MASTER THESIS

Enhancing self-management for chronic care patients: experiences with venous phlebotomy, expectations of and willingness to use a new home blood-sampling device and its impact on societal costs

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01-07-2020

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Abstract

Introduction: Diabetes mellitus, cardiovascular diseases, chronic kidney disease or thyroid diseases are four chronic diseases which require regular monitoring by performing blood tests. Venipuncture is an invasive procedure that can cause pain and anxiety. Frequent blood-sampling especially causes discomfort and inconvenience and may thereby negatively affect daily life. Besides these facts, frequent blood-sampling results in high societal costs. Hem-Col is a microtube to store blood after a finger prick which makes self-management possible. Phlebotomy self-management by using Hem-Col may result in cost-reduction and better healthcare outcomes.

Aim: To investigate experiences of chronic care patients with venipuncture, their expectations of and willingness to use Hem-Col as home blood-sampling device and the impact on societal costs when Hem-Col is implemented.

Methods: An online survey was distributed among patients with diabetes mellitus, cardiovascular diseases, chronic kidney disease and thyroid diseases. A patient-level simulation model was developed to represent a hypothetical cohort of these chronically ill patients in the Dutch population.

Results: In total, 1313 patients participated in the survey of which 31% experience the time spent on the phlebotomy appointment as a burden, 32% indicate that phlebotomy appointments affects their daily schedule, 12% experience anxiety and 46% experience physical inconveniences. Long waiting times and crowded phlebotomy locations are the most important factors for dissatisfaction with phlebotomy locations. Of all respondents, 71% prefer to use Hem-Col to monitor their chronic disease. The costs are expected to decrease with €76 per patient per year.

Discussion: Blood-sampling with Hem-Col is considered more user-friendly compared with venous phlebotomy at location. Long waiting times and crowded phlebotomy locations can be avoided when patients have the possibility to use Hem-Col. Implementing Hem-Col for the purpose of monitoring chronic diseases is likely cost-saving as it is expected to reduce societal costs.

Keywords: chronic diseases; phlebotomy; self-sampling; surveys and questionnaires; health technology assessment; cost-analysis

Contents

Introduction

In 2018, approximately 58% of the Dutch population (~9.9 million people) are diagnosed with at least one chronic disease [1]. More specifically, ~1.2 million people suffer from diabetes mellitus [2], ~1.6 million people suffer from cardiovascular diseases [3], ~1,7 million people suffer from chronic kidney disease [4] and ~0,6 million people suffer from thyroid diseases [5-8]. The prevalence is increasing with age, with 95% of the people above the age of 75 years suffering from at least one chronic disease [1]. The number of people that are diagnosed with a chronic disease will further increase due to aging and growth of the Dutch population resulting in a larger chronic disease burden [9].

Patients with diabetes mellitus (DM), cardiovascular diseases (CVD), chronic kidney disease (CKD) or thyroid diseases (TD) are monitored by blood testing; one to four times a year [10-14]. Venipuncture, the process of obtaining intravenous access to collect blood, is an invasive procedure that can cause pain, distress and anxiety [15, 16]. Frequent blood sampling especially causes discomfort and inconvenience for the patient [17]. Approximately 10% of the world population has a phobia of needles resulting in fear and avoidance behavior [18]. Besides the fact that phlebotomy is experienced as inconvenient, it is incurred with high healthcare costs due to the large number of patients that need to be monitored over time [19-21].

Self-management is becoming increasingly important in healthcare [22]. It can improve disease control and quality of life and therefore reduce unscheduled care [22], which may result in cost-reduction and better healthcare outcomes [23]. Phlebotomy self-management can be made possible by collecting blood from a finger prick in a tube and sending it to the laboratory by mail. Patients can choose where and when they want to perform the blood-sampling, which reduces the impact on their daily routines. At-home blood-sampling empowers patients by giving them the opportunity to take more control of their own healthcare [24]. Furthermore, the blood is no longer drawn from a vein but collected after a finger prick which is less invasive [23]. Many studies indicate that, in general, a finger prick is preferred over venipuncture since it is experienced as being less painful [25-28], although contradictory results have also been reported [29].

Several blood-sampling methods are offered as an alternative to venipuncture and to support self-management. Microsampling or reduced volume sampling techniques have benefits in terms of storage, shipment and ease of sampling [30]. Some drawbacks are the varying hematocrit content which results in sample inhomogeneity and therefore complicates the analysis of the sample and blood-volume dependent results [30].

In point-of-care testing (POCT), blood is drawn at home and immediately tested. The time between the conducted test and result is minimized allowing quick decision making [31]. However, the diagnostic accuracy of POCTs is often lower than reference laboratory tests and these devices are often more expensive [31, 32]. Hem-Col (designed by Labonovum, Limmen, The Netherlands) can overcome these drawbacks. Hem-Col is a microtube to store blood after a finger prick and allows reliable measurement of analytes after days of storage before separating cells from plasma [23]. This results in a larger time frame for laboratories to analyze the sample. Hem-Col tubes have the size of regular blood collection tubes which makes analyzing by common laboratory equipment possible (figure 1) [23]. Hem-Col is available to consumers outside hospital laboratories but is not yet implemented in current clinical practice. Implementing Hem-Col in clinical practice would provide the ability for physicians to order Hem-Col for patients when blood testing is needed. Even though multiple blood-sampling devices have been developed in the last years, this study will solely focus on Hem-Col because of its promising factors as both patients and laboratories can benefit from this self-sampling device. Furthermore,

Figure 1: Hem-Col tube

the blood analytes that are frequently requested for testing in the standard protocols to monitor DM, CVD, CKD or TD can be tested with Hem-col tubes [10, 12-14, 33, 34]. In addition, Hem-Col might be able to reduce societal costs since less phlebotomy locations are needed when used at a large scale [23] implying that less time will be spent on blood-sampling at phlebotomy centers.

The aim of this study is to gain insight into the experiences of chronic care patients with venipuncture to monitor their disease and their expectations of and willingness to use Hem-Col for blood-sampling. Furthermore, a cost analysis will be performed to investigate the impact of Hem-Col on societal costs.

Methods

The experiences with venipuncture, the expectations of and willingness to use Hem-Col were investigated by a survey. A health economic model was developed to quantify the effect on costs from a societal perspective.

Survey

Qualitative interviews with ten DM patients served as input for the design of the survey, by providing insight into their perspectives on phlebotomy. The final survey was constructed in Qualtrics XM and consisted of four sections, containing a total of 32 questions. The questions in the first section concerned demographic factors such as age, gender and province. In the second section, questions were asked about the respondents' chronic disease(s) and details on their phlebotomy appointments, details like how often they have them, at what location and how much time they usually take. The third section focused on how the phlebotomy is experienced and whether respondents prefer a finger prick over venipuncture. Hem-Col was introduced in the fourth section, after which respondents were able to share their expectations of such a system. At the end of the survey, respondents were asked whether they would be interested to use Hem-Col. The full survey (translated to English) can be found in appendix A. The needed survey sample size in order to draw conclusions for the total group was ~400 respondents (appendix B).

The survey was distributed among several Dutch patient associations and Facebook support groups for patients with DM, CVD, CKD or TD. To participate in the survey, a person needed to be diagnosed with at least one of the chronic diseases and blood testing had to take place at least once a year to monitor the disease. The minimum age to participate was 18 years. All responses were anonymous and only fully completed responses were saved.

To investigate whether the respondents represent the entire cohort of chronic care patients in the Dutch population, the distribution of respondents among Dutch provinces, as well as their age and gender were compared with the Dutch population. Age and gender were compared specifically with the chronic care patients within the Dutch population. To determine whether a statistical significant difference exists between the respondents and the Dutch population, a χ^2-test was performed for gender and distribution among the provinces, and a one-sample t-test was performed for age.

Data were analyzed using Excel, SPSS (version 26) [35] and R (version 3.6.1) [36], using the package corrplot (version 0.84) [37] and ggplot2 (version 3.2.1) [38]. SPSS was used to determine significant differences between subgroups by performing a χ^2-test. R was used to create a correlation matrix to show the correlation between numeric variables and to create a generalized linear model for the non-numeric variables to determine significant interactions.

