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Physicians' very brief (30-sec) intervention for smoking cessation on 13671 smokers in China: a pragmatic randomized controlled trial

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ABSTRACT

Background and aims Three to 10 minutes of smoking cessation advice by physicians is effective to increase quit rates, but is not routinely practised. We examined the effectiveness of physicians' very brief (approximately 30 sec) smoking cessation intervention on quit rates among Chinese outpatient smokers. **Design** A pragmatic, open-label, individually randomized controlled trial. **Setting** Seventy-two medical outpatient departments of hospitals and/or community health centers in Guangdong, China. **Participants** Chinese adults who were daily cigarette smokers (n = 13671, 99% males) were invited by their physician to participate during outpatient consultation. Smokers who were receiving smoking cessation treatment or were judged to need specialist treatment for cessation were excluded. **Interventions** The intervention group (n = 7015) received a 30-sec intervention including physician's very brief advice, a leaflet with graphic warnings and a card with contact information of available cessation services. The control group (n = 6656) received a very brief intervention on consuming vegetables and fruit. A total of 3466 participants in the intervention group were further randomized to receive a brief booster advice from trained study personnel via telephone 1 month following their doctor visit. **Measurements** The primary outcome was self-reported 7-day point prevalence abstinence (PPA) in the intervention and control groups at the 12-month follow-up. Secondary outcomes included self-reported 30-day abstinence and biochemically validated abstinence at 12-month follow-up. **Findings** By intention-to-treat, the intervention (versus control) group had greater self-reported 7-day abstinence [9.1 versus 7.8%, odds ratio (OR) = 1.14, 95% confidence interval (CI) = 1.03–1.26, P = 0.008] and 30-day abstinence (8.0 versus 6.9%, OR = 1.14, 95% CI = 1.03–1.27, P = 0.01) at 12-month follow-up. The effect size increased when only participants who received the intervention from compliant physicians were included (7-day PPA, OR = 1.42, 95% CI = 1.11–1.74). The group difference in biochemically validated abstinence was small (0.8 versus 0.8%, OR = 1.00, 95% CI = 0.71–1.42, P = 0.99). **Conclusion** A 30-sec smoking cessation intervention increased self-reported abstinence among mainly male smokers in China at 12-month follow-up (risk difference = 1.3%), and should be feasible to provide in most settings and delivered by all health-care professionals.

Keywords Physicians, RCT, smoking cessation, Tobacco, pragmatic, very brief intervention.

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INTRODUCTION

Smoking is the leading cause of morbidity and premature mortality [1,2]. Approximately one in 10 deaths world-wide are attributable to smoking [3]. In 2015, there were 933.1 million daily smokers in the world [3], and half will die prematurely from smoking-related diseases [4,5]. Without massive smoking cessation and strategies to prevent smoking initiation, the World Health Organization (WHO) target—a 30% reduction in smoking prevalence by 2025 [6]—seems impossible. 'Offer help to quit tobacco use', a policy of the WHO's 'MPOWER', is an effective measure for tobacco control; however, globally, it shows the slowest progress among all six MPOWER strategies [7]. In particular, most low- and middle-income countries do not provide cost-covered cessation services and medications [7]. Even in countries that provide such services, the services often have low rates of engagement which limit their

population impact (use of cessation treatment services in developing countries 4–28%) [8]. In China, the use of the medication for quitting in quit attempters was only approximately 2% [9].

Physicians' cessation advice during their usual medical consultations increases abstinence rates [10,11], and it is an affordable intervention [12]. However, providing such advice for 3–10 minutes, although described as a 'brief' intervention by the WHO [13], is unrealistic and impractical in busy settings where physicians often have only 5–10 minutes for each patient. In most countries, fewer than half the physicians delivered such brief advice [14,15]. Barriers for physicians to provide patients with smoking cessation advice include lack of time [16] and lack of training in smoking cessation treatment. Only 44% of the countries that signed the Framework Convention on Tobacco Control integrated brief advice into existing cessation treatment services [17]. To facilitate physicians' compliance, very brief physician advice—lasting only 1–3 minutes—may be more feasible than 'brief' advice.

To date, the absolute risk of smoking, as stated by the WHO, is that one in two smokers will be killed by smoking [4]. Although this message is easy to understand, it has not been used as a key warning message on tobacco packaging [18] and has not been used in mandatory health warnings world-wide [19]. In developing a very brief (approximately 30 sec) intervention, we included the 1-in-2 absolute risk of smoking in a new AWARD (Ask, Warn, Advise, Refer and Do-it-again) model. The AWARD model is a simple protocol in delivering very brief smoking cessation advice including five steps: (1) ask whether the patient smokes; (2) warn about the risk—that one in two smokers or even two in three smokers who started smoking at younger age and smoked heavily will be killed by smoking [4]; (3) advise to quit as soon as possible; (4) refer to existing smoking treatment services; and (5) do-it-again—repeat the advice if smokers continue to smoke or relapse. The AWARD model does not require assessment of smokers' readiness to quit (assess) or a quit plan (assist), as stated in the commonly used 5A model. The model emphasizes the very brief but strong warnings, and refers all patients to smoking cessation services that are available. Our previous trial showed that briefly trained smoking cessation ambassadors had delivered cessation advice using AWARD to 920 community smokers in 27 outreach health promotion sessions [20]. The training of using AWARD could be as short as 1 hour [21].

Systematic reviews showed that physicians' brief intervention for smoking cessation increased abstinence rates by 47–78% [10,11,22]. From these reviews, we identified five randomized controlled trials (RCTs) in which the interventions are brief, taking less than 2 minutes [23–27], and two of the five trials showed the effectiveness of the intervention on promoting abstinence outcomes at 1-year follow-up, with risk ratios (RRs) from 1.42 to 1.62 [23,24]. The five RCTs are either too dated or on relatively small samples. Two recently published RCTs examined the effectiveness of physicians' very brief (1-minute) smoking cessation advice [21,28]. One RCT conducted in Guangdong, China showed that physicians' very brief advice (less than 30 sec) increased self-reported 7-day point prevalence abstinence at 12-month follow-up by approximately twofold [intervention 18.9% versus control 5.8%, RR = 3.28, 95% confidence interval (CI) = 0.94–11.41]. The other RCT, conducted in Beijing, showed that physicians' very brief advice increased self-reported 6-month prolonged abstinence at 12-month follow-up by onefold [intervention 15.7% versus control 7.8%, adjusted odds ratio (aOR) = 2.26, 95% CI = 0.97–5.26]. Both trials revealed that physicians' very brief smoking cessation advice increased smokers' 1-year quit rate with a large effect size. However, these results were non-significant, owing to small sample sizes.

