Proactive recruitment in clinical trials: an idea whose time has come

A recently pulished study reported on the reach and efficacy of proactive telephone counselling for smoking cessation.[1] Based on a large (N=3008) randomised clinical trial (RCT), smokers who received proactive phone counselling were more likely to report short-term (4 months) and mid-term (6 months) abstinence than those who received mailed quit tips. The paper is described as being the first trial to assess the efficacy of proactive telephone counselling to smokers in the general population. However, a prior study by our group used very similar methodology to recruit US smokers into a clinical trial of cessation induction.[2]

Briefly, our prior study recruited smokers via proactive, cold calls. Since the primary focus of the trial was cessation induction among smokers unmotivated to quit, the screening process provided enrolment options for those wanting to quit (cessation arm) versus those not wanting to quit (non-cessation arm). Interested and eligible individuals in the non-cessation arm were recruited into a 6-month RCT (N=616) testing (1) nicotine replacement therapy-aided smoking reduction, (2) motivational advice and (3) no treatment. Relative to the no-treatment control condition, smokers in both the reduction and motivational interventions were more likely to make a 24 h quit attempt (OR=4.2 and 5.6 for reduction and motivation groups, respectively) and report a 7-day point prevalence abstinence at 6 months (OR=4.5 and 6.3). There were no differences between reduction versus motivational advice groups on either quit attempts or abstinence. Like Tzelepis *et al*, our results demonstrated (1) the feasibility of proactive recruitment, particularly of smokers unmotivated to quit, and (2) that a telephone-based intervention can effectively promote cessation among these recalcitrant smokers.

The benefits of proactive recruitment into cessation trials are noteworthy. Primary among these is the potential to recruit a large sample that is typically more representative of the general population than would be recruited through reactive channels. For example, a pilot study to our RCT mentioned earlier used reactive methods with the aim of recruiting roughly the same study population. In this pilot study,[3] advertising in the local media resulted in an apparent sampling bias. Although we restricted eligibility to smokers who self-reported as not wanting to quit, quit rates were higher than expected based on national norms, which suggests that reactive methods have the inherent effect of selecting more motivated smokers. As Tzelepis *et al* and others[4] point out, recruitment bias is common in clinical trials of smoking cessation. Proactive recruitment can circumvent some of these issues by targeting specific demographic areas, that is, oversampling of under-represented populations.

Proactive recruitment does have its drawbacks, however. With the advent of do-not-call lists and the increase in cell-phone-only households, pure random digit dialling (RDD) has become increasingly inefficient. Very large numbers of calls are required to reach sufficient numbers of eligible and enrolled participants. For example, in the Tzelepis *et al* study, 43 710 households were reached, of which only 3008 (7%) included an eligible smoker, and of these, 1562 (52%) were enrolled in the trial. For our RCT of smoking reduction and motivational advice, 13 787 households were contacted, of which 1213 (9%) were eligible and interested in the non-cessation arm, and of these, 616 (51%) were formally enrolled in the trial. Thus, the ratio of households contacted to recruited participants was 22:1 and 28:1 for our study and Tzelepis' study, respectively. Although uncertain, it is possible that the increasing ratio from our study to the Tzelepis study reflects the increasing inefficiency of RDD methods. Others have proactively recruited smokers using targeted mailings within established medical settings.[5 6] Our research group has recently turned to online channels as a means of proactive recruitment to enrol smokers in a clinical trial.[7] The process is largely the same as with RDD, including both benefits and drawbacks, but, on the whole, it is quicker and more cost-efficient.

Another unfortunate consequence of proactive recruitment is that it increases the difficulty of collecting biological samples of smoking behaviour. Given that participants are geographically dispersed, it is difficult to collect a breath or urine sample in a timely manner (ie, concurrent with self-reported abstinence). Other studies have used either mailed samples, usually of saliva,[8 9] or remote, third-party specimen collection,[10] though both options are subject to moderate rates of non-response. Neither the Tzelepis study nor ours included biological verification of abstinence. The Society for Research on Nicotine and Tobacco's guidelines for population-based studies that include minimal contact with participants suggest that the absence of biological corroboration is acceptable.[11]

Proactive recruitment methods are a viable option to effectively and efficiently recruit large numbers of participants in clinical research, including intervention trials. Researchers will have to carefully weigh the benefits and consequences of pursuing this option, but it clearly represents a methodological option worth considering.

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