Various survey outcomes served as input parameters for the health economic model since they affect the costs incurred with phlebotomy, such as the amount of phlebotomy appointments per year,

the location of the appointments and the time spent per appointment (including travel time). The dependency on others and whether the respondents were willing to use Hem-Col were also implemented as parameters in the model. A χ^2-test was performed in R to determine whether or not these survey parameters are dependent on the chronic disease or age group of the respondents.

Model

A patient-level simulation model was developed in Excel to represent the Dutch population that is suffering from DM, CVD, CKD or TD. Two simulations were conducted; one simulation represents current practice (i.e. phlebotomy) and in the other simulation patients may use Hem-Col based on the probability derived from the survey. In both simulations, each hypothetical patient was assigned one of the four chronic diseases, a gender and an age, based on data from literature. Even though chronic diseases occur often alongside each other like DM, CVD and CKD [13, 33, 39, 40], only one disease was assigned to each patient to simplify the model. The primary outcome measure was the incremental cost for the Hem-Col as compared with current practice. Health effects are assumed to be negligible since Hem-Col will not induce health effects in the long term because the test results are similar to equivalent tests performed in a regular laboratory. In addition, phlebotomy appointments take only a short period of time, indicating that a potential short-term negative impact on quality of life can also be considered negligible. In accordance with Dutch guidelines, all costs were therefore evaluated from a societal point of view, over a time horizon of one year.

Costs

Since the procedure of analyzing blood analytes is the same for Hem-Col as the current practice due to the exact same size of the tubes, these costs are not taken into account. However, the volume of collected blood after a finger prick varies considerably, so the dilution of the buffer with blood must be examined. An internal standard of known concentration, in this case lithium, is added to the tubes beforehand to examine the dilution factor. The costs of the dilution and examination were calculated by taking the average cost of three Dutch laboratories [41-43] and were added to the costs of the Hem-Col method. The tariff for the order of the blood tests, which is the same for all phlebotomy locations and Hem-Col, and the costs of shipment by mail were also added to the Hem-Col costs. The general costs of the Hem-Col device were provided by Labonovum.

Phlebotomy can be performed at four different types of locations in the Netherlands: the hospital, a service phlebotomy center, the GP's office and at home. The costs for phlebotomy at the hospital were calculated by taking the average reimbursement tariff of five hospitals [44-48], and the costs for the other locations were calculated by taking the average tariff per location of ten large laboratories [41-43, 49-55].

Besides the costs for phlebotomy itself, patients may have to deal with many more costs. Potential costs for travel, parking, productivity losses and time spent by an informal care-giver must all be taken into account. Almost all hospitals have a paid parking lot, so parking costs are added to the traveling costs to the hospital. Traveling costs are also incurred when Hem-Col is used since patients have to send it by mail. The maximum distance to the mail box was derived from PostNL [56].

Productivity loss costs are incurred due to the patient not being able to work during the hours of the phlebotomy appointment. Full production loss costs are accounted for until the age of 65. Of

the Dutch population, 12.1% is still employed after the age of 65 years and 1.8% is still employed after the age of 75 years [57]. The production loss costs for these age groups were calculated by multiplying with these percentages. Furthermore, patients may be dependent on others for the phlebotomy appointment resulting in costs of productivity loss of an informal care-giver. Traveling costs, parking costs and costs of productivity loss were derived from the Institute for Medical Technology Assessment [58].

Hem-Col tubes can be split into two parts when it is broken at the snap area (figure 2). The lower part contains no blood and can be disposed as residual waste which is way cheaper to process than medical waste [59]. The medical waste costs were derived by taking the average of two waste process organizations: Renewi and Suez (information obtained after personal communication).

All costs were converted to 2020 prices using consumer price indices (CPI) provided by the Dutch Central Bureau of Statistics [60]. An overview of the costs can be found in table 1.

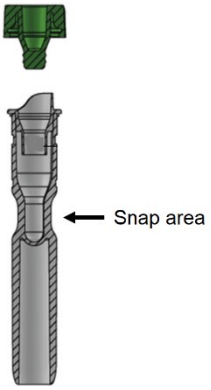

Figure 2: Snap area Hem-Col tube

*Table 1: Costs overview. *Package contains 1 tube, +€1,95 for an extra tube.*

Parameter	**Category**	**Deterministic value**	**95% CI**
Phlebotomy cost	Hospital	€ 9.04	€9.08 to €9.99
	Phlebotomy service center	€ 15.34	€14.09 to €16.60
	GP's office	€ 18.13	€17.92 to €18.34
	At home	€ 25.16	€19.36 to €30.96
	Hem-Col*	€ 20.42	€10.42 to €30.43
Traveling cost	Hospital	€ 6.08	€3.10 to €9.07
	Phlebotomy service center	€ 0.45	€0.52 to €1.52
	GP's office	€ 1.02	€0.23 to €0.67
	Hem-Col	€ 1.02	€0.52 to €1.52
Production loss cost per hour	Male age 18-64	€ 40.74	€20.78 to €60.70
	Male age 65-74	€ 4.91	€2.51 to €7.32
	Male age 75+	€ 0.73	€0.37 to €1.09
	Female age 18-64	€ 33.97	€17.32 to €50.61
	Female age 65-74	€ 4.10	€2.09 to €6.10
	Female age 75+	€ 0.61	€0.31 to €0.91
	Informal care giver	€ 15.05	€7.68 to €22.42
Waste cost	Regular tube	€ 0.0122	€0.0062 to €0.0182
	Hem-Col tube	€ 0.0068	€0.0035 to €0.0101

Probabilistic sensitivity analysis

Monte Carlo simulations were performed for a probabilistic sensitivity analysis, using 10,000 iterations of 10,000 hypothetical chronic care patients. All input parameters were represented by a distribution to acquire probabilistic values and 95% confidence intervals. The gamma distribution was used to derive probabilistic values for the cost parameters. The SE was calculated for the phlebotomy costs. The SE of other cost parameters could not be calculated and was therefore set at 25% of the deterministic value. Beta or Dirichlet distributions were used for probability parameters. Some of the

probability parameters which were derived from survey outcomes had zero observations. Since it is not possible to derive a value from the Dirichlet distribution when the α (i.e. the number of observations) is equal to zero, 1 was substituted for α when this resulted in a parameter probability of 0.03 or lower. A maximum of 0.03 was considered acceptable for these parameter probabilities, otherwise the probability of the parameter was set to 0. An overview of all parameters is provided in appendix C.

A one-way sensitivity analysis was performed to determine the effect of individual parameters on the cost outcome. A value of information analysis was performed to establish the value of additional information and potentially enhance decision-making on whether to implement Hem-Col in clinical practice. The expected value of perfect information (EVPI) was calculated which represents the expected costs of uncertainty in the model.

Results

In total, 1363 patients completed the survey of which 1313 patients were included in the analysis (figure 3). Patients with multiple diseases were according to their diseases assigned to the DM, CVD, CKD and/or TD group for analysis.