In this study, we conducted a three-arm RCT to assess the effectiveness of physicians' very brief smoking cessation intervention (30-sec advice plus printed materials) in outpatient clinics of hospitals and community health centers in Guangdong, China. We hypothesized that the intervention group would have a higher prevalence of self-reported abstinence than the control group.

METHODS

Study design

This parallel, multi-site, pragmatic RCT (allocation ratio for intervention and control was 1 : 1) recruited smokers from 72 outpatient clinics of hospitals and community health centers in two large cities (Guangzhou and Shenzhen) and five rapidly expanding cities (Zhuhai, Zhongshan, Dongguan, Jiangmen and Shantou) in Guangdong Province, China. At the 1-month follow-up, the intervention group was further divided into two subgroups to assess the effectiveness of booster telephone advice on smoking cessation led by trained study personnel. The protocol was slightly amended twice in December 2015 and August 2016 (Supporting information, Appendix 1) to include more hospitals and community health centers as recruitment sites, and a fidelity survey on the participating physicians' compliance to the intervention protocol. The trial design was highly pragmatic, based on the PRECIS-2 (PRagmatic Explanatory Continuum Indicator Summary) criteria [29] (Supporting information, Appendix 2). Supporting information, Appendix 3 shows the schedule or enrolment and follow-up assessments.

Ethical approval was granted by the University of Hong Kong, the Hong Kong West Cluster of Hospital Authority (HKU/HA HKW) Institutional Review Board (UW 14–419). An independent data monitoring

committee, including two external professorial staff from the School of Nursing of the University of Hong Kong, was set up to review the collected data. They determined that the effect sizes were stable and that we could cease recruitment before reaching the target number (Supporting information, Appendix 4).

Physicians' training

We invited physicians of outpatient clinics in major hospitals, which were recommended by Guangzhou and Guangdong Health Bureaus and Shenzhen Tobacco Control Associations, to participate in a 1-hour training work-shop. The work-shop covered topics including smoking prevalence and trends, the WHO Framework Convention on Tobacco Control, MPOWER measures, the AWARD model and purpose and design of this RCT. We organized a total of 30 work-shops from 2014 to 2016, and 398 physicians and 941 other health-care professionals attended the training. In addition, 26 physicians, who were trained by their colleagues, participated in the RCT.

Recruitment procedures

During usual medical outpatient consultations (January 2015–September 2016), the physicians determined the eligibility of their patients for the trial. The inclusion criteria were (1) aged 18 years or older, (2) currently smoking at least one cigarette per day, (3) Chinese residents who could communicate in Chinese and (4) having a telephone. Exclusion criteria were (1) receiving any smoking cessation treatment or participating in any smoking cessation trials, (2) needing special care to quit due to chronic disease and/or other reasons and (3) having communication difficulties. Eligible smokers were informed by their physicians about the trial with an information leaflet (Supporting information, Appendix 5) and invited to participate. The physician then randomized participants to either the intervention or control group with the 'sequentially numbered, opaque, and sealed envelopes' (SNOSE) method; delivered the intervention; and reminded participants about the 3-day follow-up telephone interview. Trained study personnel called participants within 3 days following the doctor visit and invited them to complete a brief baseline survey. Participants were not compensated for participation in the survey. Physicians received RMB¥20 (≈US$ 2–3) for each participant recruited into the study.

Randomization, masking and blinding

Participants were randomly assigned on an individual level to intervention or control groups by their physician at baseline. Our research assistant (RA), who was not involved in the recruitment procedures, generated a random sequence list of the group allocation (intervention or control) with a random-number generator and sequentially numbered identifiers. The RA inserted a group assignment paper (red for the intervention group and green for the control group) in a SNOSE for randomization. After participants provided a written consent at baseline recruitment, the physicians opened the envelope to determine the group assignment and delivered the intervention. Hence, both physicians and participants were concealed from the group assignment before participants' consent. At the 1-month follow-up telephone interview, participants from the intervention group were randomly allocated into the intervention A (IA) or intervention B (IB) groups through a computer-assisted patient interview system following their completion of the follow-up phone survey. Hence, the group assignment at 1-month follow-up was not revealed to physicians, participants and telephone interviewers (outcome assessors). Because the intervention for all trial groups was behavioral, all physicians, participants and telephone interviewers at 1-month follow-up were not blinded from the according intervention; however, the telephone interviewers at the 3-, 6- and 12-month follow-up and researchers who ran the analysis were blinded to the group allocation of all participants.

Interventions

Participants in the intervention group all received very brief (approximately 30 sec) 'WAR' smoking cessation advice, which originated from the AWARD model [20] from the physician as follows: 'According to the WHO, one in two smokers will be killed by smoking. I warn you that the latest research showed that about two in three smokers will be killed by smoking ('W'arn). You must quit immediately ('A'dvise). Here is a leaflet and a card showing the telephone number of the smoking cessation clinic where professionals will help you quit smoking. Please seek their help as soon as possible ('R'efer)'.

We encouraged physicians to make eye contact, speak solemnly, show a red leaflet (Supporting information, Appendix 6) and gesticulate to emphasize the absolute risk of smoking, and then courteously hand patients a card (Supporting information, Appendix 6). The leaflet covered diseases caused by smoking and second-hand smoke exposure, explicit pictorial health warnings, motivational messages to quit and benefits of quitting. The card showed the physician's name, the WAR advice, contact information of the smoking cessation clinics and follow-up telephone interview schedule. These materials were used to supplement physicians' 30-sec advice and save physicians' time in handling further enquiries.

The control group received very brief (approximately 30 sec) health advice concerning eating fruit and vegetables, the pictorial information leaflet and the reminder card

on eating more fruit and vegetables (Supporting information, Appendix 7).

Baseline and follow-up data collection

Supporting information, Appendix 3 lists all the baseline, follow-up and outcome variables assessed in this study. Lay interviewers (without being formally trained on knowledge of tobacco control) conducted the telephone follow-ups with a tablet installed with a survey program. At the 3-day follow-up, we collected additional baseline information on smoking and quitting so that the physicians did not need to ask these questions during interventions, and participants were not subjected to questioning for longer than the very brief advice. At 1 month, in the intervention group, after completing a short follow-up survey, the telephone interviewers were notified of the new group allocation (groups IA or IB). In group IA, the interviewer provided the same WAR smoking cessation advice. No such additional intervention was provided to group IB or controls.

