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## 38 Blood collection in the field – results and lessons from the polish test study

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- ▶ This study was an unique opportunity to compare the assay results from both field-collected dried blood spot samples and respondent-matched venous-blood draws, the so-called gold standard values
  - ▶ The collection of dried blood spot samples at respondents' homes can yield high-quality biomaterial, but the logistics for the handling of the venous samples poses major challenges
  - ▶ Straightforward correction formulae accounting for fieldwork conditions were determined, but due to small sample size further, more extensive validation studies are needed
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### 38.1 Introduction

Deriving blood-marker values from a venous draw is still the gold standard in medicine. The values obtained from dried blood spots (DBS) are, therefore, likely to be challenged: Collecting DBS is cheaper and easier to administer in a survey context (McDade et al., 2007) and the scope of assays available for the analysis of biomarkers in DBS is growing, though still much smaller relative to the analyses possible using venous blood. The obtained DBS results differ in absolute values from the venous results. For the blood markers that SHARE intended to analyse, the literature still provides scarce evidence on the relevance of the information acquired from DBS collected under fieldwork conditions and its comparability with results obtained from venous blood (Sugden et al., 2015).

The Polish test study to be introduced in this chapter takes this challenge head-on. Our aim was twofold. First, we collect venous blood samples in addition to DBS samples under sometimes difficult circumstances during the fieldwork of a population survey and compare the analyses results from both types of blood samples. Second, the study serves as the basis of a potential wider collection of biomaterials among a large and representative population.

Polish country-specific bioethical regulations require all studies that collect human blood or other biomaterials to involve professionally trained medical staff; they do not allow the appointment of trained lay interviewers. Yet, the

financial resources required for interviewers and nurses to jointly conduct the survey and collect DBS in the full sample were too high.

Hence, we implemented a small-scale test study in Poland in which nurses visited the respondents after the completed standard SHARE interview. The blood collection was conducted during a separate nurse visit with SHARE Wave 6 pretest respondents. To use the full potential of nurses' engagement, both DBS and venous blood were taken and the collection was supplemented with an additional short questionnaire and a health examination. Thus, the Polish test study provides important input into the future application of DBS in large, representative surveys.

In this chapter, we outline the concept and implementation of blood sample collection in the field through this small-scale experiment. We describe unanticipated obstacles that affected the data collection and, as a result, reduced the initially expected number of participating respondents. Nevertheless, as shown in Section 3, the collected samples allowed for a meaningful comparison of the DBS and venous blood results, and the exercise has provided a number of useful lessons for the conduct of similar studies in the future.

## **38.2 Wave 6 pretest in Poland: Follow-up nurse visits**

The test study to collect DBS and venous blood was conducted as a follow-up of the SHARE Wave 6 pretest and required the engagement of several research centres and contractors. The study was led by the Collegium Medicum at the Jagiellonian University in Krakow (JUK) in cooperation with the Polish SHARE country team from the Centre for Economic Analysis (CenEA). The University of Southern Denmark in Odense (SDU) granted support with medical matters and surveyed the quality of the DBS samples sent to the SHARE biobank before intermediate storage. The venous blood samples were analysed at JUK. The University of Washington in Seattle (UW) conducted the analyses of the DBS. The Munich Center for the Economics of Ageing (MEA) coordinated the entire process and assisted with legal issues and overall study guidelines. Fieldwork was handled by the Polish survey agency Kantar TNS, who also conducted the entire SHARE Wave 6 fieldwork in Poland.

The pretest of SHARE Wave 6 in Poland took place in June and July 2014. During the interview, the respondents were asked whether they would be willing to participate in the additional blood collection. Of the 137 respondents, who were interviewed in the pretest, 63 agreed to a subsequent nurse visit.

Eventually, only 36 participated in the test study. The final drop-out number of those, who initially had agreed to participate, was higher than expected and the reasons are difficult to identify, possibly related to the significant delay between the pretest interview and the nurse visit which finally took place in early 2016 due to unanticipated administrative and procedural delays. Even though in the meantime the survey agency kept contact with the respondents by phone or personally to remind them about the study and to secure their participation, a timelier visit may have helped to improve the final participation rate.

During their visit, the nurses obtained informed written consent from the respondents. Then, they collected the DBS samples, followed by blood pressure and other anthropometrical measurements and a brief health-focused paper-and-pencil questionnaire. The visit finished with the collection of venous blood. The tubes with venous blood were put in a cooler and were supposed to be delivered immediately to local blood banks, all written materials and DBS samples were shipped to Kantar TNS. Later, the DBS samples were sent in two batches to SDU. Within three days following collection, the venous blood samples were transported by courier on dry ice to the main laboratory at the JUK.