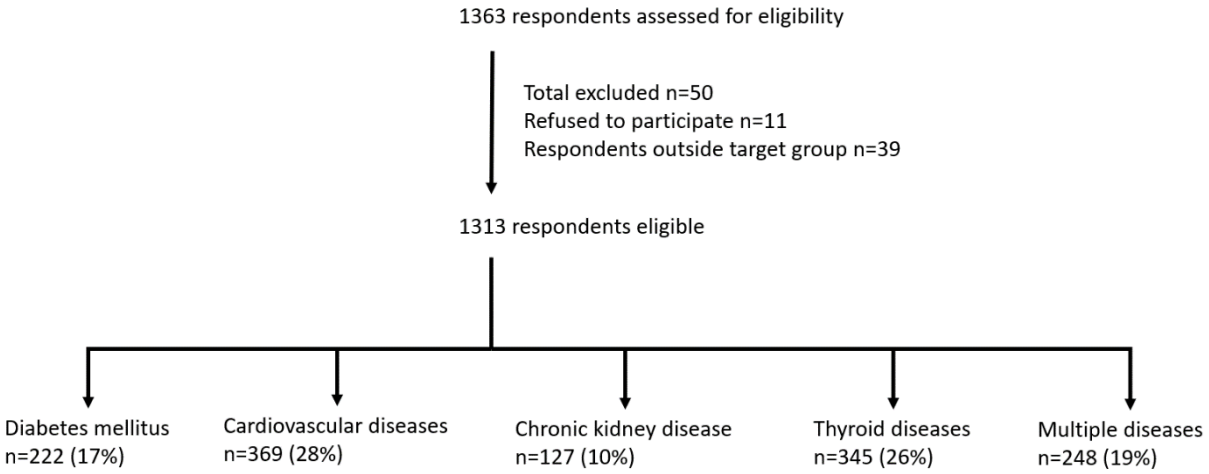

Figure 3: Flow chart of survey responses.

Characteristics

Of the responding chronic care patients, 428 (33%) were male (table 2). The mean age of the respondents was 54.3 years (SD= 15.9), the mean amount of phlebotomy appointments per year was 4.5 (SD=6.4) and the mean time spent per appointment including travel time was 2.0 hours (SD= 0.9). As the location of the phlebotomy appointment, most patients visit the hospital (50%), followed by the phlebotomy service center (40%), the GP's office (7%) and their home (3%).

The mean age of CVD-patients is 64.5 years which is 12-15 years higher than the mean age of DM-, CKD- and TD-patients (table 2). Patients with CKD have the most phlebotomy appointments (i.e. 6 times per year), visit the hospital most often for a phlebotomy appointment (i.e. 73%) and spent most time at the appointment including travel time (i.e. 2.5 hours) compared with the other chronic diseases. Most CVD-patients go to the phlebotomy service center for an appointment (i.e. 46%) and they spent the least time per appointment including travel time (i.e. 1.9 hours). Compared with the other groups, fewer CVD-patients experience the time spent per appointment as a burden (i.e. 21%) and fewer CVD-patients stated that the appointment affects their daily schedule (i.e. 26%). More DM-

patients prefer not to go to the appointment (i.e. 21%) or experience anxiety (i.e. 14%) compared with CVD-, CKD- and TD-patients. Most CVD-patients do not experience venous phlebotomy as painful (i.e. 62%), while for the other groups this is 50% or lower. TD-patients experience less physical inconveniences after phlebotomy (i.e. 62%) compared with the other groups.

*Table 2: Characteristics of participating patients with DM, CVD, CKD and/or TD. Significant difference between a patient group and the total group ***p<0.001, ** p<0.01,* p<0.05*

	Total	**DM**	**CVD**	**CKD**	**TD**
Participants [n(%)]	1313 (100%)	388 (24%)	545 (34%)	199 (13%)	463 (29%)
Male [n(%)]	428 (33%)	146 (38%)*	312 (57%)***	59 (30%)	35 (8%)***
Age in years [mean(sd)]	54.3 (15.9)	51.8 (18.7)***	64.5 (10.4)***	51.0 (16.0)	49.2 (13.0)***
Phlebotomy appointments per year [mean(sd)]	4.5 (6.4)	4.3 (6.9)***	4.5 (8.9)***	6.2 (4.9)***	4.5 (3.7)***
Location			***	***	***
Hospital [n(%)]	656 (50%)	210 (54%)	220 (40%)	146 (73%)	231 (50%)
Phlebotomy service center [n(%)]	523 (40%)	150 (39%)	248 (46%)	43 (22%)	194 (42%)
GP's office [n(%)]	96 (7%)	19 (5%)	48 (9%)	7 (4%)	37 (8%)
At home [n(%)]	36 (3%)	9 (2%)	29 (5%)	3 (2%)	1 (<1%)
Time spent including travel time in hours [mean(sd)]	2.0 (0.9)	2.1 (0.9)	1.9 (0.8)**	2.5 (1.0)***	2.0 (0.8)
Time spent seen as a burden [n(%)]	410 (31%)	141 (36%)**	114 (21%)***	70 (35%)	176 (38%)***
Feeling before phlebotomy appointment		***	***		
I don't care [n(%)]	959 (73%)	253 (65%)	429 (79%)	154 (77%)	337 (73%)
I prefer not to go [n(%)]	189 (14%)	80 (21%)	63 (12%)	20 (10%)	67 (14%)
Anxiety [n(%)]	163 (12%)	55 (14%)	53 (10%)	25 (13%)	59 (13%)
Grade for anxiety scale 0-10 [mean(sd)]	6.7 (2.0)	6.8 (2.2)	6.9 (1.9)	7.2 (1.8)	6.5 (2.1)
Fear of needles [n(%)]	85 (52%)	30 (55%)	23 (43%)	15 (60%)	34 (58%)
Venous blood-sampling is painful		**	***		**
Yes [n(%)]	73 (6%)	34 (9%)	29 (5%)	11 (6%)	22 (5%)
No [n(%)]	705 (54%)	195 (50%)	338 (62%)	98 (49%)	224 (48%)
Sometimes [n(%)]	533 (41%)	159 (41%)	178 (33%)	90 (45%)	217 (47%)
Feeling dependent on others [n(%)]	210 (16%)	71 (18%)	86 (16%)	34(17%)	78 (17%)
After the phlebotomy					
Bruises [n(%)]	643 (49%)	174 (45%)*	258 (47%)	114 (57%)*	253 (55%)**
Bleeding [n(%)]	217 (17%)	64 (16%)	94 (17%)	25 (13%)	92 (20%)*
Muscle pain [n(%)]	88 (7%)	31 (8%)	19 (3%)***	13 (7%)	41 (9%)*
Lightheaded [n(%)]	56 (4%)	25 (6%)*	16 (3%)*	4 (2%)	22 (5%)
Passing out [n(%)]	15 (1%)	7 (2%)	4 (1%)	2 (1%)	7 (2%)
None of the above [n(%)]	575 (44%)	174 (45%)	249 (46%)	81 (41%)	177 (38%)***
Affects their daily schedule [n(%)]	413 (32%)	133 (34%)	140 (26%)***	74 (37%)	166 (36%)*

Representativeness

A significant difference was found in the mean age between the responding patients and literature for the groups DM (51.8 versus 66.3 years; p<0.001), CVD (64.5 versus 76.5 years; p<0.001), CKD (51.0 versus 66.7 years; p<0.001) and TD (49.2 versus 58.9 years; p<0.001) [61-64]. A significant difference was found in gender between the responding patients and literature for the groups DM (male 38% versus 53%; p<0.001), CVD (male 57% versus 52%; p=0.02) and TD (male 8% versus 16%; p<0.001) [61-64]. Finally, a significant difference was found in distribution among Dutch provinces between the

respondents and literature for the DM- (p=0.04), CVD- (p<0.001) and TD-patients (p<0.001) [65]. However, for CKD-patients no significant difference was found in gender (male 30% versus 29%; p=0.89) and distribution among Dutch provinces (p=0.43) [61-65]. Only the responding CKD-patients are representative for the Dutch population in terms of gender and province.

Experiences, expectations and preferences

When considering patients' experiences with phlebotomy locations, the statements 'It's always busy' and 'I have to wait for a long time' were chosen the most, 58% and 54% respectively (figure 4). CKD-patients are most dissatisfied and CVD-patients are least dissatisfied with venous phlebotomy appointments. The most important factors mentioned by the patients for using an at-home blood-sampling device are: the system must be safe and trustworthy (i.e. 97%), be easy to use (i.e. 92%), contain clear instructions (i.e. 90%) and be easy to send (i.e. 89%) (figure 5). An adjustable lancet was valued more within the DM group compared with the other groups.

Of all responding patients, 35% preferred a finger prick, 22% preferred venous sampling, 37% had no preference and 6% did not know (figure 6). Among DM-patients, the preference for a finger prick was higher (i.e. 45%) and the preference for venous sampling was lower (i.e. 17%) compared with other groups.