At 3-, 6- and 12-month follow-up the interviewers, who were blinded to the group allocation, contacted participants to complete a phone survey. At 6 and 12 months, participants who reported abstinence during the past 7 days were invited to complete a biochemical validation within a month at the place of recruitment. Self-reported quitters with exhaled carbon monoxide below 4 parts per million (p.p.m.) and salivary cotinine below 10 ng/ml, which were measured with a PiCO Smokerlyzer (Bedfont Scientific, Kent, UK) and NicAlertstrips (Nymox Pharmaceutical Corporation, St Laurent, QC, Canada) were classified as biochemically validated quitters. Participants who completed a biochemical validation (no matter if the validation result was positive or negative) were provided with RMB¥200 (≈US $30) as compensation for their time and travel expenses.

Outcomes

The primary outcome was self-reported 7-day point prevalence abstinence (PPA) at 12-month follow-up. As this RCT recruited a large population of smokers, including those without intention to quit and were unlikely to agree to biochemical validation, and used a very low-intensity intervention, misrepresentation of smoking status was considered low [30]. Also, self-reported abstinence is clinically meaningful to smokers and can be assessed under usual conditions; hence, self-reported abstinence was chosen as the primary outcome. The secondary outcomes included (1) 7-day PPA at the 6-month follow-up; (2) biochemically validated quit rates at 6 and 12 months; (3) interviewer-verified quit rates at 6 and 12 months (see Supporting information, Appendix 11 footnote); (4) self-reported 30-day continuous abstinence at 6 and 12 months; (5) self-reported smoking reduction (cigarettes or other tobacco consumption reduced by at least half compared with baseline) at 1, 3, 6 and 12 months; (6) self-reported quit attempts (intentionally stopped smoking for at least 24 hours) at the fourth follow-up; (7) self-reported use of smoking cessation service, including visiting smoking cessation clinics or calling the quit lines at the four follow-up; and (8) any weight gain, based on their self-report weight at 3, 6 and 12 months compared with baseline.

Fidelity survey

Participating physicians were invited to complete a 16-item fidelity survey, which assessed their delivery of key components of the intervention protocol during August 2016 to May 2017 (Table 1). We assumed that if the physicians reported full compliance to the intervention, all their patients should receive the intervention as stated in the protocol. Therefore, we defined participants whose physician was compliant as 'compliant physicians' participants'.

Pre-registered hypothesis

We hypothesized that the intervention group would have a higher prevalence of self-reported tobacco abstinence at the 12-month follow-up than the control group (https://clinicaltrials.gov/ct2/show/NCT02494960?term=NCT02494960&rank=1).

Statistical analysis

Conservatively assuming a natural quit rate of 1% in the control group and a moderate effect with a relative risk of 1.6 (i.e. 1.6% in the intervention group) with $\alpha = 0.05$ and power of 90%, the required sample size was 12864. Assuming a retention rate of 80%, the revised sample size was 16080 using the calculator GPower version 3.1.

The primary comparison was the quitting outcomes between the intervention and control group, and the secondary comparisons included group IA versus control, group IB versus control and groups IA versus IB. All data analyses were conducted using SPSS version 24.0 for Windows (SPSS Inc., Chicago, IL, USA). The main analysis was by intention-to-treat, with participants lost to follow-up treated as smokers. The number needed to treat (NNT), which shows the number of treated subjects needed to have one additional successful outcome, was computed by taking the reciprocal of the risk difference between the intervention and control group. Sensitivity analyses included modified complier average causal effect (mCACE) [31] analysis, including compliant physicians' participants only (Supporting information, Appendix 8), and analysis

TABLE 1 Fidelity survey on physicians' compliance to the intervention protocol (n = 90 of 424 physicians who participated in the RCT).

	Row %					
	Never	*Rarely*	*Half-half*	*Mostly*	*Always*	*Don't remember*
Intervention group						
1. Warned about the risk of smoking[a]	4	1	3	3	88	0
2. Advised to quit smoking immediately	1	0	2	3	92	1
3. Delivered the red leaflet	0	0	1	1	98	0
4. Delivered the red card	0	0	1	1	93	4
5. Advised to eat more fruit and vegetables	93	0	1	0	1	4
6. Advised to eat at least 5 bowls of fruit and vegetables	94	0	0	0	0	6
7. Delivered the green leaflet	96	0	0	0	0	4
8. Delivered the green card	96	0	0	0	0	4
Control group						
9. Warned about the risk of smoking[a]	51	2	6	2	36	3
10. Advised to quit smoking immediately	31	3	4	8	51	2
11. Delivered the red leaflet	96	0	0	0	0	4
12. Delivered the red card	89	0	0	0	0	11
13. Advised to eat more fruit and vegetables	6	0	4	1	87	2
14. Advised to eat at least 5 bowls of fruit and vegetables	10	1	6	3	79	1
15. Delivered the green leaflet	1	0	1	1	94	2
16. Delivered the green card	1	0	1	1	94	2

	n (row %)	
	Yes	No
Physicians who were compliant to the intervention for the intervention group	78 (87%)	12 (13%)
Physicians who were compliant to the intervention for the control group	26 (29%)	64 (71%)

[a]The warning message was: 'According to WHO, one in two smokers will be killed by smoking. I warn you that the latest research showed that about two in three smokers will be killed by smoking'. The red leaflet and the red referral card (Supporting information, Appendix S4) included the risk of smoking and details of smoking cessation clinics. The green leaflet and the green card (Supporting information, Appendix S5) were interventions for the control group. Physicians who answered 'always' or 'mostly' in items 1–4 and 'never' or 'rarely' in items 5–8 were identified as being compliant to the protocol for the intervention group. Physicians who answered 'never' or 'rarely' in items 9–12 and 'always' or 'mostly' in items 13–16 were identified as being compliant to the protocol for the control group. Gray cells indicate the criteria of being compliant. RCT = randomized controlled trial.

using multiple imputation procedure. Planned subgroup analysis by analyzing the odds ratios of 7-day PPA at 12 months and *P*-values for interaction by participants' socio-demographic and smoking/quitting history was conducted.

