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Review

Recruitment barriers for prophylactic vaccine trials: A study in Belgium

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ABSTRACT

Recruitment of volunteers is one of the main challenges in clinical trial management, and there is little information about recruitment barriers for preventative vaccine trials. We investigated both the recruitment barriers and recruitment strategies for preventive vaccine trials in Belgium. A 10 min survey was used as well as interviews of staff at all clinical trial sites in Belgium that regularly perform vaccine trials. We observed that there are successful recruitment strategies and few recruitment issues for trials involving healthy adults and those over 65 years old. However, challenges face the recruitment of paediatric populations, pregnant women, patients and the very elderly (over 85 years old). From these results, we identified three priority areas to increase recruitment for prophylactic vaccine trials in Belgium. These are: the lack of public knowledge about infectious diseases; the lack of resources of healthcare professionals to take part in clinical trials; and the burden to potential volunteers to take part in a trial. These were discussed with stakeholders and solutions were proposed.

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1. Introduction

Clinical trials are crucial for the progress of medicine. They test whether an intervention – for example a new drug, vaccine or diagnostic tool – is safe and works for its targeted use in man. The number of subjects needed to prove this is carefully calculated, however, reaching this recruitment target is one of the greatest challenges in clinical trial management [1]. The validity of the study results can therefore be affected by missed recruitment targets. Poor recruitment causes costly delays and even early termination of trials, which slows down drug development. A study in the UK showed that approximately half of clinical trials achieve their recruitment target, and approximately one third of trial terminations occur during the recruitment stage [1]. Frequent barriers for volunteering include travel time and inconvenient visit schedules [2–6]. The selection criteria, the protocol, training in recruitment, resources and experience of the research team also affect recruitment [1–5,7–9].

Belgium is an important country for clinical trials. It has the second highest clinical trial site density in the world [10,11] and approximately 1500 sponsor-driven and academic trials running throughout the year [12]. Belgium is a key country in vaccinology with the presence of major companies and several small and medium sized Belgian enterprises active in the vaccine field. There is also a strong academic presence in vaccinology, and the Belgian Federal Agency for Medicines and Health Products has a dedicated vaccines spearhead. In 2010, 6.5% of newly started clinical trials in Belgium were to test a preventative or therapeutic vaccine [11].

There is a large body of literature about recruitment barriers but little is specific to prophylactic vaccine trials (PVT). Unlike patient studies, PVT typically involve subjects who have never had the disease targeted by the candidate PV. Furthermore, the motivations to volunteer can be very different. These include altruism and personal benefit (for example health benefits or financial compensation, 5,13–15). It is important to gain more insight into PVT recruitment barriers in order to facilitate the development of innovative vaccines that will improve public health. Some studies observed that the travel distance to the trial site, age, and safety concerns affect study recruitment or enrolment (for a review, see 16). However, to our knowledge, no studies have assessed the broader aspects of recruitment barriers for PVT, from the perspectives of researchers and healthcare professionals. The present study addresses this knowledge gap by assessing recruitment barriers for PVT in Belgium.

2. Methods

2.1. Survey

The survey was built using an online tool (SurveyMonkey Inc, CA, USA). It was tested and validated for functionality on different devices (desktop, tablet and smartphone) and for time to complete (<10 min). The survey was sent by email to individuals involved in a PVT in Belgium between 2011 and 2015, and Belgian clinical research associations. Survey invitees (>100 people) were allowed to send the survey link onto their community. As a result, we cannot measure the response rate.

The survey was open between the 17th of November and the 18th of December 2016. Respondents were asked multiple choice questions about: their professional background; their experience in recruiting different subject populations; the impact and frequency of different recruitment barriers; and the success of various recruitment strategies. Subject populations were identified from clinical trial applications submitted to the National Regulatory Authority, 2011–2015. Recruitment barriers and strategies were identified from a literature review, not all specific to PVT (Supplementary Tables 1 and 2). Respondents could leave a comment after each question so that we could gather information not captured in the multiple choices. Responses were submitted anonymously. Results are presented as the percentage of participants reporting each response (one decimal place). Comments were analysed qualitatively.

2.2. Interviews

From January to March 2017, we interviewed researchers at the four major sites where PVT are regularly performed in Belgium: the Centre for Vaccinology (CEVAC), Ghent University Hospital; Leuven University Vaccinology Centre, KU Leuven; SGS, Antwerp; and Centre for the Evaluation of Vaccination, University of Antwerp. We also interviewed a former investigator from ImmuneHealth, Charleroi, who ran PVT in the past. The aims of the interviews were to gain detailed perspectives on recruitment and identify potential future strategies to improve recruitment. Responses were analysed qualitatively.

The survey and interview questions are found in the Supplementary Information.

3. Results

3.1. Survey respondent demographics

We received 34 responses to our survey. Nine were excluded because no questions about recruitment were answered. Retained respondents came from the private sector (CRO, n = 7; investigator site, n = 2; sponsor organisation, n = 5) and a public investigator site, n = 8 (Supplementary Fig. 1). Three respondents reported that they came from an "other" organisation: a "university/ethics committee"; a "hospital with a clinical research centre"; and a "public investigator and sponsor site". Most respondents are involved in 1–3 PVT per year (52%). The rest are involved in 4–6 (36%) or more than 10 (12%) PVT per year (Supplementary Fig. 2).

Respondents' experience in trials with different subject populations was inferred from survey responses (see Supplementary Information). Most respondents have experience in trials that recruit healthy adults (88%), the elderly over 65 years old (76%) and/or patients (72%). Respondents had least experience in paediatric trials (infants, 52%; and adolescents, 48%) and trials involving pregnant women (36%, Supplementary Fig. 3).

3.2. Survey results about recruitment targets

Recruitment is most successful for healthy adults and the elderly (65 + years old; 69.6% and 43.5% "never miss" target, respectively; 0% often/always miss, Fig. 1). Combining the "often" and "always" miss scores, the most difficult to recruit are: the very elderly (85+, 50%); infants and children (13.6%); adolescents (4.5%); and patients (4.5%). Of those that have experience recruiting pregnant women (37.5%), more reported that they "sometimes miss" their recruitment targets (29.2% of total responses).

The most common topics in the comments (n = 17) were about difficulties recruiting young children (n = 7) and the very elderly (n = 4). Other comments mentioned difficulties recruiting healthy volunteers (n = 2) and specific patient populations (n = 2). Two respondents reported that: it's difficult to find volunteers that haven't already been vaccinated with a certain vaccine (e.g. hepatitis B vaccine); vaccination in Belgium is relatively complete, which alludes to the previous point; and the protocol is sometimes not aligned with Belgium's vaccination schedule for infants, which is a barrier for comparator studies.

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