The most important reasons for preferring a finger prick were 'quicker' and 'easier' (table 3). The most important reason for preferring venous sampling was 'being used to it'. Of the patients who did not know their preference, 64% never experienced a finger prick. The reason 'being used to it' was given more often among DM-patients (i.e. 60%) and less often among TD-patients (i.e. 13%) for preferring a finger prick compared with the other groups. The reason 'hard to find my vein' was given more often among CKD-patients (i.e. 47%) for preferring a finger prick compared with the other groups. Of the DM-patients who did not know their preference, only 23% never experienced a finger prick.

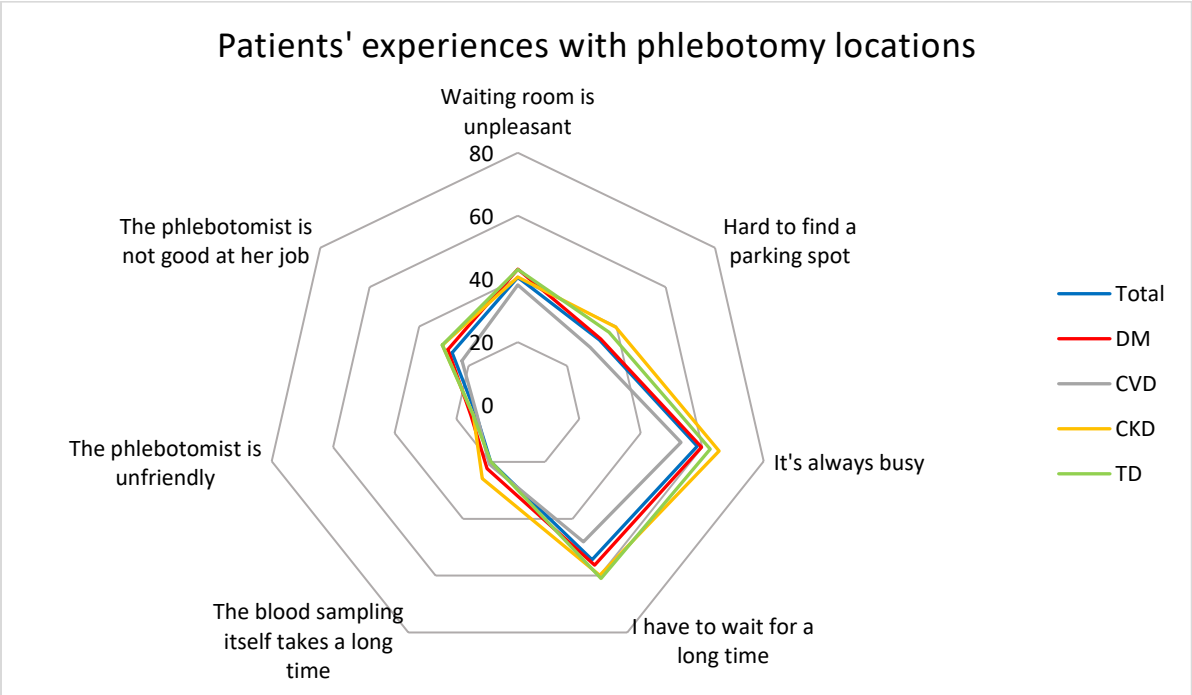

Figure 4: Experiences with venous phlebotomy at location on a scale of 0-100. A higher value indicates that more patients agree with the statement.

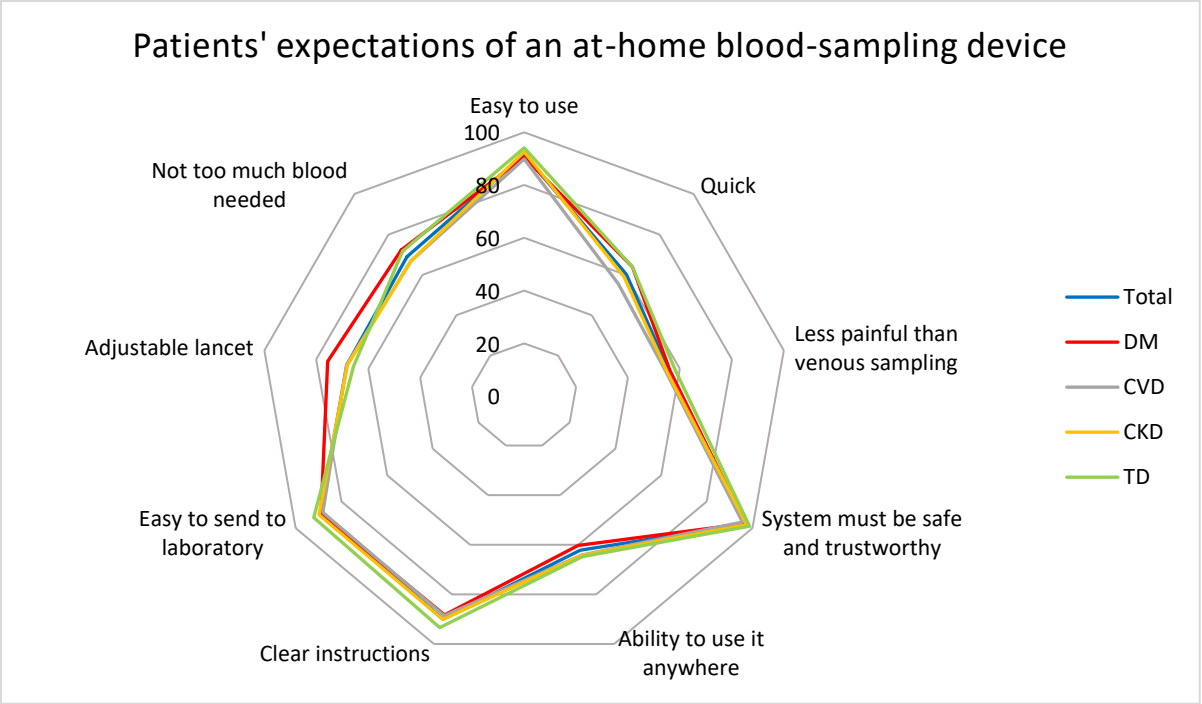

Figure 5: Expectations of an at-home blood-sampling device on a scale of 0-100. A higher value indicates that more patients agree with the statement.

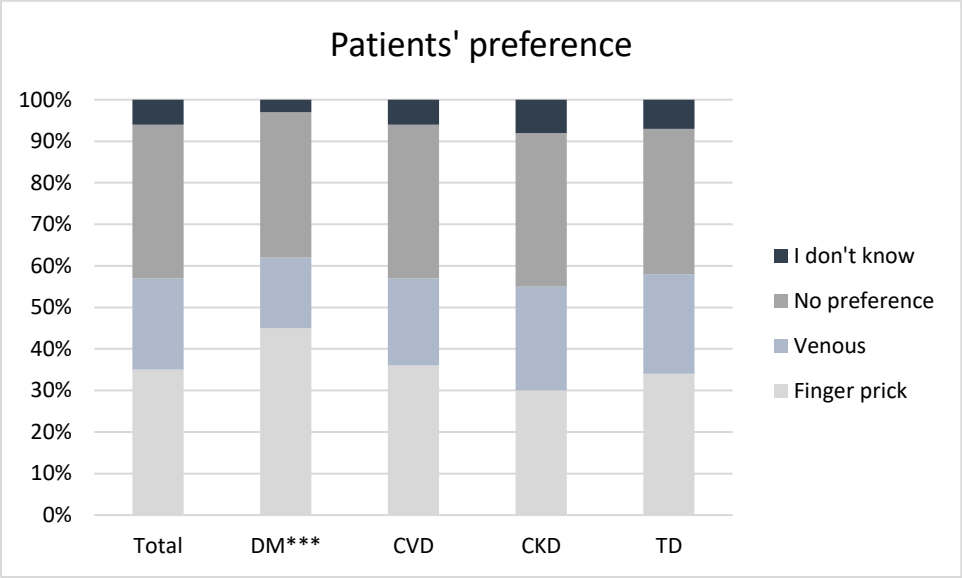

*Figure 6: Patients' preference for a sampling method. Significant difference between a patient group and the total *** p<0.001*

