Letter to the Editor

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Self-sampling at home using volumetric absorptive microsampling: coupling analytical evaluation to volunteers’ perception in the context of a large scale study

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To the Editor,

Because of the many advantages, dried blood microsampling has received a lot of interest in many application fields, including clinical trials, therapeutic drug monitoring and toxicology [1, 2]. As it involves minimally invasive sampling by a minimally trained individual, self-sampling, at any time or place, is possible, matching the emerging principle of ‘patient-centric’ sampling [3]. However, despite being advocated as an ideal tool, large-scale studies combining the appreciation of self-sampling at home by untrained people with the actual quality of the resulting samples are lacking [4–7].

Here, we report on a large-scale evaluation of self-sampling at home by volunteers participating to a study assessing the half-life of the direct alcohol marker phosphatidylethanol (PETH) (Van Uytfanghe et al., unpublished). PETH is a highly selective and sensitive marker for alcohol intake, consisting of a group of phospholipids of which PETH 16:0/18:1 (palmitoyl-2-oleoyl-sn-glycero-3-phosphoethanol) is the most abundant and most commonly measured species [8]. The study utilized non-assisted volumetric absorptive microsampling (VAMS), in which consenting (Ghent University Hospital Ethics Committee approval n° 2018/1514) volunteers performed a fingerprick at home at three time points and self-sampled blood, using 10 µL sampling devices (Mitra®, Neoteryx). The entire project was conducted remotely: following online enrollment, written instructions (Supplementary Material S1) with referral to an online instruction video were sent along with sampling kits (Supplementary Material S2), which were also sent back to the lab via regular mail. Apart from online and e-mail instructions, stressing the importance of correct sampling, there was no interaction with the participants. Of the 796 volunteers subscribing to generate three fingerprick blood samples (with 2 weeks intervals), 687 (86.3%) completed the study. The age range was evenly spread from 18–60 years, 63% were female, and 79% had a higher degree of education. PETH 16:0/18:1 was quantified using an ISO 17025-accredited liquid chromatography-tandem mass spectrometric method [9].

The success of self-sampling in a home setting was evaluated based on four different (objective and subjective) aspects.

The first aspect was the need for extra sampling material. Only 18 participants needed an additional lancet, while 10 participants requested an additional sampling kit (8 of these specified problems with the first sampling). This is less than 5% of the total participants.

A second parameter was the quality of the tip of the VAMS devices upon arrival at the laboratory, following visual inspection by two independent assessors. White spots or some dark red spots on the tip indicated sample under- or overfilling (see Supplementary Material S4 for some illustrations). For the three time points, respectively 92, 93 and 91% of the samples passed this quality check. This translates in ~83% of the participants having been able to generate samples of good quality in three subsequent samplings. We found no indication that failures were dominant in one of the subgroups (i.e. related to age, sex or education).
In total, four VAMS samplers were provided to the participants (i.e. one spare sampler, as most participants had never performed a fingerprick and self-sampling before). Although not explicitly asked, 1/5 of the participants used this extra sampler to collect a replicate sample (in 91% of instances this was at the first time point, i.e. the very first time they performed the procedure). This availability of replicates allowed objective assessment of a third parameter: the overall quality of the samples. For those duplicates that passed the visual quality inspection and had a concentration above 10 ng/mL (0.014 µM, the lower limit of quantitation), the difference between the duplicates was determined (n=87). From this, an estimate of the imprecision of the method, home-sampling included, could be calculated, using the standard deviation $s = \sqrt{\frac{\sum_{i=1}^{n} (A_i - A_i')^2}{2n}}$ (with $A_i$ and $n$ representing the difference between and number of duplicates, respectively). The imprecision thus obtained, 14%, was slightly but significantly higher (Chi2-test, $\alpha=0.05$) than the estimate of the imprecision derived under controlled circumstances for sampling, 11%. The latter was calculated based on repeated measurement of in-house controls, sampled by dipping VAMS into whole venous blood, over a 15-month time frame (n=212 duplicates) [5]. Using the sum of squares, it could be estimated that home-sampling accounted for 9.0% of the total imprecision of the method. The overall imprecision was deemed acceptable, when applying international guidelines on incurred sample reanalysis [10] and considering the in-house allowed expanded measurement uncertainty ($k=2$, 38%) for PEth [9].

Finally, the volunteers’ appreciation of self-sampling at home was evaluated. Before getting access to their results, 4 months after the sample collection, a brief online questionnaire (Supplementary Material S3) had to be filled out (anonymized), consisting of nine questions, which was completed by 501 participants (73%). The results of the responses are summarized in Figure 1. Seventy seven percent of the respondents had never executed fingerprick sampling before and a vast majority (>90%) judged the clarity of the instructions to be good or very good (which is in line with the good quality of the samples). On a scale of 1 (not painful) to 10 (very painful), 64% scored the painlessness <4. Regarding applicability, user-friendliness and acceptability, again most participants were positive about this sampling technique. This also translates in the fact that almost 80% would prefer this type of sampling over a conventional blood draw by trained personnel, if needed on a monthly basis.

There are several limitations of this study. First, we had an overrepresentation of participants with a higher degree of education; a bias likely owing to announcement via Ghent University social media. Second, volunteers participating to this study, which was conducted in the context of an initiative coined “Tournée Minérale” (which is similar to e.g. “Dry January”, in which persons voluntarily abstain from alcohol for a month), may have been intrinsically motivated. As no payment was foreseen, the only incentive for participation was insight into the individual PEth value and its decrease during one month of abstinence. We consider it likely that the participants’ intrinsic motivation was one of the keys for the success of this study.

In conclusion, the results of this large-scale and entirely remotely executed study support the feasibility of patient-centric home-sampling by non-experienced volunteers. The evidence can be found in: (i) the limited

![Figure 1: Summary of the questions and results of the questionnaire.](https://example.com/figure1.png)

Questions are above the answers, the number between brackets indicates the number of possible answers. For questions 1–6 possible answers were from left to right: very (dark green), rather (light green), neutral (yellow), not (orange), absolutely not (red) and “did not look at it” (blue); *: the % for “not” was zero; $: “neutral” was not an option. For the original answers and questions, we refer to the Supplementary Material S3.
requests for extra sampling material, (ii) visual inspection of the sample quality, (iii) the limited increase of the imprecision due to self-sampling and (iv) a positive assessment via a questionnaire. The success of future routine home sampling can only be obtained when patients collect good quality samples. As was the case in our study, it will be important that patients are incentivized and intrinsically motivated.

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References


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