To account for any correlation of outcomes within each recruitment site, a generalized estimating equation model adjusting for socio-demographic and smoking characteristics assessed at baseline or 3-day follow-up was used instead of *t*-tests and multivariate logistic regression analyses, as originally stated in the protocol. The homogeneity of treatment effect across recruitment sites or cities was checked by testing the interaction between recruitment site/cities and group allocation as a fixed effect in the logistic model using the Wald test. We found no evidence of heterogeneity (i.e. all *P*-values of interaction terms > 0.1). Logistic regression models were used in the mCACE analysis, because the heterogeneity in the intervention compliance among different physicians and recruitment sites had been removed. We also assumed the missing outcomes are dependent upon observed data (missing at random) and used multiple imputation procedure to impute the missing data in another sensitivity analysis. To restrain false-positive findings from assessing the primary and secondary outcomes, the Benjamini–Hochberg procedure [32] was applied to calculate new thresholds for statistical significance. All the above statistical details were described in detail in Supporting information, Appendices 8 and 12.

RESULTS

Of the 27418 patients being screened from 7 January 2015 to 18 September 2016, 13671 (49.9%) were randomized to the intervention (n = 7015) and control (n = 6656) groups (Fig. 1). At the 1-month follow-up, the intervention group was equally divided into group IA (n = 3466) and group IB (n = 3549). Owing to a shortage of manpower and delays in fund transfers from Hong Kong to mainland China, approximately 13.5% (1 month), 35.5% (3 months), 14.1% (6 months) and 11.4% (12 months) of the participants were not contacted at the respective follow-up. Attrition among three trial groups at all follow-ups showed no significant differences. Supporting information, Appendix 9 shows that living in Shenzhen, being male and more smoking days in the past month were

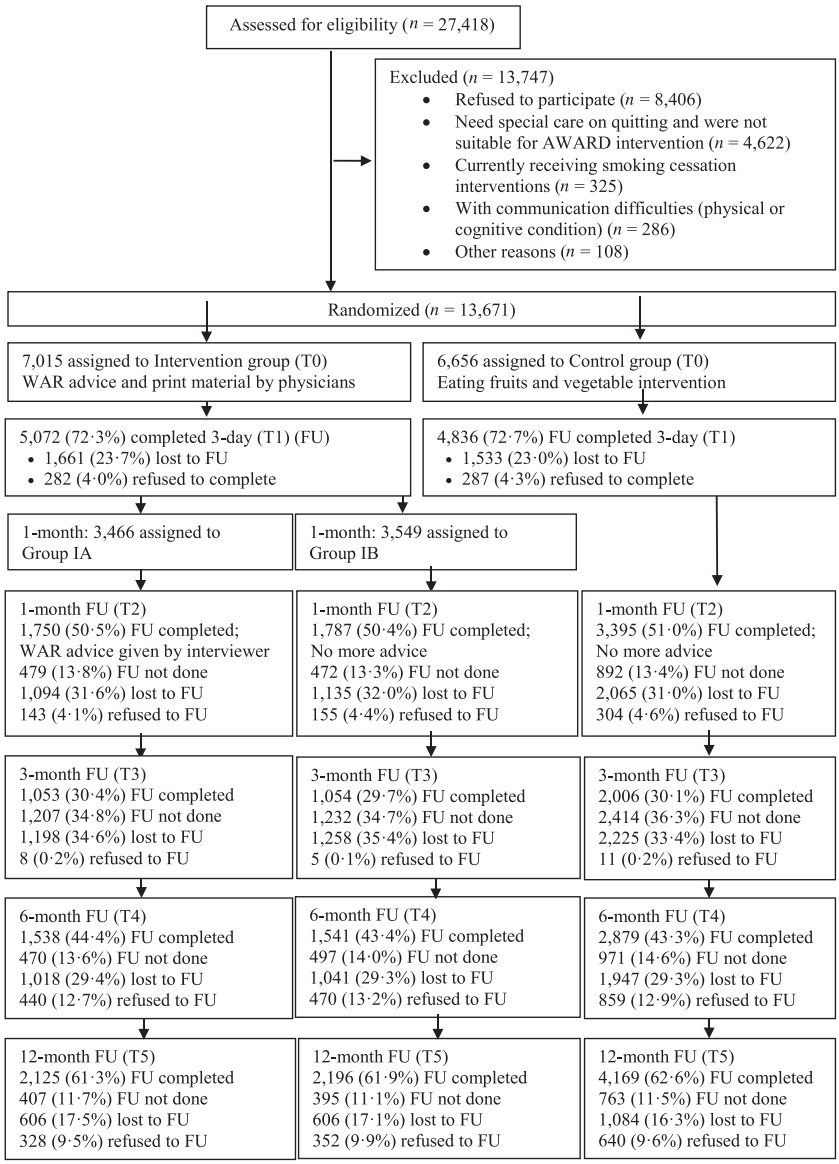

FIGURE 1 Consolidated Standards of Reporting Trials (CONSORT) flow-chart. FU = follow-up; WAR advice = very brief smoking cessation advice including 'warn', 'advise' and 'refer' components

associated with the follow-up completion at 6 and 12 months.

Table 2 shows that most socio-demographic and smoking characteristics showed no substantial differences among the trial groups. More participants in group IA (versus controls) (53.7 versus 51.8%, respectively; OR = 1.12, 95% CI = 1.01–1.25, $P = 0.03$) and group IB (55.7 versus 51.8%, respectively; OR = 1.21, 95% CI = 1.09–1.34, $P < 0.01$) reported either quit attempts or smoking reduction by 50% 3 days after the baseline intervention.

Only 90 of 424 physicians completed the fidelity survey. These physicians could be matched with 9939 trial participants (72.8% of all participants). Of the 90 physicians, 87% reported that they typically or always followed the protocol in delivering the intervention to the intervention group, including the WAR advice and the print materials (Table 2). Approximately half warned the control group participants about the risks of smoking and approximately one-third advised the control group participants to quit. Only 29% of physicians were identified as compliant for the control group. In all trial participants (Table 3), 5940 (43.4%) were identified as compliant physicians' participants. More participants in group IA (62.9%) and group IB (61.5%) than the control group (29.7%) were compliant physicians' participants.

Using intention-to-treat (ITT), the intervention group showed a significantly greater self-reported 7-day PPA (9.1% vs. 7.8%; OR = 1.14; 95% CI = 1.03–1.26; Risk difference = 1.3%) and 30-day PPA (8.0% vs. 6.9%; OR = 1.14; 95% CI = 1.03–1.27) than the control group

TABLE 2 Socio-demographic characteristics assessed at baseline.

