

Relating Onset of Health Conditions to Changes in Tobacco/Nicotine Use — Analyses based on the U.S. PATH Study *

by

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1. SUMMARY

Introduction: Evidence is limited on how the onset of health conditions affects tobacco/nicotine use. We report analyses from adults in the U.S. PATH study relating changes in established cigarette and/or e-cigarette use between Waves 1 and 4 to onset of conditions in Waves 2 or 3. **Methods:** Nine conditions had sufficient onsets for analysis. The main analyses adjusted for sex and age. Additional analyses excluded other tobacco/nicotine product users, controlled for more variables, restricted changes in one product to never users of the other, or restricted attention to changes occurring after onset of the condition.

Results: In the main analyses, onset of each condition predicted significantly increased overall e-cigarette initiation rates, with highest odds ratios (OR) for any major respiratory condition (2.86, 95% confidence interval (CI) 2.10–3.90) and cancer (2.51, 1.52–4.14). Each onset also predicted higher cigarette smoking initiation rates, but ORs were lower than for e-cigarette initiation, and only significant for any cardiovascular condition (1.65, 1.31–2.08), high blood pressure (1.34, 1.13–1.58), and any major smoking-related condition (1.35, 1.12–1.62). For quitting smoking only six conditions showed increased ORs, significant only for high cholesterol (1.29, 1.02–1.62). The additional analyses generally confirmed these patterns. Relationships with re-initiating cigarettes or becoming dual users of cigarettes and e-cigarettes were inconsistent. Onset

of conditions also tended to reduce amount smoked by smokers.

Conclusions: While PATH is nationally representative, its sample size does not always allow precise estimates. There is concern about accuracy of statements by some older participants claiming to be Wave 1 never smokers but Wave 4 ever smokers. Nevertheless the previously unreported association between onset of the health conditions and e-cigarette initiation (which mainly occurs in Wave 1 cigarette smokers) appears real. [Contrib. Tob. Nicotine Res. 32 (2023) 1–10]

ZUSAMMENFASSUNG

Einleitung: Es gibt nur begrenzte Evidenz dazu, wie das Auftreten von Erkrankungen den Konsum von Tabak/Nikotin beeinflusst. In diesem Artikel wird über Analysen aus der U.S. PATH Studie berichtet, in der die Veränderung der Konsumgewohnheiten bei erwachsenen Nutzern von herkömmlichen Zigaretten bzw. E-Zigaretten der Phasen 1 und 4 im Vergleich zu deren Konsum beim Auftreten von Erkrankungen während der Phasen 2 und 3 untersucht wird. **Methoden:** Eine für die Analyse ausreichende Fallzahl konnte bei neun Erkrankungen erreicht werden. Die Hauptanalysen wurden nach Alter und Geschlecht adjustiert. In weiteren Analysen wurden Nutzer anderer Tabak-/Nikotinerzeugnisse ausgeschlossen, der Einfluss von zusätzlichen

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Variablen kontrolliert, die Analyse von Veränderungen bei einem Erzeugnis auf diejenigen Probanden beschränkt, die niemals andere Produkte konsumierten, bzw. der Schwerpunkt der Analysen auf Veränderungen gelegt, die nach Einsetzen der Erkrankung auftraten.

Ergebnisse: In den Hauptanalysen war das Auftreten von Erkrankungen ein signifikanter Prädiktor für insgesamt erhöhte Initiationsraten bei E-Zigaretten, wobei die höchsten Odds-Ratios bei allen schweren Atemwegserkrankungen (2,86, 95% Konfidenzintervall 2,10–3,90) sowie Krebserkrankungen (2,51, 1,52–4,14) beobachtet wurden. Jede neu auftretende Erkrankung war auch ein Prädiktor für höhere Initiationsraten bei Zigaretten, jedoch waren die ORs niedriger als bei E-Zigaretten und nur bei kardiovaskulären Erkrankungen (1,65, 1,31–2,08), Hypertonie (1,34, 1,13–1,58) sowie schweren durch das Rauchen bedingten Erkrankungen (1,35, 1,12–1,62) signifikant. Für den Rauchverzicht wurden lediglich bei sechs Erkrankungen erhöhte ORs beobachtet, welche nur bei Hypercholesterinämie signifikant waren (1,29, 1,02–1,62). In den weiteren Analysen wurden diese Trends generell bestätigt. Die Zusammenhänge zwischen der Wiederaufnahme des Zigarettenrauchens oder dem Beginn eines gleichzeitigen Konsums von herkömmlichen Zigaretten und E-Zigaretten waren inkonsistent. Das Auftreten von Erkrankungen führte zudem bei Rauchern tendenziell zu einer Reduzierung der Anzahl der gerauchten Zigaretten.

Schlussfolgerungen: Es handelt sich bei PATH um eine national repräsentative Studie, jedoch lässt die Stichprobengröße nicht in jedem Fall präzise Schätzungen zu. Es gibt Bedenken bezüglich der Richtigkeit von Angaben einiger älterer Probanden. Diese gaben in Phase 1 der Studie an, Nichtraucher zu sein, während sie in Phase 4 angaben, bereits vorher Raucher gewesen zu sein. Dennoch scheint sich der in der Wissenschaft bisher nicht berichtete Zusammenhang zwischen dem Auftreten einer Erkrankung und dem Beginn des Konsums von E-Zigaretten (dies ist hauptsächlich bei Rauchern herkömmlicher Zigaretten der Phase 1 der Fall) zu bestätigen. [Contrib. Tob. Nicotine Res. 32 (2023) 1–10]

RESUME

Introduction: Les preuves sont limitées, qui éclairent la façon dont l'apparition de troubles peut affecter le tabagisme ou consommation de nicotine. Nous relayons ici les analyses pratiquées sur des sujets adultes dans le cadre de l'étude U.S. PATH faisant état de modifications entre la consommation de cigarettes traditionnelles et/ou de leur variante électronique telle que rapportée lors des phases 1 et 4 de l'étude et la consommation rapportée en phases 2 ou 3 en cas d'apparition des troubles.