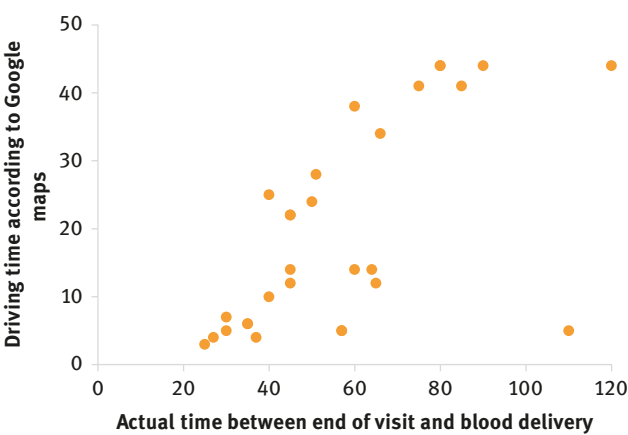
The venous blood samples were analysed for the following biomarkers: Vitamin D, triglycerides (TG), total cholesterol TC, high density lipoprotein (HDL), low density lipoprotein (LDL), C-reactive protein (CRP), HbA1c (glycated haemoglobin), fasting glucose, BDNF and the cytokines TNF- $\alpha$  and IL-6. The DBS samples were sent to the laboratory at UW and have been analysed for TG, TC, HDL, CRP, HbA1c, and Cystatin C (CysC). Thus, the results from five markers are available for both types of blood samples.

### **38.3 Blood collection in the field: Challenges, obstacles and lessons learnt**

As previously noted, one of the main shortfalls of the study was the unexpected delays related to a number of contractual and procedural demands. Therefore, the final nurse visits happened much later than was announced during the interview. This delay may have affected the high degree of withdrawal from the study among respondents, who initially had agreed to participate. Thirty-six respondents eventually participated in the study, among them one refused to participate in the DBS and venous blood collection and four others refused one or the other.

The geographic distribution of respondents' households with respect to the nearest local blood bank turned out to be a larger challenge than expected. 21

local blood banks had been selected all over the country because the venous blood samples collected by the nurses were expected to be delivered in portable coolers to those blood banks within one hour after collection. Though the nurses were instructed to deliver the samples as soon as possible, Figure 38.1 shows a relatively large difference between the expected time of delivery (based on Google Maps driving time) and the actual time recorded by the nurses. The additional time needed may be due to the quality of the roads and weather conditions during the study or other unanticipated delays. In addition, the extended delivery time may have influenced the quality of blood samples, a factor that should be accounted for in the analyses of further studies.



**Figure 38.1:** Expected and actual time of delivery of blood samples to local blood banks.  
**Source:** Based on SHARE Wave 6, Polish pretest supplementary blood collection data.

### 38.4 Initial results: Comparing DBS and venous blood

Apart from testing the complex fieldwork procedures involved in venous blood collection in the field, a key issue of interest behind the exercise was the comparison of the collected DBS and venous blood samples (Crimmins et al., 2014). Although such comparisons have been previously made in laboratory settings, we know of no other field exercise which would allow for this. In Table 38.1, we present the initial results based on the data collected during the nurse visits.

**Table 38.1:** Comparison of laboratory results of DBS and plasma.

		Mean	Min	Max
<b>HbA1c</b>	DBS value	5.4	4.7	6.5
	Wet blood value	5.8	4.9	8.1
<b>Total cholesterol</b>	DBS value	356	230	486
	Plasma value	173	92	237
<b>HDL</b>	DBS value	106	77	141
	Plasma value	50	34	65
<b>Triglycerides</b>	DBS value	308	165	1301
	Plasma value	178	61	1523
<b>CRP</b>	DBS value	3.0	0.3	11.0
	Plasma value	4.1	0.1	26.5

**Source:** Based on SHARE Wave 6, Polish pretest supplementary blood collection data.

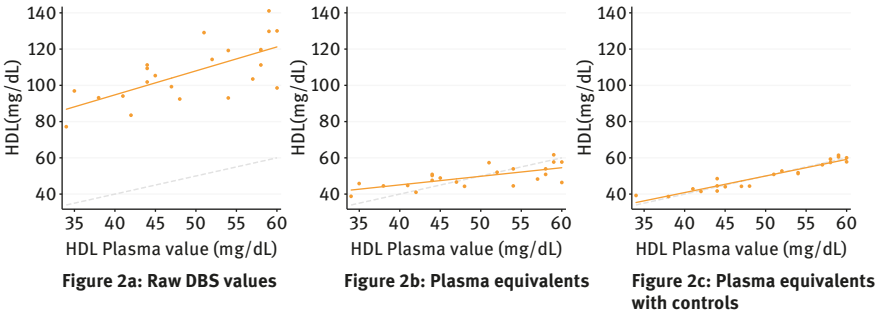
Apart from a few descriptive statistics, we present an approach to adapt the non-standard DBS results from the main SHARE DBS study to hypothetical gold standards.

