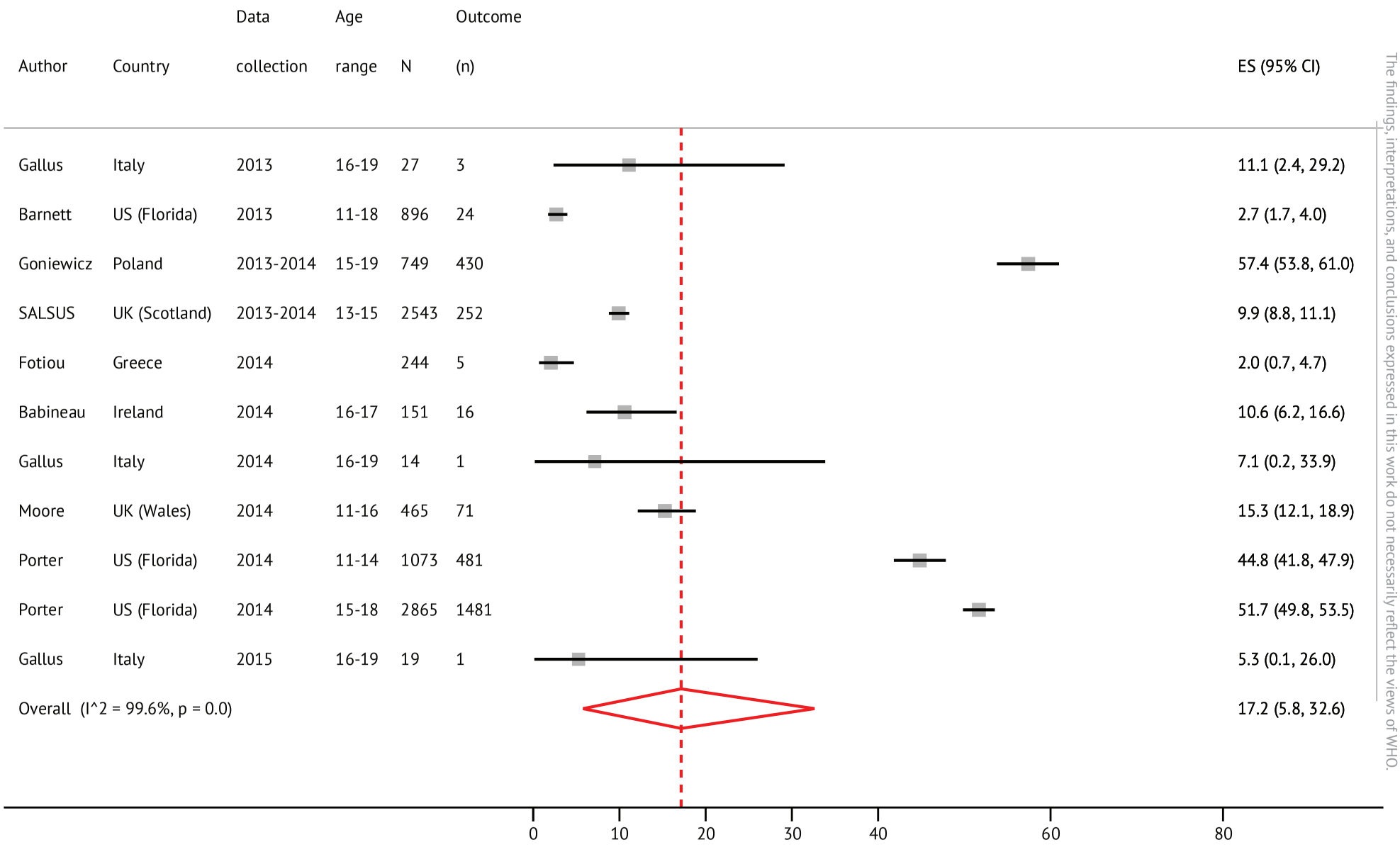


Figure 21: Pooled analysis of current e-cigarette use among smoking youth from 2013-2015