*Table 3: Reasons for having a preference for a particular sampling method. Significant difference between a patient group and the total group *** p<0.001, ** p<0.01,* p<0.05*

	Total	**DM**	**CVD**	**CKD**	**TD**
Reasons for preferring a finger prick					
Quicker [n(%)]	316 (69%)	131 (75%)*	115 (59%)***	41 (69%)	115 (74%)
Easier [n(%)]	301 (65%)	118 (68%)	109 (56%)***	39 (66%)	108 (69%)
Less painful [n(%)]	194 (42%)	89 (51%)**	64 (33%)***	29 (49%)	69 (44%)
No bruises [n(%)]	172 (37%)	61 (35%)	73 (38%)	23 (39%)	61 (39%)
I am used to it [n(%)]	154 (33%)	104 (60%)***	65 (34%)	18 (31%)	21 (13%)***
Hard to find my vein [n(%)]	133 (29%)	44 (25%)	56 (29%)	28 (47%)***	50 (32%)
No bleeding afterwards [n(%)]	83 (18%)	30 (17%)	43 (22%)*	10 (17%)	25 (16%)
No muscle pain [n(%)]	55 (12%)	20 (12%)	20 (10%)	6 (10%)	19 (12%)
Afraid of needles [n(%)]	44 (10%)	21 (12%)	12 (6%)*	8 (14%)	15 (10%)
Different reason [n(%)]	12 (3%)	3 (2%)	8 (4%)	1 (2%)	3 (2%)
Reasons for preferring venous sampling					
I am used to it [n(%)]	163 (57%)	39 (58%)	69 (61%)	30 (59%)	64 (57%)
Less painful [n(%)]	114 (40%)	25 (37%)	40 (35%)	22 (43%)	53 (47%)*
Uncomfortable to use a finger prick [n(%)]	107 (38%)	33 (49%)*	45 (39%)	15 (29%)	37 (33%)
I don't want to do it myself [n(%)]	35 (12%)	10 (15%)	14 (12%)	3 (6%)	14 (13%)
Different reason [n(%)]	7 (2%)	0 (0%)	2 (2%)	3 (6%)	2 (2%)
Reason for not knowing preference					
Never experienced a finger prick [n(%)]	54 (64%)	3 (23%)***	21 (62%)	11 (69%)	23 (68%)

Hem-Col

Of all responding patients 66% indicated being interested in Hem-Col, 15% indicated not being interested and 20% was indifferent (table 4). The most important reasons for being interested were the ability to do the blood-sampling yourself and the blood-sampling taking less time. Of all responding patients 71% are willing to use Hem-Col; 81% of this group wants to use it for all tests that monitor their chronic disease (table 5). DM-patients were most willing to use Hem-Col (i.e. 77%) while CVD-patients were least willing to use Hem-Col (i.e. 63%). DM-patients were willing to pay a contribution of €1.66 for the Hem-Col which is lower than CVD-, CKD- and TD-patients, although this difference is not significant.

*Table 4: Reasons for being interested in Hem-Col versus not being interested in Hem-Col. Significant difference between a patient group and the total group *** p<0.001, ** p<0.01,* p<0.05*

	Total	**DM**	**CVD**	**CKD**	**TD**
Interested [n(%)]	859 (66%)	288 (74%)***	324 (60%)***	122 (61%)	314 (68%)
Reasons					
I can do it myself [n(%)]	643 (75%)	218 (76%)	240 (74%)	90 (74%)	247 (79%)
Easier to plan into my schedule [n(%)]	463 (54%)	181 (63%)***	137 (42%)***	64 (52%)	182 (58%)
Takes less time [n(%)]	510 (60%)	194 (67%)***	151 (47%)***	90 (74%)***	197 (63%)
No travelling needed [n(%)]	467 (54%)	170 (59%)	159 (49%)*	84 (69%)***	170 (54%)
Different reason [n(%)]	55 (6%)	17 (6%)	27 (8%)	5 (4%)	21 (7%)
Not interested [n(%)]	196 (15%)	39 (10%)***	96 (17%)***	34 (17%)	69 (15%)
Reasons					
Uncomfortable to do it myself [n(%)]	103 (52%)	15 (38%)	50 (52%)	14 (41%)	41 (59%)
Fear to do it myself [n(%)]	59 (30%)	9 (23%)	22 (23%)*	9 (26%)	27 (39%)*
I see it as a trip [n(%)]	15 (8%)	6 (15%)	10 (10%)	3 (9%)	2 (3%)*
Different reason [n(%)]	67 (34%)	18 (46%)	39 (41%)	13 (38%)	16 (23%)*
Indifferent [n(%)]	256 (20%)	61 (16%)***	125 (23%)***	43 (22%)	80 (17%)

*Table 5: Willingness to use Hem-Col among participants. Significant difference between a patient group and the total group *** p<0.001, ** p<0.01,* p<0.05*

	Total	**DM**	**CVD**	**CKD**	**TD**
Willingness to use hem-col [n(%)]	933 (71%)	299 (77%)**	344 (63%)***	139 (70%)	348 (75%)*
For all blood tests [n(%)]	751 (81%)	244 (82%)	282 (82%)	95 (68%)***	281 (81%)
Contribution willing to pay [mean(sd)]	€2.15 (4.44)	€1.66 (3.35)	€1.95 (3.83)	€2.01 (5.00)	€2.40 (4.81)

Interaction and correlation between parameters

A significant interaction was found between all chronic diseases (p<0.001) meaning they occur alongside each other within these patient groups. Several significant interactions were found between the willingness to use Hem-Col and other parameters. Patients who usually go to the service phlebotomy center for an appointment (p=0.002), spent more time per appointment (p=0.007) or experience difficulty in finding a parking spot (p=0.005) are more likely to be willing to use Hem-Col. Patients who are suffering from other chronic diseases are less likely to be willing to use Hem-Col (p=0.03).

Survey parameters for the health economic model

To obtain the parameters for the health economic model, it was examined whether chronic diseases were significantly different from one another in terms of a parameter. In case a significant difference exists, the probabilities and mean values were dependent on the chronic disease. The same was done for the age groups. The amount of phlebotomy appointments differed significantly between chronic diseases (p<0.001) and age groups for CVD-patients (p=0.001). The location of the phlebotomy appointment differed significantly between chronic diseases (p<0.001) and age groups within the diseases DM, CVD and CKD (p_{DM}<0.001 , p_{CVD}=0.003 and p_{CKD}<0.001). The time spent per appointment differed significantly between chronic diseases (p<0.001) and age groups for CVD-patients (p_{CVD}<0.001). However, larger differences in the time spent per appointment were observed between locations than age-groups for CVD-patients, so the time spent per appointment was chosen to depend

on chronic disease and location of the appointment (location-time p<0.001). The dependency on others differed significantly between age groups for CVD-patients (p=0.005), so the probability of being dependent on others was split per chronic disease and age group for CVD-patients. The willingness to use Hem-Col differed significantly between chronic diseases (p<0.001) and age groups for CVD-patients (p<0.001). An overview of all model parameters can be found in appendix C.

Cost analysis

Although the cost of phlebotomy itself increases with €25.82 per patient per year when using Hem-Col, the overall societal cost (i.e. -€76.68 per patient per year) remains negative indicating costs can be reduced when Hem-Col is implemented (figure 7). The average cost savings are mainly attributable to a decreased time spent per phlebotomy appointment, resulting in a reduction of the production loss cost with €83.95 per patient per year. The travel cost and informal care cost per patient per year decrease as well, with €6.85 and €11.67 respectively. The decrease in waste cost per patient per year (i.e. €0.03) can be considered negligible.