Méthodologie: Neuf troubles présentaient suffisamment de cas de déclenchement pour une analyse. Les principales analyses furent ajustées selon le sexe et l'âge. Des analyses supplémentaires exclurent les utilisateurs d'autres produits contenant du tabac ou de la nicotine, surveillèrent un plus grand nombre de variables, restreignirent l'analyse des modifications pour un produit particulier aux personnes n'ayant jamais fumé un autre produit ou focalisèrent leur attention sur les modifications se produisant après l'appari-

tion des troubles.

Résultats: Dans les analyses principales, l'apparition de chaque trouble fut indicatrice d'une augmentation significative des taux généraux d'initiation au vapotage, avec des rapport des cotes au plus haut dans le cas des affections respiratoires majeures (2,86, intervalle de confiance de 95%, 2,10–3,90) et des cancers (2,51, 1,52–4,14). Chaque apparition était aussi un indicateur de taux plus élevés d'initiation à la cigarette; toutefois, les rapport des cotes étaient inférieurs à ceux relatifs à l'initiation au vapotage et n'étaient significatifs que pour les troubles cardiovasculaires (1,65, 1,31–2,08), pour l'hypertension artérielle (1,34, 1,13–1,58) et pour toutes les affections majeures liées au tabagisme (1,35, 1,12–1,62). Eu égard à l'abandon du tabac, seuls six troubles affichèrent des rapport des cotes en augmentation et n'étant significatifs que dans le cas d'un taux de cholestérol élevé (1,29, 1,02–1,62). En règle générale, ces schémas furent confirmés par les analyses complémentaires. Les liens avec la reprise du tabagisme ou le glissement vers une consommation combinée de cigarettes traditionnelles et de cigarettes électroniques manquaient de constance. L'apparition de troubles tendait aussi à réduire les quantités fumées par les utilisateurs.

Conclusions: L'étude PATH est certes représentative au niveau national; néanmoins, la taille de son échantillon ne permet pas toujours de dégager des estimations précises. Il y a lieu de s'inquiéter de la véracité des déclarations de certains participants plus âgés affirmant entrer dans la catégorie des personnes n'ayant jamais fumé lors de la phase 1 alors qu'ils affirment avoir déjà fumé lors de la phase 4. Toutefois, la relation précédemment passée sous silence entre l'apparition de troubles et l'initiation à la cigarette électronique (qui intervient principalement chez les fumeurs de la phase 1) semble réelle. [Contrib. Tob. Nicotine Res. 32 (2023) 1–10]

2. IMPLICATIONS

In the past smokers who were discovered to have smoking-related diseases have been encouraged to quit smoking, with such advice not always being followed. There is now the possibility of switching to new products such as e-cigarettes. If these products prove to be safer alternatives this could be a useful option for improving health outcomes in diseased populations.

3. INTRODUCTION

There is an extensive literature on the extent to which use of, and changes in the use of tobacco products affects the subsequent risk of cancer, chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD) and other diseases (1). However, there is far less literature available on how onset of disease might affect subsequent use of tobacco/nicotine products. Smokers with smoking-related disease may often be advised to reduce their consumption or quit, but the extent to which smokers may actually do so is not well established. Many of these studies (e.g., GOLČIĆ *et al.* (2) and GUMMERSON *et al.* (3) for cancer, BRUMMETT *et al.* (4) and KIM *et al.* (5) for heart disease,

and HIRAI *et al.* (6) and HIRAYAMA *et al.* (7) for COPD or respiratory disease) determine changes in smoking habits only in a group with a defined disease or group of diseases, and do not collect comparable data in a healthy control group. Even, where they do (e.g., PALMER *et al.* (8) and WESTMAAS *et al.* (9) for cancer, KWON *et al.* (10) for diabetes and hypertension, and LIU *et al.* (11) and JONES (12) for COPD or respiratory disease) they tend to limit attention to quitting, not considering the possibility that those with a diagnosis with a poor outcome might increase their smoking, or re-initiate it (possibly because they wish to enjoy their final days while they still can), or switch to other tobacco/nicotine products, such as e-cigarettes. Furthermore, most studies are relatively short-term, not allowing useful information to be obtained on survival or other health changes, few, (e.g., (13–15)) reporting on any health outcome.

Here we report detailed analyses investigating the effects of onset of a range of diseases on aspects of established cigarette smoking and e-cigarette use. These are based on adult data from those who were adults (aged 18+ years) in Waves 1 to 4 of the Population Assessment of Tobacco and Health (PATH) study (16, 17), a nationally representative longitudinal cohort study in the U.S. supported by federal funds. The publicly available databases (<https://doi.org/10.3886/ICPSR36231.v18>) provide extensive information on tobacco/nicotine product use, health status and other factors at each follow-up Wave. Wave 1, conducted in September 2013 to December 2014, involved 45,971 individuals, 13,651 adolescents aged 12–17 years and 32,320 adults aged 18+ years. Wave 2 was conducted in October 2014 to October 2015, and Wave 3 in October 2015 to October 2016. By Wave 4, conducted in December 2016 to January 2018, there were data on 33,821 adults. 6,065 were from a new cohort, and of the remaining 27,756, 5,131 were adolescents at Wave 1 and were thus excluded, leaving 22,625. Of these 20,594 had cigarette smoking at both waves, 19,576 had e-cigarette data at both waves, and 18,018 had information on both types of tobacco/nicotine product use at both waves.

