

A new job: research volunteer?

Giovan Maria Zanini^a, Claudio Marone^{b, c}

^a Health Department of Canton Ticino, Bellinzona, Switzerland

^b Department of Internal Medicine, Ospedale Regionale di Bellinzona e Valli, Bellinzona, Switzerland

^c G. M. Zanini and C. Marone are President resp. past President of the Research Ethics Committee of Canton Ticino, Southern Switzerland

Summary

We report three years of experience with a newly introduced register for healthy research volunteers in Canton Ticino, Southern Switzerland. The aim of the register was to encourage responsible participation in medical research, and to detect fraud due to volunteers taking part in more than one study at the same time.

All healthy volunteers participating in drug studies approved by the Research Ethics Committee were included in the register and given a special code. During three years, in a population of 1436 volunteers involved in 152 studies, 192 subjects (13.4%) were identified as habitual or regular volunteers (they participated regularly, limiting the pause between studies to the minimum of three months as required by the regulations of the Re-

search Ethics Committee). Among them, only three subjects gave false information and were identified. Most volunteers participated in studies only sporadically (54% in one, 21% in two over three years) and 82.4% of the volunteers were involved, on average, in only one study per year.

Our register permits fraud detection as well as analysis of the research population from an epidemiological point of view. It has been well accepted from both volunteers and research organisations. It is simple and represents a substantial contribution especially for organisations, which need to recruit a large number of subjects for their research.

Key word: regular volunteer; register; fraud

Introduction

Clinical studies involving healthy volunteers are essential in the development of new drugs. Pure altruism is rarely the primary motivator of volunteers. Instead, financial compensation represents the most important incentive [1]. In addition to legal concerns about the sum offered, unresolved ethical issues are under discussion, since volunteers are often economically vulnerable individuals belonging to specific demographic groups. The opportunity for an easy additional income can stimulate the volunteer to participate in an excessive number of studies, with subjects taking part in studies at close time intervals [2, 3]. At a regional scale, a strict control on the individuals involved in research studies is important for the following reasons:

1. to encourage responsible participation, avoiding potential negative consequences for the subject's health and ensuring high-quality research;

2. to detect fraud due to volunteers taking part in more than one study at the same time

In addition to protect the health of volunteers exposed to multiple drugs, quality of the studies is improved by excluding potential drug interferences of substances with long pharmacokinetics. With this double aim, we conceived and set up a healthy volunteers register. We obliged the investigators to announce every study with healthy subjects to the register, and we suggested a pause of three complete calendar months between the end and the beginning of the successive study for all volunteers, according to the regulations of the Research Ethics Committee. Here, we report three years of experience with the register for volunteers in our region (Canton Ticino, Southern Switzerland).

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Material and methods

All research studies, including studies involving healthy volunteers, have to be approved by the Research Ethics Committee of Canton Ticino, where recruited healthy subjects have to be announced. The centralised structure of our Ethics Committee guarantees that the information relative to all drug studies throughout the country involving healthy volunteers is registered. The investigator allots each volunteer a code which contains the subject's initials, date of birth (DD,MM,YY), gender (M/F), and an international abbreviation for the volunteer's nationality. The data are verified by means of an official identity document. This structure permits the adequate identification of each volunteer and gives the opportunity for a demographic analysis of the study participants.

The study in which the subject takes part, together with the earliest possible date for a new participation are registered with the code. The investigator is responsible

for determining the interval of exclusion from other drug studies, which is at least three months starting the first day of the month following the end of the previous study. In other words, the investigator has the faculty of prolonging the free interval in case of drugs with long pharmacokinetics, but is not allowed to shorten the period to less than three months. Volunteers are informed of the register and recruited in a study only if they respect the prescribed interval between two studies. If the volunteer ignores this rule, he/she is informed and excluded from the study. If the volunteer participates in two studies simultaneously, he/she is warned and banned from every study in Southern Switzerland. In such a case, the respective studies are verified on possible negative effects.

We started the registration in the year 2000 and here we report the first three years of experience.

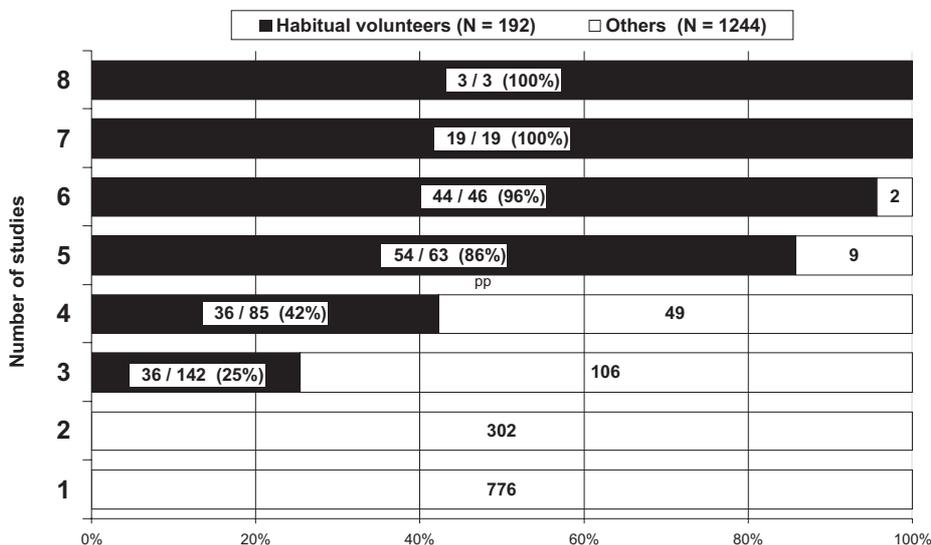
Results

In three years, 152 drug studies were performed in our region (Canton Ticino, Southern Switzerland), which required 2894 volunteers. In the registered population of 1436 individuals (58% males, 42% females) necessary for the 2894 research opportunities, we identified 192 (13.4%) habitual or regular volunteers (61% males, 39% females) who limited the prescribed three months interval between the studies in which they partic-

ipated. Among these 192 volunteers, the register detected three subjects, who gave false information and did not respect the prescribed pause interval. These individuals were warned and excluded from all present and future research studies in Southern Switzerland. Figure 1 shows the part taken from habitual volunteers in relation to the number of studies in which they have participated.

