Contemporary Clinical Trials Communications 5 (2017) 92–99

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

Beyond intention-to-treat: The effect of brief counseling for tobacco cessation in secondary analyses of a cluster randomized controlled trial in Swedish dental clinics

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ARTICLE INFO

Article history:
Received 29 June 2016
Received in revised form
4 November 2016
Accepted 14 January 2017
Available online 18 January 2017

Keywords:
Tobacco use cessation
Adherence
Per-protocol
As-treated
Instrumental variable

ABSTRACT

In experimental studies the assigned intervention measures the received intervention if full protocol adherence is achieved, but this is rarely the case in public health. The objective of this study was to estimate the effect of a brief counseling intervention delivered in Swedish dental clinics on tobacco use cessation, taking non-adherence into account. We conducted three secondary analyses. In a per-protocol analysis the experimental counseling delivered as intended was contrasted to usual care (control). In an as-treated analysis individuals were compared according to the counseling components actually received, disregarding randomization. In an instrumental variable analysis the effect of the intervention among those who would always be treated as assigned was estimated. Logistic regression was used to examine the association between tobacco cessation outcomes (seven-day abstinence, three-month abstinence, half-reduction, quit attempts) and the defined exposure to the intervention. Protocol adherence in the intervention group was 73.4%. The per-protocol analysis closely replicated the results of the intention-to-treat analysis, showing a statistically significant effect of the brief counseling on the reduction in tobacco consumption *OR* = 1.81, 95% CI [1.06, 3.07], but no significant effect for other outcomes. In the as-treated analysis, receiving more counseling components compared with no tobacco counseling increased the likelihood of half-reduction. The instrumental variable yielded biased results. We conclude that despite application problems, conducting per-protocol, as-treated and instrumental variable analyses in randomized trials where experimental conditions are not strictly standardized strengthens and puts in context the inference based on intention-to-treat analysis.

1. Introduction

Brief counseling complemented by oral examination in dental settings is effective in assisting patients to achieve tobacco use cessation [1]. In Sweden, the effectiveness of a brief structured counseling for tobacco use cessation delivered in dental clinics to unselected tobacco users was evaluated in the cluster randomized controlled trial FRITT (Swedish acronym for "Free from Tobacco in Dentistry"). The intention-to-treat (ITT) analysis of this trial showed a statistically significant effect on reduction by half of tobacco consumption from baseline to follow-up, but not on complete abstinence [2].

The "intention-to-treat" (ITT) analysis preserves the benefits of randomization in the comparison of alternative interventions. Therefore, it is the primary analytic approach in randomized clinical trials [3,4]. This approach estimates the effect of being assigned to a specific treatment, irrespective of whether or not the individual received, took or completed the assigned treatment. In case of non-adherence, the assigned intervention is a misclassified measure of the received intervention and the results could be a biased estimate of the treatment's effect [4].

Adherence patterns are important for an appraisal of the extent

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http://dx.doi.org/10.1016/j.conctc.2017.01.005

to which the ITT analysis yields a valid measure of the effect of the intervention. A review of randomly selected trials published in high-impact medical journals showed that protocol non-adherence was reported in 98% of the studies, whereas methods to address non-adherence in only 51% of them [5]. In many of the studies, "as-treated" (AT) or per-protocol (PP) analyses were the methods usually applied to account for non-adherence, but there was no discussion on the potential biases introduced by these methods [5]. The PP and AT analyses do not capture the causal effects if the sources of systematic error (i.e confounding) are not dealt with [6]. Instrumental variable (IV) analysis has been proposed as a method yielding an unbiased estimate of the effect of receiving the alternative treatment even in the presence of unmeasured confounders, if some central assumptions are met [4,7].

Analyses following the PP, AT or IV approaches are often overlooked in RCTs of non-pharmacological interventions. Several studies have underlined the benefits of reporting additional analysis besides ITT [6,8–10]. For instance, estimating the effect of interventions taking non-adherence into account may help to extrapolate the results to settings where the adherence pattern is different from that in the trial [8,9]. Also, results may be more informative for patients and clinicians, who are interested in the true effect of the intervention rather than in the effect of the assigned intervention [8].