4. METHODS

The main analytical method involved studying changes in established tobacco/nicotine use between Waves 1 and 4 according to whether or not onset of the condition occurred in Waves 2 or 3. The individuals included in each analysis were adults (aged 18+ years) at Wave 1, who at Wave 1 had never been told by a doctor or health professional that they had the health condition or certain related conditions, and had established smoking data available at Waves 1 and 4. For each combination of health condition and change in tobacco/nicotine use considered, the main analyses took account of the population weighting at Wave 1 and adjusted for sex (male, female) and detailed age group (18–24, 25–34, 35–44, 45–54, 55–64, 65–74, 75+ years) as at Wave 1, with estimates of the relationship between onset of the condition and change in established tobacco/nicotine use (expressed as an odds ratio (OR) with 95% confidence interval, with a positive value indicating that the change was more likely in those with onset of the condition)

calculated by weighted logistic regression for the whole population and also separately by broad age group (18–34, 35–54, 55+ years). Additional analyses tested, by including a suitable interaction term in the model, whether the association varied by sex, or by broad age group. Also Sensitivity analysis 1 excluded those who had ever used smoked tobacco/nicotine products other than cigarettes or e-cigarettes (traditional cigars, filtered cigars, pipes, hookahs, smokeless tobacco, snus and dissolvable products), while Sensitivity analysis 2 adjusted not only for sex, and detailed age group, but also for total household income (split into five levels, with those with missing values being considered as an extra level), census region (Northeast, Midwest, South, West), and use of any of the tobacco/nicotine products excluded in Sensitivity analysis 1.

Initial analysis considered 17 different changes in tobacco/nicotine habits between Waves 1 and 4. Changes 1–3 related to initiation of smoking (never smokers at Wave 1, but current or former smokers at Wave 4), quitting smoking (current smoking at Wave 1, but not currently smoking at Wave 4), and re-initiation of smoking (former smokers at Wave 1, but current smokers at Wave 4), with changes 4–6 relating to initiation, quitting and re-initiation of e-cigarettes smoking similarly defined. Changes 7–9 relate to initiation, quitting and re-initiation of smoking in those who had never used cigarettes, while changes 10–12 relate to initiation, quitting and re-initiation of e-cigarettes in those who had never smoked. The final five changes relate to current dual use of cigarettes and e-cigarettes - change 13 to current cigarette-only smokers becoming dual users, change 14 to current e-cigarette-only users becoming dual users, and changes 15–17 relating to dual users quitting, becoming current users of cigarettes only, or becoming current users of e-cigarettes only. Preliminary analysis showed that eight of these changes (5, 6, 11, 12, 14–17) occurred relatively infrequently (see Supplementary File 1 which gives the number of changes for each health condition and definition of tobacco/nicotine use change) and attention in this paper is restricted to the following nine changes:

1. Initiation of cigarette smoking (regardless of e-cigarette use),
2. Quitting of cigarette smoking (regardless of e-cigarette use),
3. Re-initiation of cigarette smoking (regardless of e-cigarette use),
4. Initiation of e-cigarette use (regardless of cigarette smoking),
7. Initiation of cigarette smoking (in never e-cigarette users),
8. Quitting of cigarette smoking (in never e-cigarette users),
9. Re-initiation of cigarette smoking (in never e-cigarette users),
10. Initiation of e-cigarette use (in never cigarette smokers) and
13. Cigarette-only smokers becoming dual users.

Initial analysis considered the onset of 18 health conditions, but it was decided to limit attention to nine of them for the reasons explained in Table 1.

Table 1. Selection of health conditions for analysis and rules used for excluding individuals for analysis.

	Health condition considered initially	Reason for excluding conditions from analyses presented	Individuals excluded on the basis of health conditions present at Wave 1
1	COPD	Not clearly distinct from 2 or 3	—
2	Chronic bronchitis	Not clearly distinct from 1 or 3	—
3	Emphysema	Not clearly distinct from 1 or 2	—
4	Any major respiratory disease (i.e., conditions 1, 2 or 3)	Included	Any of 1, 2 or 3
5	Asthma	Included	5 only
6	Other lung/respiratory condition	Not clearly defined	—
7	Any respiratory condition (i.e. conditions 1, 2, 3, 5 or 6)	Included	Any of 1, 2, 3, 5 or 6
8	Congestive heart failure	Few changes	—
9	Stroke	Few changes	—
10	Heart attack	Few changes	—
11	Some other heart condition	Not clearly defined	—
12	Any cardiovascular condition (i.e. conditions 8, 9, 10 or 11)	Included	Any of 8, 9, 10 or 11
13	High blood pressure	Included	13 only
14	High cholesterol	Included	14 only
15	Diabetes (sugar or borderline)	Included	15 only
16	Cancer	Included	16 only
17	Tobacco-related cancer	Few changes	—
18	Any major smoking-related condition (i.e., conditions 4, 7 or 12)	Included	Any of 4, 7 or 12

All analyses were limited to those without the condition of interest at Wave 1, with analyses of some conditions also excluding those with other conditions, as also shown in the Table 1. Some additional analyses were also carried out, as described below.