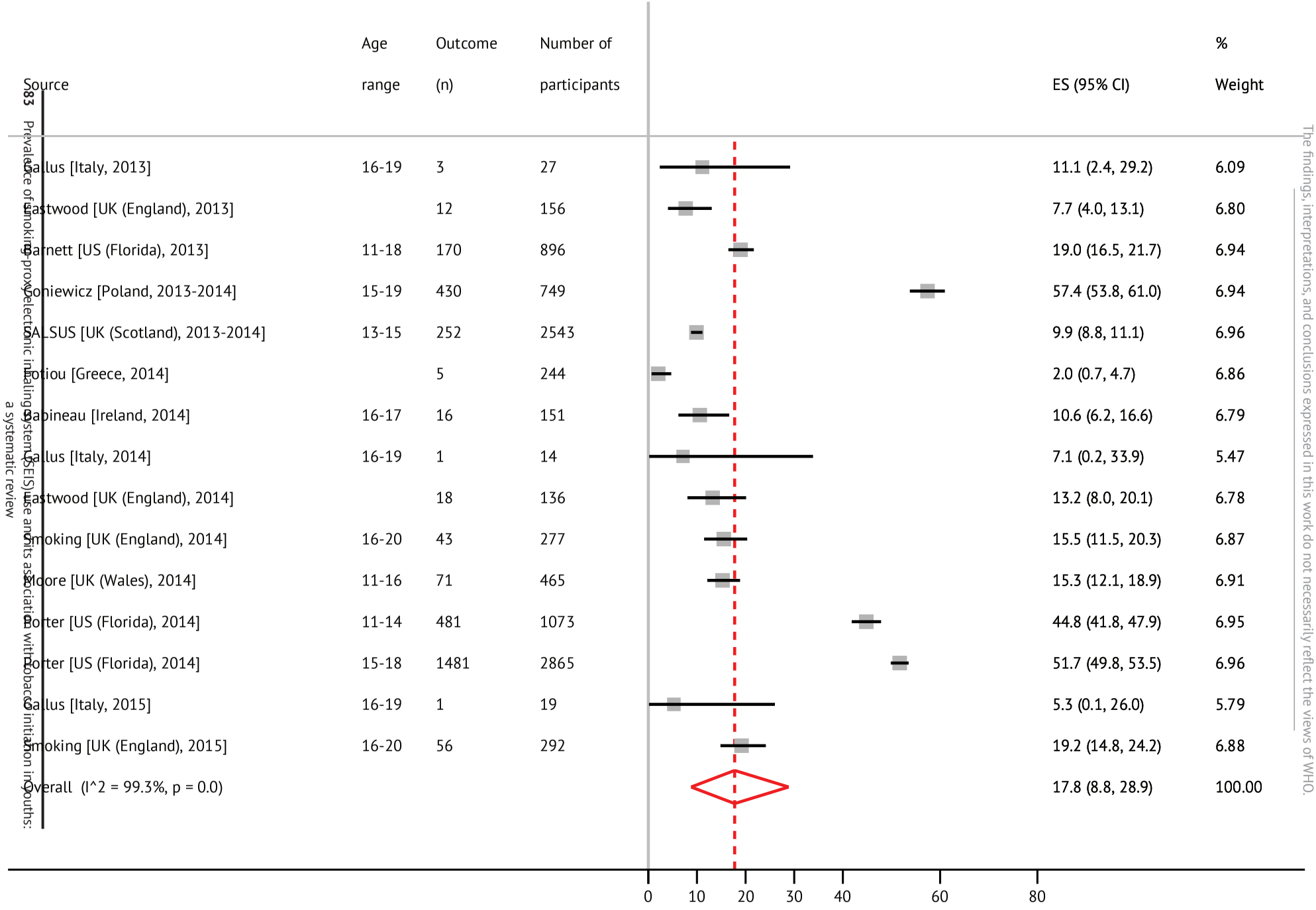


Figure 22: Pooled analyses of current e-cigarette use among smoking youth by country (2010-2015)