Assessed at initial recruitment survey		*Group IA (n = 3466) %*	*Group IB (n = 3549) %*	*Control (n = 6656) %*
City of residence	Shenzhen	2063 (59.5)	2121 (59.8)	3857 (57.9)
	Guangzhou	711 (20.5)	711 (20.0)	1411 (21.2)
	Zhongshan	391 (11.3)	443 (12.5)	842 (12.7)
	Zhuhai	165 (4.8)	158 (4.5)	304 (4.6)
	Shantau	92 (2.7)	74 (2.1)	170 (2.6)
	Jiangmen	41 (1.2)	39 (1.1)	68 (1)
	Dongguan	3 (0.1)	3 (0.1)	4 (0.1)
Sex	Male	3431 (99.0)	3510 (98.9)	6576 (98.8)
	Female	35 (1.0)	39 (1.1)	76 (1.1)
	DK/RTA	(0)	(0)	4 (0.1)
Age group (years)	18–29	854 (24.6)	844 (23.8)	1617 (24.3)
	30–39	1022 (29.5)	1088 (30.7)	1985 (29.8)
	40–49	828 (23.9)	878 (24.7)	1611 (24.2)
	50–59	477 (13.8)	461 (13)	873 (13.1)
	60–69	192 (5.5)	197 (5.6)	395 (5.9)
	70 or above	63 (1.8)	42 (1.2)	96 (1.4)
	DK/RTA	30 (0.9)	39 (1.1)	79 (1.2)
Mean age, years (SD)		39.4 (12.5)	39.2 (12.0)	39.4 (12.3)
Marital status	Single	594 (17.1)	599 (16.9)	1081 (16.2)
	Married	2780 (80.2)	2860 (80.6)	5402 (81.2)
	Divorced	28 (0.8)	21 (0.6)	43 (0.6)
	Widowed	5 (0.1)	5 (0.1)	13 (0.2)
	DK/RTA	59 (1.7)	64 (1.8)	117 (1.8)
Education level	Junior secondary or below	1353 (39.0)	1404 (39.6)	2629 (39.5)
	Senior secondary	1171 (33.8)	1235 (34.8)	2362 (35.5)
	Diploma	467 (13.5)	448 (12.6)	865 (13.0)
	Bachelor or above	378 (10.9)	374 (10.5)	638 (9.6)
	DK/RTA	97 (2.8)	88 (2.5)	162 (2.4)
Any children	No	696 (20.1)	679 (19.1)	1276 (19.2)
	One	1140 (32.9)	1179 (33.2)	2278 (34.2)
	Two or more	1509 (43.5)	1570 (44.2)	2863 (43.0)
	DK/RTA	121 (3.5)	121 (3.4)	239 (3.6)

Assessed at 3-day telephone survey		*Group IA (n = 2506)*	*Group IB (n = 2566)*	*Control (n = 4836)*
Perceived health status	Very good	136 (5.4)	135 (5.3)	215 (4.4)
	Good	1561 (62.3)	1600 (62.4)	2984 (61.7)
	Fair	700 (27.9)	681 (26.5)	1371 (28.3)
	Bad	90 (3.6)	122 (4.8)	227 (4.7)
	Very bad	3 (0.1)	3 (0.1)	9 (0.2)
	DK/RTA	16 (0.6)	25 (1.0)	30 (0.6)
Days of smoking in past 30 days (SD)		26.7 (8.3)	26.7 (8.2)	26.9 (8.1)
Mean daily cigarette consumption (SD)		16.5 (9.5)	16.0 (9.4)	16.2 (9.5)
Time to first smoking after waking	< 5 minutes	599 (23.9)	612 (23.9)	1168 (24.2)
	6–30 minutes	496 (19.8)	527 (20.5)	977 (20.2)
	31–60 minutes	444 (17.7)	436 (17.0)	855 (17.7)
	> 1 hour	657 (26.2)	699 (27.2)	1301 (26.9)
	DK/RTA	310 (12.4)	292 (11.4)	535 (11.1)
Any home smoking restriction	Yes, no smoking anywhere	223 (8.9)	262 (10.2)	493 (10.2)
	Yes, smoking is allowed at specific time or place	489 (19.5)	517 (20.1)	954 (19.7)
	No restriction	1524 (60.8)	1523 (59.4)	2934 (60.7)

(***Continues***)

Table 2. (Continued)

Assessed at 3-day telephone survey		*Group IA (n = 2506)*	*Group IB (n = 2566)*	*Control (n = 4836)*
	DK/RTA	270 (10.8)	264 (10.3)	455 (9.4)
Living with smokers	Yes	672 (26.8)	698 (27.2)	1278 (26.4)
	No	1449 (57.8)	1490 (58.1)	2888 (59.7)
	Living alone	109 (4.3)	110 (4.3)	207 (4.3)
	DK/RTA	276 (11.0)	268 (10.4)	463 (9.6)
Any quit attempt history	Yes	778 (31.0)	820 (32.0)	1514 (31.3)
	No	1459 (58.2)	1489 (58.0)	2866 (59.3)
	DK/RTA	269 (10.7)	257 (10.0)	456 (9.4)
Any quit attempt or smoking reduction	Yes	1345 (53.7)	1429 (55.7)	2505 (51.8)
after baseline	No	886 (35.4)	883 (34.4)	1872 (38.7)
	DK/RTA	275 (11.0)	254 (9.9)	464 (9.6)

DK/RTA: don't know/refuse to answer. All differences (intervention versus control; IA versus C; IB versus C; IA versus IB), except quit attempt or smoking reduction after baseline, were due to chance, i.e. randomization.

TABLE 3 Distribution of participants by group and compliance of their physicians.

	Group IA (n = 3466)	*Group IB (n = 3549)*	*Control (n = 6656)*
Participants whose physicians were compliant to the protocol	2181 (62.9)	2183 (61.5)	1976 (29.7)
Participants whose physicians were not compliant to the protocol	360 (10.4)	376 (10.6)	2863 (43.0)
Participants whose physicians' compliance was unknown	925 (26.7)	990 (27.9)	1817 (27.3)

at 12-month follow-up (Table 4). The group differences at 6 months were also significant. The results from the ITT analysis adjusted for other baseline variables, mCACE and the multivariate model with MI were consistent with the ITT analysis without covariate adjustments. In mCACE analysis, the OR of 7-day PPA and 30-day PPA was 1.42 (95% CI = 1.15–1.74) and 1.38 (95% CI = 1.11–1.71), respectively. The numbers needed to treat for 7- and 30-day PPA at 12-months were 82.7 (95% CI = 46.7–360.6) and 91.9 (95% CI = 50.9–476.9), respectively (Supporting information, Appendix 10).