The first two additional analyses considered the effect of alternative exclusions. Additional analysis A excluded those who at Wave 1 had any of the individual conditions studied, while Additional analysis B excluded those who at Wave 1 had any major smoking-related condition, and also, where appropriate, the particular condition considered.

The next set of additional analyses attempted to account for reverse causation, avoiding the possibility that, in the main analyses, some of the changes in tobacco/nicotine use between Waves 1 and 4 might have occurred before onset of the health condition studied. Additional analysis C was restricted to those who had unchanged tobacco/nicotine habits at Waves 1 and 2, and related changes in tobacco/nicotine use between Waves 1/2 and Wave 4 according to whether onset of the condition occurred in Wave 2. Additional analysis D was restricted to those who had unchanged tobacco/nicotine habits at Waves 1, 2 and 3, and related changes in tobacco/nicotine use between Waves 1/2/3 and Wave 4 according to whether onset of the condition occurred in Wave 3.

The final set of additional analyses studied changes in the number of cigarettes smoked. Three versions of it were conducted. Additional analysis E restricted attention to those smoking cigarettes at both Waves 1 and 4. Additional analysis F restricted attention to those smoking cigarettes at Wave 1 but counted quitting at Wave 4 as a reduction in amount smoked. Additional analysis G also included non-smokers (never and former smokers) at Wave 1, counting both quitting and relapse as changes in amount smoked. In these analyses, correction was made for clearly erroneous

values for the daily amount smoked for some individuals in the data reported in the PATH study using the methodology given previously in the publication which first described the problem (18). Also, for those reporting someday rather than everyday smoking, the amount smoked was divided by 3 if smokers last smoked three or more days ago, by 2 if they last smoked yesterday or the day before yesterday, and was left unchanged if they smoked in the past hour or sometime today.

In order to conduct the analyses described above, the relevant data were transferred to a ROEELE database, and analysed using the ROEELE program (Release 59, Build 49). All these analyses could also be run using the GLM Package and the Step Function from the R Program (<https://www.r-project.org/>).

5. RESULTS

Main and sensitivity analyses

There were 22,526 individuals who were aged 18 or over at Wave 1, and had smoking data at Waves 1 and 4. 10,868 (48.2%) were males, with 10,694 (47.5%) aged 18–34, 7,023 (31.1%) aged 35–54 and 4,807 (21.3%) aged 55+ years. At Wave 1 there were 1,796 with any major respiratory condition (COPD, chronic bronchitis or emphysema), 2,278 with asthma, 4,004 with any respiratory disease (major, asthma or other lung/respiratory condition), 1,623 with any cardiovascular condition (congestive heart failure, stroke, heart attack or some other heart condition), 5,325 with high blood pressure, 3,912 with high cholesterol, 2,877 with diabetes, 542 with cancer, and 3,232 with any major smoking-related condition, based on the groupings shown in Table 1.

Table 2. Changes in tobacco/nicotine product use between Waves 1 and 4 in relation to onset of health condition in Waves 2 or 3^a.
Note that initiation and quitting of cigarettes is regardless of e-cigarette use, and that initiation of e-cigarettes is regardless of smoking habits.

Change in product use in relation to onset of health condition	OR for main analysis ^b	OR excluding other tobacco/nicotine product users ^c	OR controlling for three more variables ^d
<i>Initiation of smoking</i>			
Any major respiratory condition	1.11 (0.85–1.44)	0.91 (0.65–1.27)	1.01 (0.78–1.32)
Asthma	1.14 (0.84–1.56)	0.95 (0.63–1.43)	1.08 (0.79–1.48)
Any respiratory condition	1.05 (0.86–1.28)	0.82 (0.63–1.07)	0.98 (0.80–1.19)
Any cardiovascular condition	1.65 (1.31–2.08)	1.96 (1.49–2.59)	1.61 (1.27–2.04)
High blood pressure	1.34 (1.13–1.58)	1.23 (0.99–1.52)	1.28 (1.08–1.52)
High cholesterol	1.05 (0.89–1.23)	0.88 (0.71–1.08)	1.03 (0.87–1.22)
Diabetes	1.15 (0.95–1.38)	1.17 (0.93–1.47)	1.11 (0.92–1.33)
Cancer	1.41 (0.96–2.05)	1.55 (0.98–2.46)	1.34 (0.92–1.97)
Any major smoking-related condition	1.35 (1.12–1.62)	1.51 (1.20–1.89)	1.28 (1.06–1.54)
<i>Quitting of smoking</i>			
Any major respiratory condition	0.97 (0.75–1.24)	1.86 (1.22–2.83)	1.07 (0.83–1.39)
Asthma	0.90 (0.64–1.27)	0.96 (0.50–1.82)	0.96 (0.68–1.36)
Any respiratory condition	1.06 (0.86–1.32)	1.47 (1.00–2.17)	1.16 (0.93–1.44)
Any cardiovascular condition	1.16 (0.87–1.54)	0.98 (0.56–1.74)	1.27 (0.95–1.69)
High blood pressure	1.09 (0.87–1.37)	1.84 (1.20–2.83)	1.16 (0.92–1.45)
High cholesterol	1.29 (1.02–1.62)	1.75 (1.17–2.62)	1.34 (1.06–1.70)
Diabetes	1.08 (0.82–1.42)	1.37 (0.86–2.18)	1.17 (0.89–1.54)
Cancer	0.77 (0.47–1.25)	1.38 (0.59–3.23)	0.81 (0.50–1.33)
Any major smoking-related condition	1.05 (0.84–1.30)	1.73 (1.18–2.56)	1.16 (0.93–1.44)
<i>Initiation of e-cigarettes</i>			
Any major respiratory condition	2.86 (2.10–3.90)	3.36 (1.76–6.42)	2.02 (1.47–2.79)
Asthma	1.57 (1.05–2.35)	1.78 (0.75–4.22)	1.29 (0.85–1.95)
Any respiratory condition	2.08 (1.61–2.68)	1.41 (0.71–2.83)	1.67 (1.28–2.18)
Any cardiovascular condition	1.67 (1.16–2.42)	2.21 (1.08–4.55)	1.42 (0.98–2.08)
High blood pressure	1.55 (1.19–2.01)	1.38 (0.74–2.57)	1.28 (0.98–1.67)
High cholesterol	1.33 (1.01–1.75)	1.38 (0.76–2.49)	1.33 (1.00–1.77)
Diabetes	1.74 (1.31–2.32)	2.32 (1.37–3.92)	1.61 (1.20–2.16)
Cancer	2.51 (1.52–4.14)	3.67 (1.48–9.13)	2.14 (1.27–3.60)
Any major smoking-related condition	1.94 (1.48–2.55)	2.61 (1.50–4.51)	1.55 (1.17–2.06)