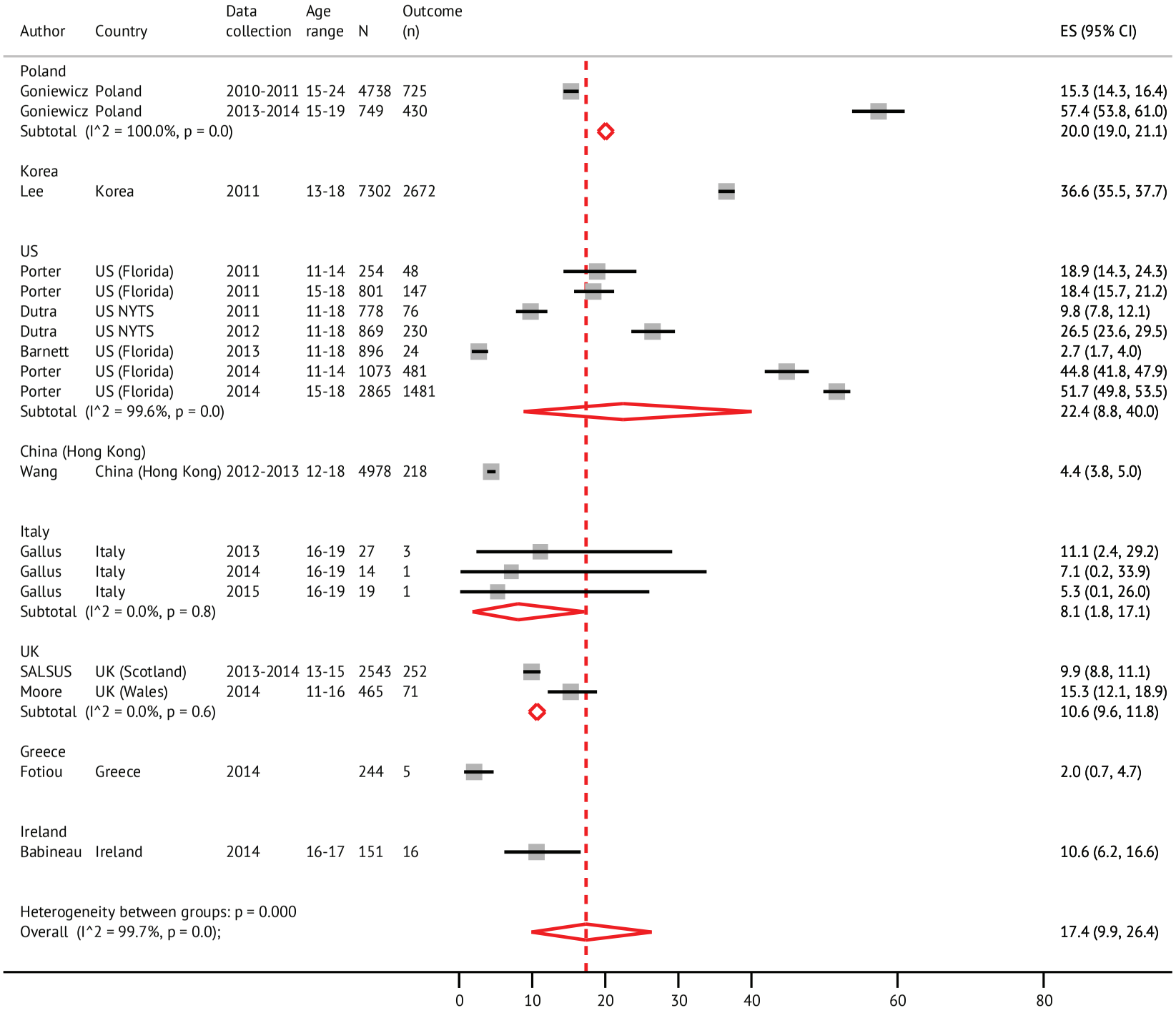
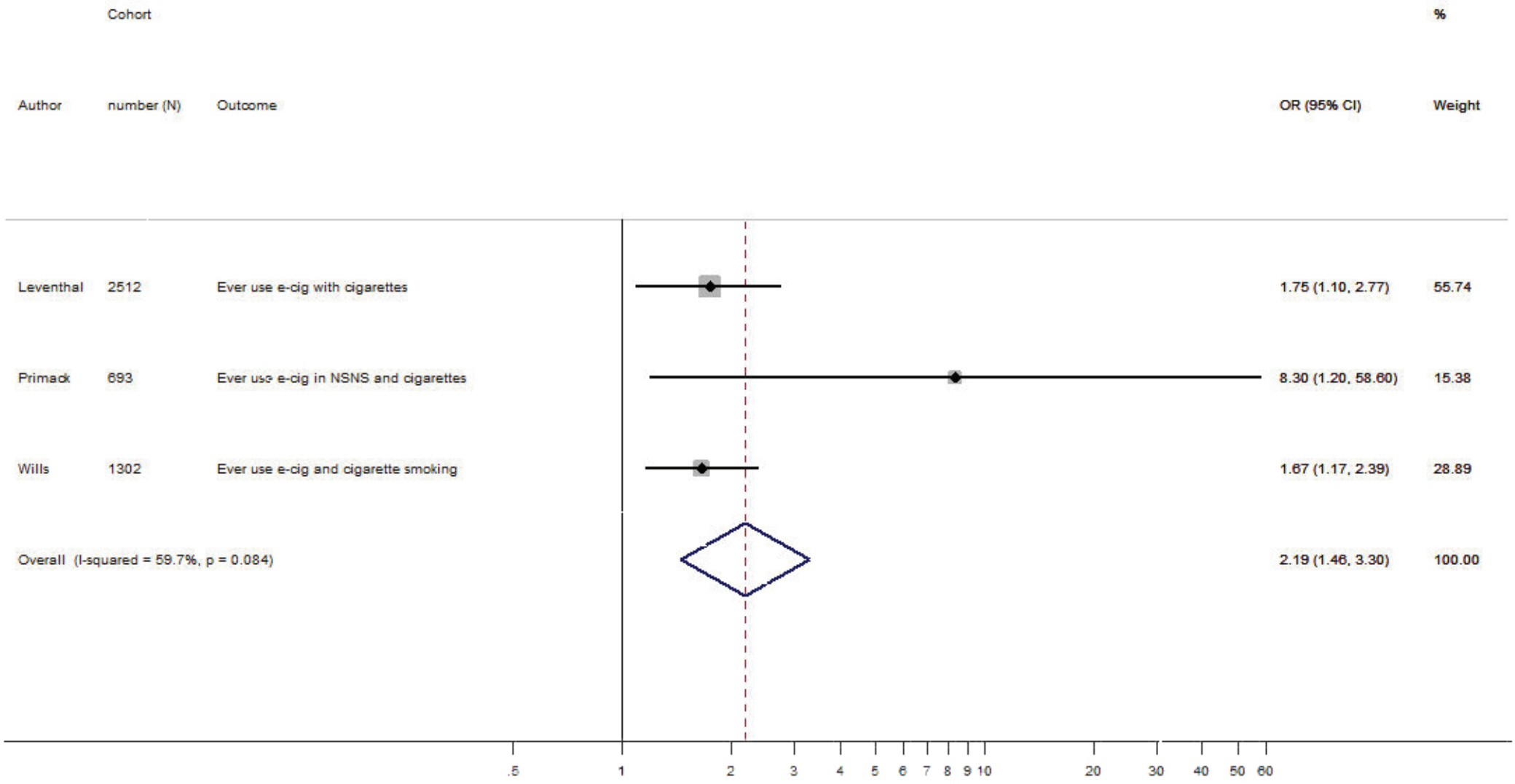


Figure 23: Pooled adjusted odds ratio for longitudinal studies assessing association of ever e-cigarette use among non-smokers at baseline with tobacco cigarette uptake



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