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Combining intensive practice nurse counselling or brief general practitioner advice with varenicline for smoking cessation in primary care: Study protocol of a pragmatic randomized controlled trial

C. van Rossem [a,*], M. Spigt [a,b], E.S. Smit [c,d], W. Viechtbauer [e], K.K. Mijnheer [f], C.P. van Schayck [a], D. Kotz [a]

[a] CAPHRI School for Public Health and Primary Care, Department of Family Medicine, Maastricht University, Maastricht, The Netherlands
[b] General Practice Research Unit, Department of Community Medicine, The Arctic University of Norway, Tromsø, Norway
[c] CAPHRI School for Public Health and Primary Care, Department of Health Promotion, Maastricht University, Maastricht, The Netherlands
[d] Amsterdam School of Communication Research/ASCoR, Department of Communication Science, University of Amsterdam, Amsterdam, The Netherlands
[e] MHeNS School for Mental Health and Neuroscience, Department of Psychiatry and Psychology, Maastricht University, Maastricht, The Netherlands
[f] Eindhoven Corporation of Primary Health Care Centres (SGE), Eindhoven, The Netherlands

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ABSTRACT

Introduction: Combining behavioural support and pharmacotherapy is most effective for smoking cessation and recommended in clinical guidelines. Despite that smoking cessation assistance from the general practitioner can be effective, dissemination of clinical practice guidelines and efforts on upskilling has not lead to the routine provision of smoking cessation advice among general practitioners. Intensive counselling from the practice nurse could contribute to better smoking cessation rates in primary care. However, the effectiveness of intensive counselling from a practice nurse versus usual care from a general practitioner in combination with varenicline is still unknown.

Materials and methods: A pragmatic randomized controlled trial was conducted comparing: (a) intensive individual counselling delivered by a practice nurse and (b) brief advice delivered by a general practitioner; both groups received 12-weeks of open-label varenicline. A minimum of 272 adult daily smoking participants were recruited and treated in their routine primary care setting. The primary outcome was defined as prolonged abstinence from weeks 9 to 26, biochemically validated by exhaled carbon monoxide. Data was analysed blinded according to the intention-to-treat principle and participants with missing data on their smoking status at follow-up were counted as smokers. Secondary outcomes included: one-year prolonged abstinence, short-term incremental cost-effectiveness, medication adherence, and baseline predictors of successful smoking cessation.

Discussion: This trial is the first to provide scientific evidence on the effectiveness, cost-effectiveness, and potential mechanisms of action of intensive practice nurse counselling

Abbreviations: GP, general practitioner; PN, practice nurse; NRT, nicotine replacement therapy; SGE, Eindhoven Corporation of Primary Health Care Centres; CO, carbon monoxide; MI, Motivational Interviewing; MEMS®, Medication Event Monitoring System; ICER, incremental cost-effectiveness ratio; T0, baseline questionnaire; T9, questionnaire at 9 weeks' follow-up; T12, questionnaire at 12 weeks' follow-up; T26, questionnaire at 26 weeks' follow-up; T52, questionnaire at 52 weeks' follow-up; PRECIS, Pragmatic-Explanatory Continuum Indicator Summary.

* Corresponding author at: CAPHRI School for Public Health and Primary Care, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands. Tel.: +31 43 3882202; fax: +31 43 3619344.

E-mail addresses: carolien.vanrossem@maastrichtuniversity.nl (C. van Rossem), m.spigt@maastrichtuniversity.nl (M. Spigt), e.s.smit@uva.nl (E.S. Smit), wolfgang.viechtbauer@maastrichtuniversity.nl (W. Viechtbauer), k.mijnheer@sge.nl (K.K. Mijnheer), o.vanschayck@maastrichtuniversity.nl (C.P. van Schayck), d.kotz@maastrichtuniversity.nl (D. Kotz).

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combined with varenicline under real-life conditions. This paper explains the methodology of the trial and discusses the pragmatic and/or explanatory design aspects.
Trial Registration: Dutch Trial Register NTR3067.

1. Introduction

Tobacco use is a prominent determinant of the global burden of disease and responsible for 31% Disability Adjusted Life Years (DALY) lost [1]. In the Netherlands, still one out of four people are daily smokers [2]. Even though most smokers would like to quit [3], the number of quit attempts and their success rate is low [4]. Increase of smoking cessation can be achieved by improving the efficacy and effectiveness of smoking cessation treatments.