Figure 1

Study participation frequency of the volunteers and part taken from habitual volunteers in relation to the number of studies in which they have participated.



Discussion

The term volunteerism hides a certain degree of hypocrisy, since financial compensation is the primary incentive for participating in a research study. Some authors consider that it is more correct to pay volunteers and consequently encourage professionalism [4]. This attitude is often reinforced by the need to recruit a sufficient number

of subjects. However, our society and our rules are very conservative and cautious and Research Ethics Committees have the task to guarantee that compensation is adequate for the engagement of the subject (time, number of blood samples), but not for the risks.

Our analysis is reassuring. In fact, most re-

search volunteers participated in studies only sporadically: 54% in one, 21% in two over the three years period. From the 142 (9.9%) volunteers who took part in three studies, 106 (7.4%) interposed a long pause interval between the successive studies (figure 1). The fact that 82.4% of the volunteers were involved, on average, in only one study per year demonstrates that the financial incentive is important but limited to a punctual purpose, as declared spontaneously by a few volunteers. For some older volunteers the intensive annual free check-up rather than the financial compensation was the reason for participation, as was shown before [5].

Nevertheless, we were surprised by the subgroup of 192 volunteers (13.4%), who considered research participation almost a job. Those volunteers we defined as habitual or regular volunteers. All these volunteers interposed only a three months' interval (as prescribed in our regulations) between studies, except when indicated longer by the investigator based on the drug pharmacokinetics. As depicted in figure 1, beside occasional volunteers (1 or 2 studies in three years) and volunteers who participated more intensively (3 to 5 studies), our register identified habitual volunteers who exploited all given opportunities (6 to 8 studies in three years). We suspect that, given no limiting rules, these subjects would have asked irresponsibly for participation in additional studies. This possibility has also been suggested by Hassar et al. [6], who reported 11 out of 79 volunteers who participated in up to 18 drug studies in a three year period. Thus, habitual volunteerism in drug research is a real problem. Regular volunteers do not differ regarding gender but they are older than sporadic volunteers (median age 31.5 vs 28 years and mean age 33.3 vs 30.6 years respectively; difference in mean age: 2.7 years with 95% confidence interval of 1.2-4.1 years). Is this a sign suggesting social problems? Habitual participation of

middle-aged people rather than young students suggests the need to increase a minimal insufficient income by a supplementary gain. With our register, it is possible to define the modality of participation based on the time schedule. We think that our procedure is scientifically and ethically more adequate than the French approach [7], where the limitation depends on the amount of money earned during one year, without any limitation related to the number of studies.

Our register permits the immediate detection of fraud, ie subjects who do not respect the imposed pause interval or who take part in more studies at the same time. We identified 3 (0.2%) individuals who tried to break the rules. They represent only a small percentage, also because all subjects were informed of the register and study protocol at the moment of the enrolment discussion. Furthermore all participants were aware of the fact that abuse implied definitive exclusion from any further study. The three fraudulent individuals, who have been warned and definitively excluded, were identified in the first months after the introduction of the register: this demonstrates its educational role.

In conclusion, our register has demonstrated efficacy in detecting fraud and has turned out to be a valuable tool for researchers to limit habitual volunteerism with potential negative consequences for the subject's health and the research quality. Moreover, it has proved to be helpful for epidemiological studies.

Correspondence:

Prof. Dr. med. Claudio Marone
Department of Internal Medicine
Ospedale Regionale di Bellinzona e Valli
CH-6500 Bellinzona
Switzerland
E-Mail: claudio.marone@eoc.ch

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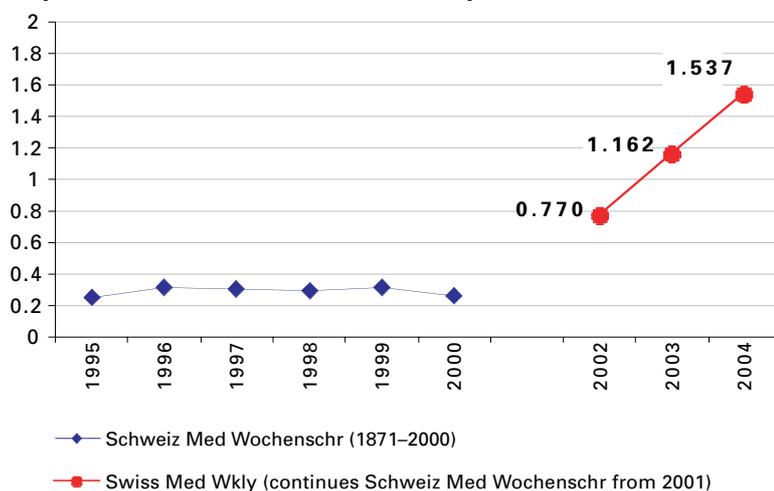
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