^a Numbers of adults changing tobacco/nicotine habits between Waves 1 and 4 are shown in Supplementary File 1 for each combination of health condition and change for the main analysis. Numbers for the other analyses are shown in the detailed results (Supplementary File 2).

^b Adjusted for sex and broad age groups

^c Excluding users of traditional cigars, filtered cigars, pipes, hookahs, smokeless tobacco, snus, and dissolvable products

^d Also adjusted for income, region and use of the products included in footnote b

OR = odds ratio with 95% confidence interval.

Table 2 summarizes the main results for initiation and for quitting of cigarette smoking, and for initiation of e-cigarettes. Note that initiation of e-cigarettes is regardless of cigarette smoking status, so includes those who become dual users as well as those non-smokers who become e-cigarette users, those becoming dual users forming the majority of cases (see Supplementary File 1). Similarly initiation and quitting of cigarettes is regardless of e-cigarette use, though here relatively few of those who initiated cigarettes would have used e-cigarettes at Wave 1. Note also that, as shown in Supplementary File 1, each of the changes in tobacco/nicotine status studied in the main analysis in Table 2 occurred quite often (from a minimum of 114 times for initiating smoking following onset of cancer to a maximum of 1,094 times for initiating e-cigarettes following onset of high blood pressure) so the OR estimates shown are reasonably precise.

For initiation of cigarettes, there was no evidence of a significant ($p < 0.05$) relationship for any of the respiratory conditions, or for high cholesterol, diabetes, or cancer.

However, for any cardiovascular condition, high blood pressure and any major smoking-related condition, there was evidence of a positive relationship, a relationship which was also seen in the sensitivity analyses. None of the interactions with age were significant. However, there was a significant interaction with sex for high blood pressure, where the positive relationship was seen only in males, and for high cholesterol, where some positive relationship was seen in males, but some negative relationship was seen in females. For quitting cigarette smoking, there was no significant evidence that smokers were less likely to quit following onset of any of the health conditions considered. For most of the conditions, there was no significant relationship, but some of the analyses showed a significant positive relationship. In the main analysis, this was only significant for high cholesterol, and the same was true following adjustment for more variables. However, evidence of a positive relationship was more clearly seen where other tobacco/nicotine product users were excluded. Here, there was a significant positive relationship, not only with high chol-

Table 3. Other changes in tobacco/nicotine habits between Waves 1 and 4 in relation to onset of health conditions in Waves 2 or 3 (main analyses)^a.

Health condition	ORs for change in tobacco/nicotine habits					
	Re-initiating cigarettes	Initiating cigarettes in never e-cig users	Quitting cigarettes in never e-cig users	Re-initiating cigarettes in never e-cig users	Initiating e-cigarettes in never smokers	Smokers becoming dual users
Any major respiratory condition	1.22 (0.57–2.61)	1.08 (0.83–1.41)	0.97 (0.74–1.27)	1.14 (0.48–2.70)	3.36 (1.57–7.16)	1.49 (0.98–2.27)
Asthma	0.95 (0.41–2.30)	1.15 (0.84–1.57)	0.77 (0.52–1.14)	0.93 (0.36–2.38)	1.96 (0.79–4.83)	0.65 (0.32–1.33)
Any respiratory condition	0.98 (0.54–1.76)	1.03 (0.85–1.26)	1.06 (0.84–1.34)	0.89 (0.45–1.76)	1.99 (1.02–3.88)	1.53 (1.06–2.21)
Any cardiovascular condition	0.73 (0.35–1.51)	1.64 (1.30–2.07)	1.12 (0.82–1.52)	0.60 (0.25–1.41)	1.82 (0.77–4.32)	1.42 (0.83–2.42)
High blood pressure	1.17 (0.73–1.88)	1.32 (1.11–1.57)	0.97 (0.75–1.25)	0.99 (0.57–1.73)	1.33 (0.76–2.33)	0.91 (0.58–1.42)
High cholesterol	1.18 (0.76–1.84)	1.04 (0.88–1.23)	1.24 (0.96–1.59)	1.29 (0.80–2.09)	1.21 (0.65–2.25)	1.45 (0.94–2.23)
Diabetes	1.80 (1.09–2.98)	1.14 (0.95–1.38)	1.05 (0.78–1.41)	2.02 (1.18–3.46)	4.23 (2.45–7.29)	1.02 (0.60–1.75)
Cancer	0.81 (0.25–2.64)	1.39 (0.94–2.05)	0.66 (0.38–1.15)	0.86 (0.24–3.12)	2.36 (0.63–8.78)	0.57 (0.19–1.74)
Any major smoking-related condition	0.95 (0.52–1.74)	1.33 (1.11–1.61)	1.03 (0.81–1.31)	0.94 (0.48–1.84)	2.20 (1.17–4.14)	0.95 (0.62–1.46)