Primary care is in a strategic position to play an important role in smoking cessation: it has a wide reach into the population, it is easily accessible for smokers [5], it is a familiar environment and there is access to professional and effective help [6,7]. Smokers who are considered to be difficult to reach, e.g., smokers with a low social-economic status or psychological illnesses; heavy smokers; and smokers from different ethnic backgrounds, may be more easily reached in primary care. In countries were the primary care system is well developed, such as the Netherlands, around 80% of the smokers visit their primary healthcare centre each year [2].

Smoking cessation treatments available in primary care can be categorized into behavioural support and pharmacological aids. Behavioural support can be given within a continuum of care, from less intensive and one-time support (brief advice) to more intensive behavioural support with multiple sessions (counselling). There is a strong dose–response relationship between number of sessions, total contact time, and abstinence showing that intensive counselling increases the chance of a successful quit attempt compared to less intensive support [8]. Effective pharmacological aids include nicotine replacement therapy (NRT), antidepressants bupropion and nortriptyline, and the partial nicotine receptor agonists varenicline and cytisine [9–11]. Varenicline had better quit rates in clinical trials compared to bupropion and NRT [12–14]. Combining behavioural support and pharmacotherapy is most promising and recommended in clinical guidelines [8,15–17].

The availability and effectiveness of multiple smoking cessation strategies from the general practitioner (GP) [6], dissemination of clinical practice guidelines, and efforts on upskilling, have not led to the routine provision of smoking cessation advice among GPs [18–20]. A survey in Australia found that GPs were very pessimistic about giving cessation advice, and only half of the GPs would give such advice in an ideal situation [20]. However, practice nurses (PNs), as an alternative workforce in primary care, have recently been introduced in the Netherlands with the aim to reduce the workload of GPs. They are expected to improve the quality of care by cost-effectively managing chronic illnesses and performing health promotion tasks such as smoking cessation [21]. Evidence for the effectiveness of PN smoking cessation counselling is limited, but results are positive and suggest the same effectiveness as the English Smoking Cessation Services [22]. Since PNs have more time for counselling than GPs, intensive counselling by the PN can contribute to higher smoking cessation rates in primary care.

Furthermore, a recent meta-analysis showed some evidence that the combination treatment increases smoking cessation success, but most studies used NRT [23]. Evidence on the effectiveness of combining counselling and varenicline is still limited and it could be that the effect of counselling is less evident when using varenicline, or that the effectiveness of varenicline is amplified by intensive counselling. Though, recent trials show promising results in favour of the combination of counselling and varenicline [24–26]. For example, when varenicline was combined with an intensive 240-minute counselling program, more than half of the patients was prolonged abstinent at 6 months of follow-up, which was significantly better than the combination of placebo with the same intensive counselling program (58.1% vs 26.4%, OR 3.87, 95% CI 2.11–7.11) [24]. Nonetheless, more support for the effect of combining varenicline with intensive versus less intensive counselling is needed. Moreover, reasons why the combination of intensive counselling and pharmacotherapy is most successful are still unknown. One of the underlying mechanisms to this effect might be that counselling increases adherence to medication, which finally leads to better quit rates [27]. Intensive counselling is also more expensive than brief advice and therefore the cost-effectiveness should be considered. Previous clinical trials were very explanatory using very strict in- and exclusion criteria, which limits the external validity of the outcomes. Also, most evidence on the effectiveness of varenicline resulted from research in clinical settings and not in real world primary care settings.

Therefore, there is a need for evaluating the effectiveness of intensive counselling from a PN versus usual care from a GP to provide healthcare professionals, policymakers, and insurance companies with evidence on the value of counselling from the PN and on the effectiveness of the combination treatment of intensive counselling by a PN with varenicline. When the PN is equally or more effective than the GP, smoking cessation could be shifted from the GP to the PN in order to reduce the workload of the GP and approach the preferences of the patient.

2. Materials and methods

2.1. Objectives

The primary objective was to compare the effectiveness of individual counselling by a PN combined with open-label varenicline versus brief advice by a GP combined with open label varenicline on biochemically validated prolonged abstinence from week 9 to week 26 after treatment initiation in smokers in a Dutch primary care setting.

Secondary objectives were:

- to determine the prolonged abstinence rate from weeks 9 to 52;