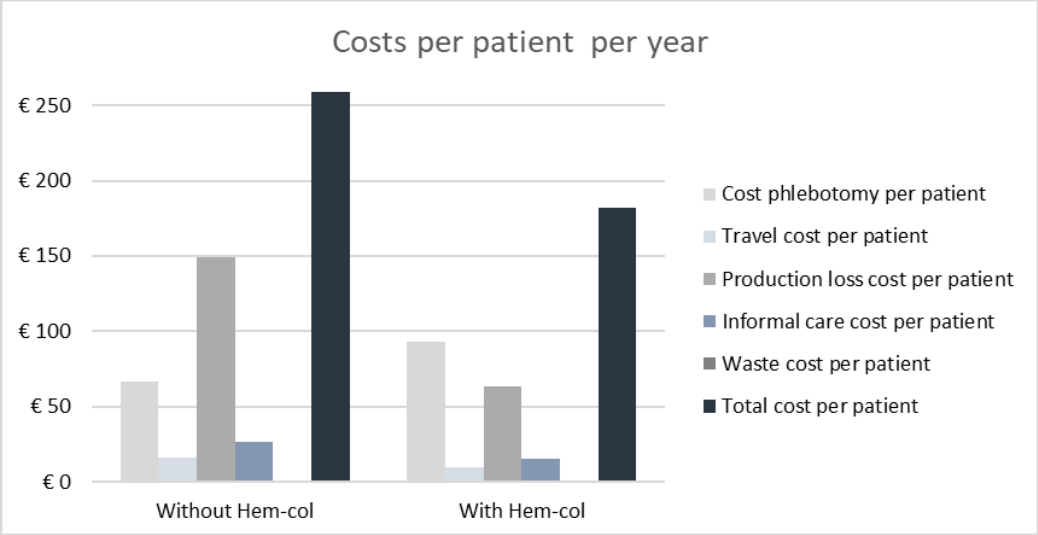

Figure 7: Micro-simulation results of 10,000 hypothetical patients per year.

Probabilistic sensitivity analysis

The result of the PSA is shown in figure 8, where the costs of current practice are plotted against the costs after implementing Hem-Col. The line represents all points where the incremental costs are equal to zero. Almost all points in the PSA are above the line indicating that the societal cost after implementing Hem-Col are likely to be lower compared with current practice. The PSA result indicates that phlebotomy with the possibility to use Hem-col costs on average €178 (95% CI €139.77 to €222.80) per patient with DM, CVD, CKD or TD on a yearly basis, as compared with €254 (95% CI €212.23 to €297.97) for current practice. The cost savings when Hem-Col is implemented are €76 (95% CI -€112.95 to -€35.55) per patient per year. This could result in annual cost savings of approximately €400 million in the Netherlands.

The cost of the Hem-Col device have the largest impact on the cost outcome due to parameter uncertainty, followed by the time spent when Hem-Col is used for blood-sampling (figure 9). The overall EVPI per chronically ill patient with DM, CVD, CKD or TD is estimated to be €0.0016 which implies that further research to decrease uncertainty is likely inefficient.

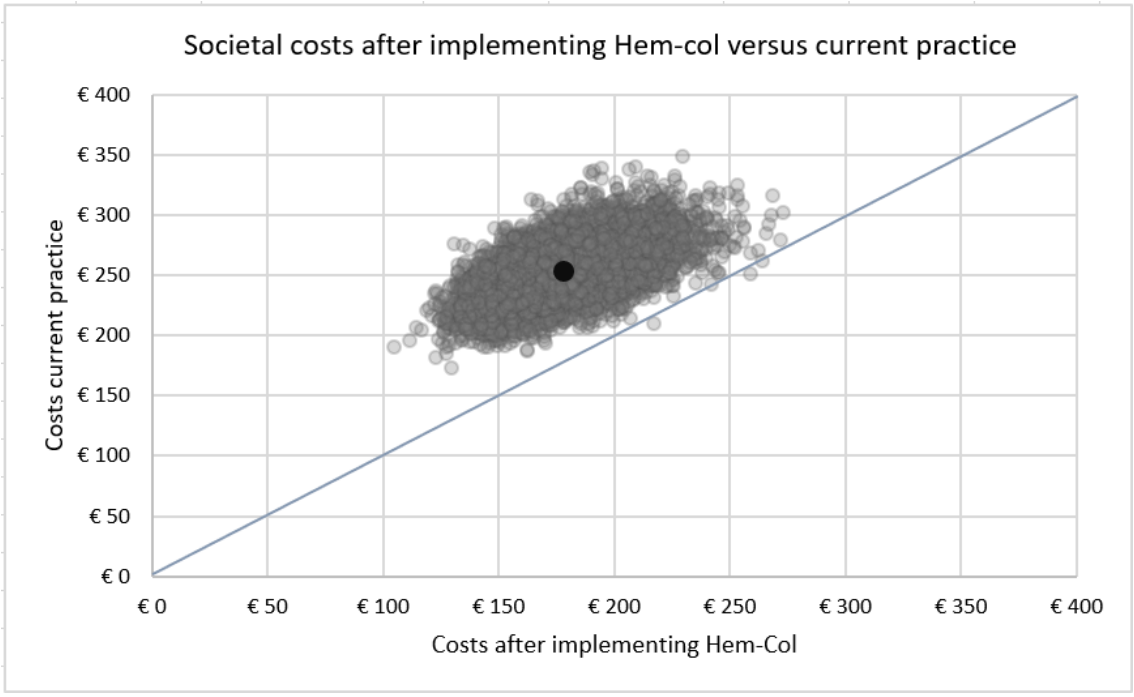

Figure 8: Result of 10,000 model iterations of 10,000 patients. The black dot represents the mean value and all costs are on a yearly basis. The line represents all points were the costs after implementing Hem-Col are equal to the costs of the current practice, meaning the incremental costs are equal to zero.

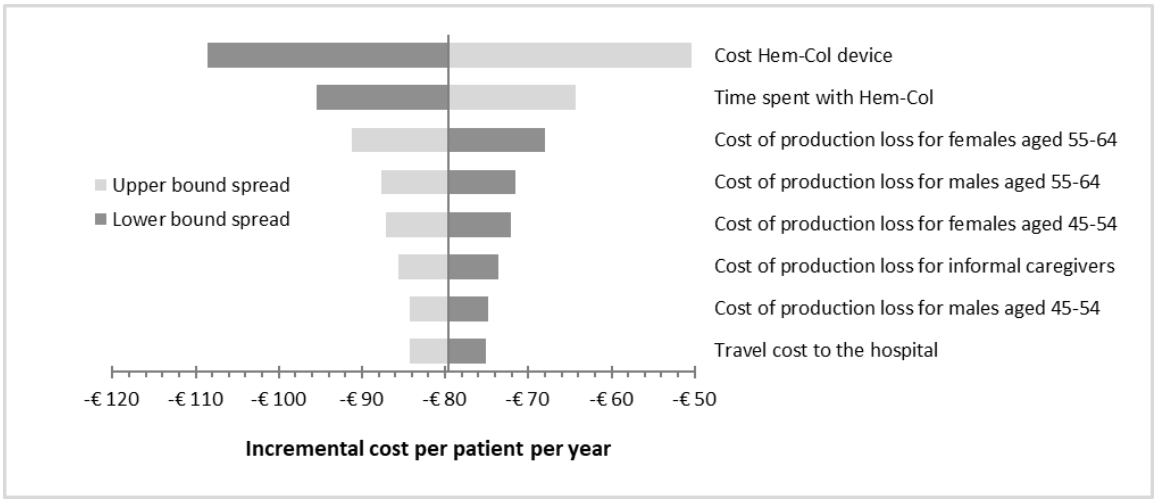

Figure 9: Tornado diagram showing the eight most influencing model parameters on the cost outcome when Hem-Col is implemented.

Conclusion

Of the chronically ill patients, approximately 70% prefer to use Hem-Col for blood-sampling to monitor their disease. Blood-sampling with Hem-Col is considered more user-friendly compared with venous phlebotomy at location. Hem-Col may reduce the burden to patients, lower the impact of the phlebotomy appointment on their daily schedule and reduce physical inconveniences. Long waiting times and crowded phlebotomy locations can be avoided when patients have the possibility to use Hem-Col. Furthermore, implementing Hem-Col for the purpose of monitoring chronic diseases is likely cost-saving as it is expected to reduce societal cost.