^a Numbers of adults changing tobacco/nicotine habits between Waves 1 and 4 are shown in Supplementary File 1 for each combination of health condition and change
OR = odds ratio with 95% confidence interval.

esterol, but also with any major respiratory condition, high blood pressure and any major smoking-related condition. There were no significant interactions with sex, but for any major respiratory condition and any major smoking-related condition, significant interactions with age were seen, with evidence of a positive relationship restricted to those aged 55 years or older.

The probability of initiating e-cigarettes was increased in relation to the onset of each health conditions studied, both in the main analysis and also in the sensitivity analyses, with the association often being significant. There were no significant interactions with sex, and only one with age where for any major respiratory condition, the relationship was more evident in those aged 35 years or older.

Table 3 more briefly summarizes the results for six further changes in tobacco/nicotine habits. As can be seen from Supplementary File 1, numbers changing tobacco/nicotine habits tended to be somewhat lower than for Table 2, with the lowest being 45 for the relationship between onset of cancer and re-initiating cigarettes in never e-cigarette users. For re-initiating cigarettes, no consistent relationships were seen with the health conditions, though a significant positive relationship was seen with onset of diabetes. Also no consistent relationships were seen for smokers becoming dual users, though again a single significant positive relationship was seen, here with any respiratory condition. The three sets of analyses restricted to never e-cigarette users gave results quite similar to those when e-cigarette users were included. For initiating cigarettes, significant positive relationships were seen, as in Table 2, for any cardiovascular condition, high blood pressure, and any major smoking-related condition. For quitting cigarettes, the ORs were again similar to those in Table 2, while for re-initiating cigarettes, the only significant positive association was again that for diabetes. For initiating e-cigarettes in never smokers a consistent positive association was seen for each health condition, as was the case in Table 2, where there was no restriction on smoking habits.

In Table 3, however, confidence intervals of these ORs were considerably wider than in Table 2, as most e-cigarette initiators are current or past smokers. Fuller details of these analyses are given in Supplementary File 2.

Additional analyses

Effect of alternative exclusions

Details of these analyses are given in Supplementary File 3. Excluding those who at Wave 1 had any of the individual conditions studied (Additional analysis A) reduced the numbers of changes in tobacco/nicotine product use in the analyses markedly, generally by at least two-fold, and in some cases by over four-fold, and it was decided not to attempt to estimate ORs based on these diminished numbers. Excluding these who, at Wave 1, had any major smoking-related condition, and also, where appropriate, the particular condition considered (Additional analysis B) reduced the numbers of changes much less, typically by about 10 to 20% compared to the main analysis. However, the original and new OR estimates were generally quite similar, with no consistent tendency for ORs to increase or decrease.

Attempting to avoid reverse causation

As described in the methods, two additional analyses were carried out, with Additional analysis C based on changes occurring after first onset of the condition in Wave 2, and Additional analysis D based on changes after first onset in Wave 3, in each analysis the change definitely occurring after the onset. Table 4 compares results for initiating smoking, quitting smoking and initiating e-cigarettes, and for four selected health conditions from the main analysis ("Original results"), Additional analysis C, Additional analysis D, and those obtained by combining the results from Additional analyses C and D. As the number of changes in the combined C+D analysis is somewhat

Table 4. Comparison of original results (adjusted for sex and age group) with those avoiding reverse causation (see footnote). Results not shown for analysis or combined analysis where number of changes following onset of the condition is less than 2.

Health condition	Tobacco/nicotine habit change		Original results	Additional analysis C	Additional analysis D	Additional analyses C + D
Any major respiratory condition	Initiating smoking	OR	1.11 (0.85–1.44)	1.22 (0.78–1.89)	–	–
		n	286	113	80	193
	Quitting smoking	OR	0.97 (0.75–1.24)	0.75 (0.47–1.20)	1.78 (1.12–2.83)	1.16 (0.84–1.61)
		n	459	218	181	399
	Initiating e-cigarettes	OR	2.86 (2.10–3.90)	3.92 (2.39–6.45)	1.74 (0.48–6.32)	3.53 (2.22–5.61)
		n	656	321	255	576
Any respiratory condition	Initiating smoking	OR	1.05 (0.86–1.28)	1.15 (0.82–1.60)	1.01 (0.32–3.20)	1.14 (0.83–1.57)
		n	553	237	163	400
	Quitting smoking	OR	1.06 (0.86–1.32)	0.83 (0.57–1.23)	1.56 (1.01–2.42)	1.09 (0.82–1.46)
		n	639	310	234	544
	Initiating e-cigarettes	OR	2.08 (1.61–2.68)	2.64 (1.73–4.05)	2.18 (0.96–4.99)	2.54 (1.74–3.70)
		n	1092	543	437	980
Any cardio-vascular condition	Initiating smoking	OR	1.65 (1.31–2.08)	2.29 (1.63–3.22)	0.93 (0.16–5.57)	2.22 (1.59–3.10)
		n	279	117	66	183
	Quitting smoking	OR	1.16 (0.87–1.54)	0.97 (0.57–1.64)	1.22 (0.63–2.35)	1.06 (0.70–1.60)
		n	331	150	123	273
	Initiating e-cigarettes	OR	1.67 (1.16–2.42)	1.83 (0.95–3.53)	1.26 (0.28–5.75)	1.72 (0.94–3.15)
		n	587	287	248	535
Any major smoking-related condition	Initiating smoking	OR	1.35 (1.12–1.62)	2.03 (1.55–2.65)	0.95 (0.24–3.87)	1.98 (1.52–2.57)
		n	521	219	139	358
	Quitting smoking	OR	1.05 (0.84–1.30)	0.79 (0.53–1.19)	1.61 (1.05–2.49)	1.10 (0.82–1.48)
		n	606	286	227	513
	Initiating e-cigarettes	OR	1.94 (1.48–2.55)	2.22 (1.39–3.55)	0.93 (0.26–3.42)	2.01 (1.29–3.12)
		n	1048	526	412	938