Of the 801 participants who reported 7-day PPA at 12-month follow-up, 115 (group IA, 37; group IB, 23; and controls, 55) participated in biochemical validation tests, and 113 were validated quitters. The group difference in biochemically validated abstinence was small (Table 4).

Table 5 and Supporting information, Appendix 11 show the findings of other secondary comparisons, which have addressed multiple comparisons (more details in Supporting information, Appendix 10). The intervention group showed a significantly greater proportion of 30-day PPA, smoking reduction by at least 50% and use of smoking cessation service at 12 months compared to the control group. Group IA showed significantly greater 7-day PPA and smoking reduction by at least 50% at 12 months than did the control group. Group IB showed significantly greater smoking reduction by at least 50% and use of smoking cessation service at 12 months compared to the control group. Very few participants reported using smoking cessation services, quitlines and cessation medications during the study period (all prevalence $< 1\%$). Outcome comparisons of groups IA versus IB revealed no significant group differences.

Subgroup analyses in Table 5 show that the intervention effect was significantly greater in smokers aged younger than 40 years than their older counterparts (aged 40–64 years), and greater in smokers with a senior secondary education level than those with a junior education or below. Smokers who had a higher degree of nicotine dependence (first-time smoking each day was 5 minutes or less after waking) had a greater OR (1.41) than did other subgroups (95% CI = 1.06–1.11); however, the interaction was non-significant.

DISCUSSION

This RCT provides the first evidence that physicians' very brief (approximately 30 sec) smoking cessation intervention during usual medical outpatient consultations increased self-reported tobacco abstinence at 12-month follow-up. The intervention also increased smoking reduction and use of the smoking cessation service. Additional brief advice by lay interviewers at 1 month follow-up (group IA) did not contribute benefits to the abstinence, probably because only half the group IA participants

TABLE 4 Main outcomes at 12-month follow-up expressed as risk differences (RD) and odds ratios (OR) showing the intervention effect from intention-to-treat (ITT) and sensitivity analyses.

	Prevalence %			*Unadjusted, ITT I: 7015; C: 6656*		*Unadjusted, PPA (6 m) I: 2879; C: 3079 (12 m): I: 4169; C: 4321*		*Unadjusted, mCACE I: 4364; C: 1976*		*Adjusted, missings handled with MI I: 7015; C: 6656*	
	Intervention (I) (IA + IB) (n = 7015)	*Control (C) (n = 6656)*	*RD (95% CI)*	*OR (95% CI)*	*P-value*	*OR (95% CI)*	*P-value*	*OR (95% CI)*	*P-value*	*aOR (95% CI)*	*P-value*
7-day PPA											
6-month	455 (6.5)	346 (5.2)	1.29 (0.29, 2.29)	1.20 (1.06, 1.36)	0.004	1.21 (1.05, 1.39)	0.008	2.03 (1.54, 2.67)	< 0.001	1.23 (1.05, 1.44)	0.01
12-month (Primary outcome)	635 (9.1)	522 (7.8)	1.21 (0.05, 2.37)	1.14 (1.03, 1.26)	0.008	1.17 (1.05, 1.29)	0.003	1.42 (1.15, 1.74)	0.001	1.14 (0.99, 1.31)	0.052
30-day PPA											
6-month	385 (5.5)	292 (4.4)	1.10 (0.18, 2.03)	1.19 (1.05, 1.36)	0.007	1.20 (1.04, 1.40)	0.01	2.14 (1.58, 2.91)	< 0.001	1.20 (0.99, 1.46)	0.07
12-month	559 (8.0)	458 (6.9)	1.09 (0.001,2.18)	1.14 (1.03, 1.27)	0.01	1.17 (1.05, 1.30)	0.005	1.38 (1.11, 1.71)	0.004	1.14 (1.01, 1.29)	0.03
Biochemically validated abstinence											
6-month	18 (0.3)	11 (0.2)	0.09 (−0.11, 0.30)	1.53 (0.78, 3.00)	0.22	1.55 (0.74, 3.25)	0.25	2.95 (0.67, 13.01)	0.11	1.78 (0.99, 3.21)	0.054
12-month	58 (0.8)	55 (0.8)	0.00 (−0.40, 0.40)	1.00 (0.71, 1.42)	0.99	1.02 (0.72, 1.45)	0.92	1.12 (0.72, 2.04)	0.83	0.95 (0.65, 1.39)	0.78

RD = risk difference; CI = confidence interval; OR = odds ratio from generalized estimation equation (GEE) models, except mCACE analysis using logistic regression models; aOR = odds ratios from multivariate GEE model with adjustment of the baseline variables in Table 1; ITT = intention-to-treat, respondents with missing information were treated as smokers; mCACE = modified complier average causal effect, analysis including participants whose physicians were compliant to the protocol according to the fidelity survey result; MI = multiple imputation; PPA = point-prevalence of self-reported abstinence; biochemically validated abstinence = abstinence validated by exhaled carbon monoxide < 4 parts per million and salivary cotinine < 10 ng/ml.

TABLE 5 Secondary outcomes at 12-month follow-up.