Discussion

One third of the patients diagnosed with DM, CVD, CKD and/or TD experience the phlebotomy appointment as a burden and indicated that it affects their daily schedule. More than half of the patients experience physical inconveniences after venous phlebotomy. Furthermore, 16% feels dependent on others and 12% experience anxiety before the phlebotomy appointment. Long waiting times and crowded phlebotomy locations are the most important factors for dissatisfaction with phlebotomy locations. An at-home blood-sampling device must be safe and trustworthy, easy to use and send, and contain clear instructions according to the chronic care patients. Although a consistent preference for a finger prick is lacking, approximately two out of three patients are interested in Hem-Col. Finally, 71% prefer to use Hem-Col to monitor their chronic disease. The most important reason for patients not willing to use Hem-Col is the expectation that it's uncomfortable to do the blood-sampling yourself. The cost per chronically ill patient with DM, CVD, CKD or TD is expected to decrease with approximately €76 on a yearly basis, indicating that Hem-Col is likely cost-saving when compared with current practice.

Dissatisfaction with long waiting times and crowded phlebotomy locations may have been aggravated due to the recent outbreak of the coronavirus. Chronic care patients are at higher risk when infected with the coronavirus which may have resulted in more negative feelings towards crowded phlebotomy locations.

Several studies indicate that, in general, a finger prick is preferred over venous sampling since it is experienced as less painful[25-28]. In this study, the percentage of patients preferring a finger prick (i.e. 35%) is higher than the percentage of patients preferring venous sampling (i.e. 22%). However, 37% of the patients indicated to have no preference so it cannot be stated that the finger prick is in general preferred among chronic care patients. About the same proportion of patients who preferred a finger prick or venous sampling found their preferred form of sampling less painful, indicating that patients' opinions vary largely within this topic.

Many patients without a preference for a blood-sampling method were interested in Hem-Col, likely due to its ability to self-manage. DM-patients are most interested in Hem-Col which is in accordance with the fact that the finger prick is preferred most by DM-patients compared with the other groups. This can be explained by the reason they mention for a finger prick: 'being used to it'. DM-patients are familiar with performing a finger prick to measure their blood glucose level throughout the day.

The reason 'hard to find my vein' was given more often among CKD-patients for preferring a finger prick compared with the other groups. CKD-patients often have a shunt which causes one arm to be unavailable for venipuncture [66]. However, the preference for a finger prick among CKD-patients was slightly lower compared with the other groups which can be explained by the possibility of blood-sampling during dialysis. When patients are on dialysis, the blood can be easily drawn without making an extra venipuncture.

CVD-patients had a lower preference to use Hem-Col, which may be explained by their age. The mean age of CVD-patients was more than ten years higher compared with the other groups. It is assumed that older people in general are less eager to learn how to use a new system, they rather hold on to a system they are familiar with [67, 68].

Patients who are suffering from other chronic diseases besides DM, CVD, CKD or TD are less likely to be willing to use Hem-Col. This can be explained by the increased amount of hospital appointments they have. Phlebotomy can be easily combined with another appointment in the hospital, which may reduce the impact of the phlebotomy appointment on the daily schedule. Therefore, these patients may value at-home blood-sampling less when compared with others.

The mean age of the respondents in this study was at least ten years lower for every group compared with the Dutch population, meaning that the respondents were not representative in terms of age. The percentage of chronically ill patients in the Dutch population that prefer to use Hem-Col may be lower. However, implementing Hem-Col in clinical practice is still cost-saving since it is mainly attributable to reduced production loss costs. The production loss costs are age-dependent, indicating that a larger amount of societal costs are saved for the patients aged between 18 and 64 years.

Patients were willing to pay €2.15 per phlebotomy appointment to use the Hem-Col device. However, the financial contribution that DM-patients were willing to make is lower which is in conflict with the highest preference they had to use Hem-Col compared with the other groups. The lower contribution can be explained by the fact that type 2 DM occurs more frequently in people with a lower socio-economic status (SES) compared with people with a higher SES [69]. This indicates that type 2 DM-patients have in general less money to spend on a financial contribution for Hem-Col.

Hem-Col is likely cost-saving as compared with current practice. In addition, the cost of the Hem-col device is a starting price meaning that the cost is likely to be reduced when Hem-Col is used on a large scale. This results in lower phlebotomy costs for Hem-Col and therefore larger cost-savings when Hem-Col is implemented in clinical practice.

The results showed that the overall uncertainty is low; even if the parameters with the largest impact on the cost outcome would vary, the implementation of Hem-Col would still be cost-saving. This demonstrates that the value of further research is expected to be low which is in line with the low EVPI. Conducting further research to decrease uncertainty is likely inefficient.

Although the results showed a negligible impact of the waste cost on the societal cost, decreasing the amount of medical waste and thereby the waste cost can be very interesting in a different context. However, the process of breaking the Hem-Col tubes is not automated yet and therefore it's doubtful whether laboratories will actually split the tubes manually.

This study provided new insights into the experiences with venipuncture, the willingness to use Hem-Col and its effect on societal cost. Survey outcomes may not be generalized directly to other countries because experiences and preferences of chronically ill patients might differ. A health economic model was created in which the parameters can be easily adapted for different countries. However, if the way the health system is organized differs significantly from the Dutch health system, more or different parameters might be needed. For example, cultural differences within a country might need addressing.

Strengths, limitations and future research

A strength of this study was the large sample size of the survey. The actual number of respondents was more than three times higher than the respondents needed in order to draw conclusions for the total group according to the sample size calculation. This increased the reliability of the results. Furthermore, survey parameters that served as model input parameters were able to be split in multiple categories due to the large sample size. For example, the probability of a patient willing to use Hem-Col depended on the chronic disease and age group. This resulted in the model being more in line with reality and therefore in high external validity. Another strength was the combination of newly acquired data with data from literature to build a health economic model with a close link to reality. This provided new insights into the costs of a self-sampling method for phlebotomy.

Several limitations were perceived in this study. Firstly, in order to analyze patient groups apart from one another, a higher number of respondents was needed for the DM- and CKD-group according to the sample size calculation. In addition, splitting model input parameters into multiple categories resulted in a few very small subgroups. Performing analysis on these small subgroups resulted in higher parameter uncertainty and therefore larger 95% CI intervals for the cost outcomes.

Secondly, respondents with multiple diseases were, according to their diseases, assigned to the DM, CVD, CKD and/or TD group for analysis. So the responses of patients with multiple diseases have a higher weight since they were taken into account multiple times resulting in a decreased reliability. Of all respondents, 19% have multiple diseases which is relatively large and therefore likely that it may have affected the outcomes.

Thirdly, after analyzing remarks made by the respondents at the end of the survey, some confusion among CVD-patients was noticed. For some CVD-patients it was not clear that Hem-Col cannot be used to examine their INR. This has probably resulted in a higher amount of phlebotomy appointments per year than the actual case and it may have affected the willingness to use Hem-Col negatively. Several CVD-patients indicated their INR is tested with a finger prick and therefore they did not see the additional value of Hem-Col. However, the cost-savings on a yearly basis may be lower but implementing Hem-Col in clinical practice is still cost-saving.

Lastly, the percentage of samples that needs to be repeated is not taken into account in the model. When patients switch to a self-sampling device, mistakes will be made, especially when it is used for the first few times. It is likely that the percentage of Hem-Col tubes that needs to be repeated is higher compared with venous sampling performed by a phlebotomist. This results in lower cost-savings and decreased satisfaction among patients which may eventually reduce the willingness to use Hem-Col.

For future research, a pilot study among DM-, CVD-, CKD- and TD-patients is recommended to investigate their experience with Hem-Col as blood-sampling device. The pilot study must focus on how promising Hem-Col is for the implementation in clinical practice.