Therefore, the objective of this study was to conduct secondary analyses in order to estimate the effect corrected for non-adherence of the brief counseling intervention evaluated in the FRITT study on cessation of tobacco use. We analyzed the effect of (a) receiving the intervention as-intended among patients randomized to the intervention group (per-protocol analysis), (b) receiving different components of the intervention (as-treated analysis), (c) receiving always the intervention assigned among patients of dental practitioners with similar propensity to adherence (instrumental variable analysis).

2. Material and methods

2.1. Study design

Details on the study design are provided elsewhere [2]. Twenty-seven dental clinics in two Swedish regions willing to be included in the study constituted the unit of randomization. Simple randomization was performed using a computer-generated random sequence with 1:1 ratio to either deliver the novel intervention (structured brief advice) or to continue with the usual practice of tobacco prevention, if any (control condition). The intervention was delivered by dentists or dental hygienists individually to patients who were tobacco users. Given the nature of the control condition, there was no standardization of intervention in this group. The follow-up time was six months.

2.2. Intervention

The intervention was developed by the Swedish National Institute of Public Health in line with the Swedish National Board of Health and Welfare guidelines on brief standardized advice in dental care for disease prevention and health promotion. It was based on the "5 A's" model centered around readiness to quit, and acknowledging the chronic nature of tobacco dependence [11,12]. It consisted of a 5 min, single-session counseling delivered during a dental visit. According to the written instructions given to the dental professional the following components had to be delivered to all patients: (a) *Ask* about tobacco use, (b) *Advise* to quit relating tobacco use with the patient's oral health (c) *Assess* willingness to quit ("Have you thought about quitting?", "Are you interested in quitting?") and (d) *Assist* by offering information about available support for tobacco use cessation and/or a leaflet about the quitting process (minimal *Assist*). For patients considering quitting, *Assist* included more specific components (setting a quit date, discussion about abstinence problems, suggestion or prescription of pharmacological treatment) and should have been followed by (e) *Arrange*, i.e. referral to Smoking Quit Line, or to other available smoking cessation resources.

2.3. Sample and data collection

2.3.1. Participants

A total of 467 patients participated in the FRITT study. The mean age was 45.6 years (*SD* 14.9), 63.4% were males, the majority had at least secondary school degree (78.9%), were full-time employed (62.5%) and were unmarried (53.1%). Concerning tobacco use, 43.6% used snus (Swedish moist smokeless tobacco product), 47.5% smoked cigarettes while only 8.9% were dual users. The average duration of use was 24.4 (*SD* 14.0) years, being highly correlated with patients' age. The majority of the participants were light or moderate tobacco users (51.2% used less than 10 cigarettes/snus pouches daily), used tobacco within 30 min after awakening (58.4%), had a history of at least one previous quit attempt (86.7%), were not considering quitting tobacco at all or in the next six months (81.1%) and never received a diagnosis of chronic disease (69.9%) [2].

The analytical sample for this study included the 452 patients (97%) who participated in the six-month follow-up. There was no significant difference in the proportions of lost to follow-up between experimental groups. The patients lost to follow-up did not differ from those retained in the study, therefore the baseline characteristics of the entire sample also apply to the analytical sample in this study.

2.3.2. Data collection

Information at the patient level was self reported both at baseline (paper-and-pencil questionnaires filled in at the clinic) and at follow-up (paper-and-pencil questionnaires filled in at the clinic, sent via postal mail or during a telephone interview). Information on the content of the intervention was collected from the dental professional both in intervention and control clinics using the same structured form, with pre-coded intervention components. The form also included information about the counseling's length (minutes). We refer to a previous paper from this study for detailed information about data collection, the eligibility and exclusion criteria for patients and clinics and the recruitment process [2].

2.4. Measures

2.4.1. Outcomes

The primary outcome was defined as complete abstinence from tobacco during the seven days prior to the follow-up survey (seven-day abstinence). Secondary outcomes were (a) sustained abstinence during the three months prior to the follow-up survey (three-month abstinence), (b) reporting at follow-up half or less of the daily average of cigarettes smoked or snus portions used reported at baseline (half-reduction) and (c) at least one quit attempt lasting 24 h or longer during the six months follow-up (quit attempts). All outcome variables were derived from self-reported information.

2.4.2. "As-intended" ("per-protocol") intervention

Adherence in this study was measured at the health care provider's level. In Table 1, the definition of the *Ask*, *Assist*, *Assess*, *Assist*