	n, Prevalence (%)			*Intervention versus control*		*Group IA versus control*		*Group IB versus control*		*Group IA versus group IB*	
	Group IA (n = 3466)	*Group IB (n = 3549)*	*Control (n = 6656)*	*OR (95% CI)*	*P-value*	*OR (95% CI)*	*P-value*	*OR (95% CI)*	*P-value*	*OR (95% CI)*	*P-value*
7-day PPA	318 (9.2)	317 (8.9)	522 (7.8)	**1.14(1.03, 1.26)**	**0.008**	**1.15 (1.02, 1.29)**	**0.02**	1.13 (1.01, 1.27)	0.03	1.01 (0.89, 1.16)	0.83
30-day PPA	279 (8.0)	280 (7.9)	458 (6.9)	**1.14 (1.03, 1.27)**	**0.01**	1.15 (1.01, 1.30)	0.04	1.14 (1.01, 1.28)	0.03	1.01 (0.88, 1.16)	0.88
Biochemically validated abstinence	36 (1.0)	22 (0.6)	55 (0.8)	1.00 (0.71, 1.42)	0.99	1.27 (0.84, 1.93)	0.25	0.75 (0.48, 1.17)	0.21	1.69 (1.05, 2.73)	0.03
Quit attempt (including quitters)	820 (23.7)	809 (22.8)	1502 (22.6)	1.06 (0.97, 1.15)	0.21	1.08 (0.98, 1.21)	0.12	1.02 (0.93, 1.13)	0.62	1.06 (0.96, 1.18)	0.25
Smoking reduction by at least 50% (including quitters[a])	655 (18.9)	645 (18.2)	1107 (16.6)	**1.12 (1.04, 1.20)**	**0.003**	**1.14 (1.05, 1.25)**	**0.003**	**1.10 (1.01, 1.19)**	**0.03**	1.05 (0.95, 1.15)	0.37
Used SC services or quitline = (all follow-ups)	12 (0.3)	19 (0.5)	12 (0.2)	**2.17 (1.27, 3.71)**	**0.004**	1.84 (0.91, 3.73)	0.09	**2.56 (1.39, 4.70)**	**0.002**	0.67 (0.35, 1.26)	0.21
Used NRT or other medications (all follow-ups)	17 (0.5)	22 (0.6)	41 (0.6)	0.92 (0.65, 1.31)	0.65	0.82 (0.51, 1.29)	0.39	1.02 (0.69, 1.52)	0.92	0.80 (0.44, 1.43)	0.45
Any weight gain	181/2119 (8.5)	200/2196 (9.1)	372/4168 (8.9)	0.96 (0.87, 1.06)	0.43	0.93 (0.82, 1.06)	0.29	0.99 (0.88, 1.12)	0.87	0.93 (0.79, 1.09)	0.36

Odds ratios (ORs) were obtained from generalized estimation equation models. All analysis were performed with intention-to-treat (participants who had missing information were treated as no behavioral or outcome change), except any weight gain including participants who provided weight data. Other analysis of the secondary outcomes are shown in Supporting information, Appendix S11. PPA = point prevalence of abstinence; bold *P*-values were considered significant by the Benjamini–Hochberg procedure with false discovery rate 10% (meaning accepting 10% of the comparisons being false positives). Further details of *P*-value adjustment are shown in Supporting information, Appendix S12. [a]Quitters were defined as self-reported quitters with 7-day PPA. NRT = nicotine replacement therapy;

TABLE 6 Subgroup analyses of the primary outcome (self-reported 7-day abstinence at 12-month follow-up).

	Groups IA + IB (n = 7015) %	*Control (n = 6656) %*	*Odds ratio (95% CI)*	$P_{interaction}$
City of residence				
Guangzhou	68/1422 (4.8)	56/1411 (4.0)	1.21 (0.88–1.67)	
Shenzhen	485/4184 (11.6)	400/3857 (10.4)	1.13 (0.98–1.30)	0.98
Others	82/1409 (5.8)	66/1388 (4.8)	1.20 (1.04–1.38)	0.74
Sex				
Male	626/6941 (9.0)	509/6576 (7.7)	1.18 (1.05,1.34)	0.23
Female	9/74 (12.2)	13/76 (17.1)	0.67 (0.27,1.68)	
Age group (years)				
18–39	372/3808 (9.8)	278/3602 (7.7)	1.28 (1.11–1.47)	
40–64	243/2896 (8.4)	224/2734 (8.2)	1.00 (0.84–1.18)	0.05
65 or above	17/242 (7.0)	14/241 (5.8)	1.23 (0.68–2.21)	0.70
Education level				
Junior secondary or below	218/2757 (7.9)	208/2629 (7.9)	0.99 (0.84–1.16)	
Senior secondary	214/2406 (8.9)	159/2362 (6.7)	1.29 (1.09–1.53)	0.02
Diploma or above	185/1667 (11.1)	139/1503 (9.2)	1.21 (0.99–1.47)	0.12
Cigarettes consumed per day				
< 20	302/2325 (13.0)	271/2299 (11.8)	1.11 (0.95–1.29)	0.67
20+	174/2193 (7.9)	138/2059 (6.7)	1.18 (0.94–1.47)	
Time to first smoking after waking				
< 5 minutes	100/1211 (8.3)	70/1168 (6.0)	1.41 (1.01–1.96)	
6–30 minutes	87/1023 (8.5)	77/977 (7.9)	1.06 (0.83–1.36)	0.13
31–60 minutes	98/880 (11.1)	86/855 (10.1)	1.11 (0.79–1.56)	0.28
> 1 hour	189/1356 (13.9)	172/1301 (13.2)	1.06 (0.86–1.32)	0.12
Any quit attempt history				
Yes	370/3474 (10.7)	305/3322 (9.2)	1.17 (1.01–1.35)	
No	191/1598 (12.0)	168/1514 (11.1)	1.08 (0.87–1.34)	0.55
Any quit attempt or smoking reduction after baseline				
Yes	364/2774 (13.1)	296/2505 (11.8)	1.13 (0.97–1.32)	
No	119/1769 (6.7)	115/1872 (6.1)	1.09 (0.85–1.39)	0.77

Odds ratios and *P*-values of interaction were obtained from generalized estimating equation models. CI = confidence interval.

received it and the influence by non-health professionals might be limited. The absence of a significant difference in the validated abstinence between the trial groups suggests possible misreporting of self-reporting abstinence status. However, in self-reported quitters at 12-month follow-up who participated in the biochemical validation, 98.3% were biochemically validated as abstinence. Only participants who reported abstinence in the past 7 days were invited for the validation, and they received the small incentive no matter whether their validation result was positive or negative. Hence, misreporting or smoking relapse immediately after telephone follow-up was not likely.

This RCT's large sample size, multi-site recruitment and simplified procedure support its generalizability. The intervention comprised two novel and impactful components: the warning concerning the absolute risk of smoking (i.e. one in two or two in three smokers are killed by smoking) and the leaflet with explicit images. The warning about the absolute risk is evidence-based, and is simpler, more direct and stronger than other warnings on harms of tobacco use. It required no specialized cessation treatment knowledge, substantially reduced training time for health-care providers and simplified quitting advice without omitting the warning regarding death. Such brief intervention may be more feasible for busy primary care settings than the standard 5A cessation counselling. The leaflet further amplified the verbal warnings with prominent colors, text fonts and threatening pictures. It could have reduced the time taken for physicians to educate smokers about the health risks of smoking, which had probably been heard by smokers before.