Additional analysis C is restricted to those with unchanged tobacco/nicotine habits at Waves 1 and 2, and relates changes in tobacco/nicotine use between Waves 1/2 and Wave 4 according to whether onset of the condition occurred in Wave 2. Additional analysis D is restricted to those with unchanged tobacco/nicotine habits at Waves 1, 2 and 3, and relates changes in tobacco/nicotine use between Waves 1/2/3 and Wave 4 according to whether onset of the condition occurred in Wave 3.

OR = odds ratio with 95% confidence interval.

n = number of changes.

reduced from that in the main analysis, the ORs for the C+D analysis have a slightly wider confidence interval. However, in 10 of the 11 cases where there were enough changes following onset of the conditions the OR was somewhat greater in the C+D analysis, though the general pattern of results was quite similar, with the most consistent and strongest association being the tendency to initiate e-cigarettes following onset of a health condition. Results for some other tobacco/nicotine habit changes are given in Supplementary File 4.

Changes in amount smoked

Table 5 shows the estimated difference in average amount smoked (in cigarettes per day) between those with an onset of the health condition stated and those without an onset. Results are shown based on continuing smoking (Additional analysis E), allowing for quitting only (F) and allowing for quitting and relapse (i.e., re-initiation) (G). The great majority of the estimates are negative, including a tendency to cut down or quit on being diagnosed with a health condition. However, many differences seen were not statistically significant at $p < 0.05$. Of the seven that were, all were negative, the most highly significant relating to heart conditions.

6. DISCUSSION

We have carried out extensive analyses of the relationship of quitting smoking to onset of various health conditions. Our main analyses adjusted for sex and broad age groups, while other analyses controlled for additional variables, excluded users of other tobacco/nicotine products, restricted attention to those who had never used e-cigarettes, or attempted to adjust for reverse causation. None of these analyses showed any strong tendency for onset of a health condition to predict quitting. Even in the analyses excluding other tobacco/nicotine product users, ORs never exceeded 1.86 and significant increases were only seen for four of the nine health conditions with sufficient data for analysis - any major respiratory condition (OR 1.86, 95% CI 1.22–2.83), high blood pressure (1.84, 1.20–2.83), high cholesterol (1.75, 1.17–2.62) and any major smoking-related condition (1.73, 1.18–2.56). Given the lack of significantly reduced ORs for any condition in any analysis, the results seem, however, to be consistent with a tendency for onset of health conditions to lead to some increase in quitting.

Other nationally representative U.S. studies in which quit rates have been compared in those with and without specific health conditions have produced rather variable

Table 5. Change in amount smoked (cigs/day) between Waves 1 and 4 in relation to onset of health conditions in Waves 2 or 3.

Health condition	Change (95% CI) ^a with 95% confidence interval and coded probability values ^b		
	Additional analysis E in continuing smokers at Waves 1 and 4	Additional analysis F in smokers at Wave 1 (allowing for quitting only) ^c	Additional analysis G in the whole Wave 1 population (allowing for quitting and relapse) ^c
Any major respiratory condition	-0.29 (-1.18 to +0.60)	-0.77 (-1.69 to +0.14)	-0.36 (-0.71 to -0.02) *
Asthma	-0.13 (-1.38 to +1.11)	+0.08 (-1.19 to +1.34)	-0.05 (-0.51 to +0.41)
Any respiratory condition	+0.06 (-0.71 to +0.84)	-0.43 (-1.21 to +0.36)	-0.23 (-0.51 to +0.04)
Any cardiovascular condition	-2.24 (-3.31 to -1.16) ***	-2.32 (-3.40 to -1.23) ***	-0.39 (-0.73 to -0.05) *
High blood pressure	-1.08 (-1.94 to -0.22) *	-1.03 (-1.88 to -0.17) *	-0.13 (-0.39 to +0.14)
High cholesterol	-0.48 (-1.35 to +0.39)	-0.64 (-1.52 to +0.24)	-0.11 (-0.37 to +0.15)
Diabetes	-0.43 (-1.43 to +0.56)	-0.21 (-1.22 to +0.79)	-0.07 (-0.37 to +0.23)
Cancer	+0.12 (-1.63 to +1.88)	+0.37 (-1.43 to +2.18)	+0.00 (-0.61 to +0.61)
Any major smoking-related condition	-0.36 (-1.16 to +0.44)	-1.18 (-1.99 to -0.36) **	-0.21 (-0.47 to +0.06)

^a All analyses are adjusted for age and sex and take person-level weights into account.