Table 38.1 shows that the distributions of the DBS laboratory results for the analysed markers are different from the distributions of the results obtained from plasma values (or wet-blood values in the case of HbA1c), which are considered the gold standard. Therefore, direct DBS data requires a different interpretation than most SHARE users would expect; they need to be converted to avoid spurious data analyses and results.

Hence, for the DBS data to be easily usable, we seek to develop an equation resulting in (converted) values that are as close as possible to the values we would have obtained from our respondents' venous blood using gold standard methods. The Polish nurse experiment provides encouraging results, indicating that this goal indeed can be reached. Figure 38.2 shows how we obtained this goal using the HDL values as an example.

Figure 38.2 plots the actual DBS values against the respondent-matched HDL values measured in plasma. The dashed line corresponds to the line of equality. Clearly, the DBS values are overall higher than their corresponding plasma values (Figure 38.2a).

Plotting the results of  $HDL_{plasma} = \beta_0 + \beta_1 \cdot HDL_{DBS}$  against the actual plasma values yields Figure 38.2b. The corrected results are much closer to the equality line and, hence, to the values obtained by gold standard laboratory methods.



**Figure 38.2:** Comparing HDL values in DBS and venous blood samples.  
**Source:** Based on SHARE Wave 6, Polish pretest supplementary blood collection data.

Extending the equation with variables for sampling conditions (namely, the estimated drying time of the DBS, shipment time to the biobank, availability of humidity protection and the interactions of all of these conditions) and controlling for the usual respondent characteristics (age, sex and body mass index), the estimated HDL values come even closer to the equality line (Figure 38.2c).

This extension indicates that the approach to converting the raw DBS values in estimated plasma equivalents can lead to values that are very close to the gold standard. However, because the Polish experiment only consists of a small number of observations, the equations to be finally applied should be obtained from further validation studies. Such a validation, aimed at converting the raw SHARE DBS values into plasma equivalents, was conducted at the University of Washington recently.

## 38.5 Conclusions and lessons learnt

A significant advantage of the DBS is the ease with which the biomarkers can be collected in different settings and conditions, either by the respondents/patients themselves or with the help of a trained lay assistant. However, although the extent of the analyses which can be conducted on DBS material continuously grows as technology develops, venous blood still allows for far more marker assays. The test study conducted in Poland on a sub-sample of SHARE respondents offered a unique opportunity to test the challenges of venous blood collection in respondents' homes together with the chance to compare the results based on venous blood collected in the field with those based on

corresponding DBS samples. We know of no other field exercise that would allow for such comparisons.

The key result of the study shows that straightforward correction formulae can be gained for the results based on DBS such that they very closely reflect the gold standard values based on venous blood. Another important lesson is that, with sufficient care and careful logistics, high-quality biomaterial can be collected at respondents' homes. However, such an approach is a complex undertaking, and time for preparations and planning as well as sufficient resources should be allocated to ensure its success. As our experience demonstrates, taking for granted certain administrative and legal procedures can result in unnecessary delays and disruptions in the flow of the study. In addition, realistic delivery times need to be considered for transporting the blood samples to local blood banks.

Regarding the adaptation of the raw DBS laboratory results to gold standard equivalents, the results of the study are promising. With this in mind and with further, more extensive validation studies in due course, we are convinced to be able to release easy-to-use biomarker data in SHARE.

## References

- Crimmins, Eileen, Jung Ki Kim, Heather McCreath, Jessica Faul, David Weir & Teresa Seeman (2014) 'Validation of blood-based assays using dried blood spots for use in large population studies', *Biodemography and social biology*, 60(1), pp. 38–48.
- McDade, Thomas W., Sharon Williams, & J. Josh Snodgras (2007) 'What a drop can do: dried blood spots as a minimally invasive method for integrating biomarkers into population-based research', *Demography*, 44(4), pp. 899–925.
- Sugden, Karen, Andrea Danese, Idan Shalev, Benjamin S. Williams & Avshalom Caspi (2015) 'Blood substrate collection and handling procedures under pseudo-field conditions: evaluation of suitability for inflammatory biomarker measurement', *Biodemography and social biology*, 61(3), pp. 273–284.