The very brief intervention showed similar benefits among smokers at different levels of cigarette consumption and with different quitting history and intention. However, smokers aged 40–64 years did not benefit greatly. This age group may have a longer smoking history than their younger counterparts and have not yet experienced adverse health outcomes, as do older smokers. Hence, our intervention may have had less of an impact on them. Moreover, our RCT revealed that less educated smokers benefited from the intervention, suggesting that future interventions need to provide more

support to smokers with low education attainment who mostly have lower ability to quit and less access to smoking cessation support [33].

The effect size in this RCT (an approximately 14% increase in abstinence) was smaller than those found in the two recent RCTs in China (one- or twofold increase) [21,28]. Those two RCTs were conducted in only one or two hospitals, so that the study procedures could be tailored and the compliance could be closely monitored. Hence, the physicians should have better compliance to the intervention protocol. In the present RCT, we were unable to tailor the study procedures in each of the 72 recruitment sites, and did not have sufficient manpower to closely monitor the compliance. Our fidelity survey showed that more than half the participating physicians frequently advised their control participants to quit, and hence a low compliance in the control group was found. When only participants whose physicians were compliant to our intervention protocol were included in the analysis, the ORs became greater. Therefore, the contamination due to non-compliance could have reduced the effect size. Another external factor of effect size is the availability of smoking cessation services. In the aforementioned RCTs the recruitment hospitals were operating smoking cessation clinics, so that motivated smokers were able to access the smoking cessation services and boost their abstinence. In contrast, in the present RCT not all participating hospitals had smoking cessation services. Our intervention only provided the telephone numbers of smoking cessation clinics in other hospitals, if there were any. Previous studies have shown that more proactive referral strategies are needed to increase uptake of smoking cessation services [34,35]. We showed that very few participants had used cessation aids, including smoking cessation services and medications. Therefore, we believe that most quit attempters quit unaided, which was difficult. Nevertheless, smoking cessation services were not available or cost-covered in most hospitals in China, as in many low- and middle-income countries [7]. Our RCT was able to show the actual intervention effect due to the very brief intervention, and apparently has higher generalizability than the aforementioned RCTs.

This study had limitations. First, only 1% of participants were female smokers. Secondly, many participants from the control group also received the brief smoking cessation intervention with equal intervention dosage, leading to unintended positive effects on smoking cessation and reduced the outcome difference. Thirdly, to minimize physicians' logistic and research duties, compliance was not documented during medical consultations. However, we successfully matched almost three-quarters of all participants with the physicians who completed the fidelity survey, enhancing the validity of the compliance analysis. Fourthly, approximately one-third of all screened smokers (8406 of 27418) refused to participate in this RCT. Hence, the results of this RCT might not be applicable to such smokers. Lastly, during our study period (2014–17), Shenzhen substantially extended the statutory smoke-free area, and large-scale promotional campaigns and law enforcement were carried out in the city. This factor might have motivated more smokers to quit, but possibly reduced the effect size due to our intervention.

CONCLUSIONS

Physicians' very brief smoking cessation intervention effectively increased tobacco abstinence by approximately 14%. This intervention can be delivered widely, and should have a greater impact than previously tested brief (but longer) interventions. We encourage hospitals and other health-care institutes to integrate the very brief smoking cessation intervention into their usual medical care guidelines.

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Declaration of interests

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Trial registration

HKUCTR-1913 (http://www.hkuctr.com/); NCT02494960 (https://clinicaltrials.gov/ct2/show/NCT02494960?term=NCT02494960&rank=1).

Author contributions

Yee Tak Derek Cheung: Conceptualization; data curation; formal analysis; investigation; supervision; validation. **Nan Jiang:** Investigation; project administration. **Chaoqiang Jiang:** Data curation; investigation; project administration; supervision. **Run Sen Zhuang:** Project administration; supervision. **Wen Hui Gao:** Project administration; supervision. **Jian Zhou:** Methodology; resources. **Jin Hong Lu:** Methodology; resources. **Hui Li:** Methodology; resources. **Jun Feng Wang:** Methodology; resources. **Yi Sheng Lai:** Methodology; resources. **Jun Sheng Sun:** Methodology; resources. **Jiu Chang Wu:** Methodology; resources. **Chiang Ye:** Methodology; resources. **Na Li:** Methodology; resources. **Gang Zhou:** Methodology; resources. **Jing Ying Chen:** Methodology; resources. **Xiu Yan Ou:** Methodology; resources. **Liu Qing Liu:** Methodology; resources. **Zhuang Hong Huang:** Methodology; resources. **Sai Yin Ho:** Conceptualization; funding acquisition. **Ho Cheung William LI:** Conceptualization; funding acquisition. **Sheng Hua Su:** Conceptualization; funding acquisition; resources. **Yan Yang:** Conceptualization; funding acquisition; resources. **Yuan Jiang:** Conceptualization; funding acquisition; resources. **Wei Hua Zhu:** Conceptualization; funding acquisition; resources. **Lie Yang:** Conceptualization; funding acquisition; resources. **Peiru Lin:** Conceptualization; funding acquisition; methodology; resources. **Yao He:** Conceptualization; funding acquisition; resources. **KK Cheng:** Conceptualization; funding acquisition. **Tai-Hing Lam:** Conceptualization; funding acquisition; investigation; project administration; resources; supervision.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix 1 Final version of study protocol.
Appendix 2 PRECIS-2 scores for trial domains.
Appendix 3 Schedule of enrolment and follow-up assessments.
Appendix 4 Independent Interim report.
Appendix 5 Information leaflet (Translated content in english).
Appendix 6 Card and leaflet (2 sides of a A4 sheet) for the intervention group.
Appendix 7 Card and leaflet (two sides of a half A4 sheet) for the control group.
Appendix 8 Further details of modified Complier average causal effect (mCACE), Generalized Estimation Equation model, and multiple imputation.
Appendix 9 Retention rate by socio-demographic and smoking characteristics at 6- and 12-month follow-up (FU).
Appendix 10 Main outcomes: risk difference (RD), number needed to treat and power.
Appendix 11 All other secondary outcomes expressed as odds ratios from generalized estimation equation models.
Appendix 12 Benjamini-Hochberg procedure.