^b *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

^c While Additional analysis E is restricted to those smoking a positive number of cigs/day at Waves 1 and 4, Additional analysis F also includes those not smoking cigarettes at Wave 4, while Additional analysis G also includes those not smoking cigarettes at Waves 1 or 4.

results. Thus a large study based on the 2018 Behavioral Risk Factor Surveillance System (11) found that adults with COPD had similar adjusted quit rates to those without COPD, despite making more quit attempts, while a smaller study based on the 1998 to 2013 Surveillance, Epidemiology and End Results study (19) found no difference in quit rates between bladder cancer cases and controls. Another study, based on the 2009 Behavioral Risk Factor Surveillance System (20), reported that the quitting rate for those without cancer (57%) was intermediate between the rate for those with tobacco-related cancer (55%) and for those with other cancers (62%). Clearer evidence that onset of a health condition is associated with increased quitting came from three studies. Based on the Health Professionals follow-up study (21) men diagnosed with cancer were more likely than matched men without cancer to quit smoking within two years (OR 2.5, 95% CI 2.0–3.0) or within four years (1.6, 1.3–2.0), though ORs varied considerably by cancer type. Based on the Cancer Prevention Study II Nutrition Cohort, WESTMAAS *et al.* (9) found that two-year quit rates were higher among smokers diagnosed with cancer than among smokers not diagnosed with cancer (31.3% vs 19.5%) with a similar difference observed after four years (43.0% vs 33.8%), the cancers considered excluding those of the lung, head and neck, oesophagus and any metastatic cancer. In an analysis based on waves of the National Health and Aging Trends study in 2011 and 2012 (22) the odds of smoking cessation were noted to increase with a new diagnosis of chronic illness since the 2011 wave.

Other changes in tobacco/nicotine use that we analyzed have rarely, if ever, been considered in other publications. However, it is interesting to note that though there is little evidence that onset of a health condition affects the probability that former cigarette smokers would re-initiate current cigarette smoking (a single marginally significant positive relationship for diabetes, one of the nine health conditions studied, being unconvincing and requiring independent replication), there is more evidence that onset of a health condition affects the probability that never cigarette smokers would initiate

cigarette smoking. Here all the ORs in the main analysis exceeded 1.0 and three (any cardiovascular condition, high blood pressure and any major smoking-related condition) were significant (at $p < 0.05$). However, none of the ORs were very large, the highest being 1.65 (95% CI 1.31–2.08), and again some independent confirmation would be valuable. Despite onset of a health condition apparently encouraging some never or former smokers to become current smokers, the results in Table 5 show some tendency for amount smoked by Wave 1 cigarette smokers to reduce between Waves 1 and 4 following onset of a health condition, though the reduction is smaller when the analyses consider the whole Wave 1 population.

Our clearest finding is that onset of a health condition consistently predicts initiation of e-cigarettes, with all the ORs in the main analysis significantly above 1, the largest values being 2.86 (95% CI 2.10–3.90) for any major respiratory condition, and 2.51 (1.52–4.14) for cancer. Though controlling for more variables, excluding users of tobacco/nicotine products other than cigarettes, and restricting attention to those who had never smoked cigarettes, made some ORs become non-significant they all remained positive. We are unaware that this finding has been reported previously. How much onset of a health condition predicts initiation of e-cigarettes may depend on their availability at the time, and public perception of their risks compared to those from cigarettes.

Our study has a number of strengths, including use of a nationally representative population which has widely been used in research, and the inclusion of detailed weighted analyses allowing for study of the effect of bias and confounding. It does, however, have some weaknesses. The sample size of 22,526 adults with smoking data at Waves 1 and 4 is not that large, and does not allow precise estimates of the OR relating some health conditions to some changes in tobacco/nicotine use. Also, disease diagnosis is not based on independent medical confirmation, severity of disease is not taken into account, and some of the disease categories combine different diseases, possibly with different effects on changes in tobacco/nicotine use. Furthermore, the

analyses relating onset of health conditions to quitting do not determine whether the quitting is long-term. The fact that errors have been discovered in the reporting of daily amount smoked (see methods) might suggest that other undiscovered errors are possible. Some older participants who stated that they have never smoked cigarettes at Wave 1 might not have bothered to mention past smoking, so that reports of current or past smoking at Wave 4, possibly affected by recent onset of a smoking-related health condition, might not necessarily imply that they had actually taken up smoking after Wave 1. Bias from this source would have the most effect on our analyses on initiation of cigarette smoking. Furthermore, details are not available on the nature and extent of any advice given to modify smoking habits. This would vary by the disease diagnosed, by U.S. state and by hospital within state. Detailed study of subsequent health effects following changes in tobacco/nicotine use after onset of health conditions is beyond the scope of this paper, though we note that the effect of changes in smoking habits (and of the advice given to modify smoking habits) is likely to vary substantially by disease, changes being likely to have the least effect in diseases with a very poor prognosis when diagnosed.

7. CONCLUSIONS

Based on analyses relating changes in tobacco/nicotine use between Waves 1 and 4 of the PATH study to onset of various health conditions in Waves 2 or 3, the clearest association noted was that for all nine health conditions studied, rates of initiation of e-cigarettes were higher in those where onset occurred than in those where it did not. The increase was consistently seen in the main and various sensitivity analyses with ORs often statistically significant at ($p < 0.05$). Positive associations were also often seen with quitting smoking, though these were weaker than for initiating e-cigarettes and rarely significant. Positive associations were also evident with initiating cigarette smoking, but these are subject to bias.

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9. DECLARATION OF INTERESTS

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