Acknowledgements

I would like to thank all patient associations and Facebook support groups for distributing the survey among members and thank all chronic care patients for their participation in the survey. I also thank the University of Twente for funding the distribution of the survey among members of the Harteraad panel.

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Appendix A: Translated survey

Welcome,

This research focuses on at-home phlebotomy possibilities for chronically ill patients. The purpose of this survey is to gain insight into your perspective. You are requested to answer a few questions about your experiences with phlebotomy appointments in the hospital or at a service phlebotomy center. Afterwards, we will ask you about your opinion of a new system that enables blood-sampling at home.

It will take approximately 10 minutes to complete the survey. The answers you provide will be processed anonymously and cannot be traced back to you. Your participation in this survey is voluntary. You have the right to quit the survey at all times without giving a reason and this will not lead to negative consequences for you. The results are owned by the University of Twente and will only be used for scientific purposes. In case you have any questions, feel free to contact the researcher via e-mail (…).

By clicking the button below, you agree to participate on voluntary basis to this research, you are at least 18 years old and you are aware of the possibility to withdraw from the survey at any time without giving a reason.

Thank you in advance for your time and effort.

- ○ I agree, start the survey
- ○ I do not agree, I wish not to participate

In case "I do not agree, I wish not to participate" was chosen, the survey ends.

---

1. What is your age?

_____

2. What is your gender?

- ○ Male
- ○ Female
- ○ Different

3. In what province do you live? Please, indicate in the figure.

4. With which chronic disease are you diagnosed that your blood needs to be tested on a regular basis? (Multiple answers are possible)

- ○ Diabetes mellitus type 1
- ○ Diabetes mellitus type 2
- ○ Cardiovascular disease
- ○ Chronic kidney disease
- ○ Thyroid disease
- ○ Different, namely:
  _____

5. How many phlebotomy appointments do you have per year to monitor this chronic disease?

- ○ 1 appointment
- ○ 2 appointments
- ○ 3 appointments
- ○ 4 appointments
- ○ 5 appointments
- ○ 6 appointments
- ○ More than 6 appointments

In case "More than 6 appointments" was chosen, the survey continues with question 6, otherwise question 6 was skipped.

6. You indicated to have more than 6 phlebotomy appointments per year, how many appointments do you have?

_____

7. Which location do you visit the most for phlebotomy?

- ○ The hospital
- ○ The service phlebotomy center
- ○ The general practitioners office
- ○ Phlebotomy appointments often take place at home

8. How much time do you spent per phlebotomy appointment, including travel time from and to the location?

- ○ Less than half an hour
- ○ Half an hour till an hour
- ○ An hour till one and a half hour
- ○ One and a half hour till two hours
- ○ More than two hours, namely:
  _____

9. Is the time spent per phlebotomy appointment a burden to you?

- ○ Yes
- ○ No

---

10. How do you feel when you think about the fact that your blood must be drawn venously?

- ○ I don't care
- ○ I don't feel anxiety, but I prefer not to go
- ○ I feel anxiety

In case "I feel anxiety" was chosen, the survey continues with question 11, otherwise question 11 and 12 were skipped.

11. How much anxiety do you experience before a phlebotomy appointment? 0 indicates that you feel no anxiety at all and 10 indicates that you feel an extreme amount of anxiety.

12. Do you fear needles?

- ○ Yes
- ○ No

13. Would you describe venous phlebotomy as painful?

- ○ Yes
- ○ No
- ○ Sometimes

14. Do you feel dependent on others to go to the hospital, the service phlebotomy center or the GP's office for the phlebotomy?

- ○ Yes
- ○ No

In case "Phlebotomy appointments often take place at home" was chosen in question 7, question 15 was skipped.

15. How do you experience the phlebotomy at your chosen location (hospital, service phlebotomy center or the GP's office)?

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
I experience the waiting room as unpleasant	○	○	○	○	○
It is hard to find a parking spot	○	○	○	○	○
It is always busy	○	○	○	○	○
I have to wait for a long time	○	○	○	○	○
The blood-sampling itself takes a long time	○	○	○	○	○
The phlebotomist is unfriendly	○	○	○	○	○
The phlebotomist is not good at her job	○	○	○	○	○

16. After blood is drawn from a vein … (multiple answers possible)

- ○ I often get bruises
- ○ I bleed frequently
- ○ I have muscle pain
- ○ I feel lightheaded
- ○ I pass out sometimes
- ○ None of the above

17. Does the phlebotomy appointment affects your daily schedule, besides the phlebotomy itself and the travel time?

- ○ Yes
- ○ No

In case "Yes" was chosen, the survey continues with question 18, otherwise question 18 was skipped.

18. How does the phlebotomy appointment affects your daily schedule?

_____
_____
_____

19. What is your preference, based only on the blood-sampling method itself; a finger prick or venous sampling? We request you to base your preference only on the method itself, and not on the location where the blood-sampling can take place (e.g. at home/hospital).

- ○ A finger prick
- ○ Venous sampling
- ○ I don't have a preference
- ○ I don't know

In case "A finger prick" was chosen, the survey continues with question 20. In case "Venous sampling" was chosen, the survey continues with question 21. In case "I don't know" was chosen, the survey continues with question 22. In case "I don't have a preference" was chosen, the survey continues with question 23.

20. Why do you have a preference for the finger prick? (Multiple answers possible)

- ○ It is less painful
- ○ I am used to a finger prick
- ○ It is quicker
- ○ It is easier
- ○ My veins are hard to find
- ○ I have a fear of needles
- ○ The bleeding stops sooner
- ○ No bruises
- ○ No muscle pain
- ○ Different, namely:

_____

The survey continues with question 23.

21. Why do you have a preference for venous sampling? (Multiple answers possible)

- ○ It is less painful
- ○ I am used to venous sampling
- ○ I don't have to do it myself
- ○ It seems uncomfortable to get enough blood in a tube after a finger prick
- ○ Different, namely:

  _____

The survey continues with question 23.

22. Did you ever use a finger prick, or someone else on you?

- ○ Yes
- ○ No

---

23. A new blood-sampling system has been developed which makes it possible for patients to do the blood-sampling themselves at home. The package will be send via mail and contains the following items (see the figure):

- A sterile cloth
- A lancet to prick the finger
- Tube to collect the blood
- A band aid
- Shipping material

The patient does the finger prick him-/herself, or someone nearby who is willing to help. After the prick, the blood can be collected in the tube. Approximately 5 blood drops are needed to fill the tube. Finally, the package can be send via mail.

What do you think when you are able to do the blood-sampling at home with a finger prick?

- ○ Great
- ○ Good
- ○ Average
- ○ Not good
- ○ Terrible

In case "Great" or "Good" was chosen, the survey continues with question 24. In case "Not good" or "Terrible" was chosen, the survey continues with question 25. In case "Average" was chosen, the survey continues with question 26.

24. For what reasons are you interested in blood-sampling at home with a finger prick? (Multiple answers possible)

- ○ I can do it myself
- ○ It is easier to schedule
- ○ It takes less time
- ○ I don't have to travel back and forth
- ○ Different, namely:
  _____

Survey continues with question 26.

25. For what reasons are you not interested in blood-sampling at home with a finger prick? (Multiple answers possible)

- ○ I think it is a hassle to do it myself
- ○ I am afraid to prick myself
- ○ I see it as a trip to go to the hospital, the service phlebotomy center or the GP's office for phlebotomy
- ○ Different, namely:
  _____

26. What do you think is important for a blood-sampling system usable at home? 5 Stars indicate that you think it's extremely important, 1 star indicates that you think it's not important.

27. A blood collection tube needs approximately 5 blood drops, do you think that is a lot?

- ○ No, that's fine
- ○ Yes, I think that is a lot but it's still doable
- ○ Yes, that seems hard to me

28. How much are you willing to spend on an additional contribution to be able to do the blood-sampling at home? The costs mentioned are per phlebotomy appointment.

- ○ Nothing
- ○ €5,00
- ○ €10,00
- ○ €20,00
- ○ €30,00
- ○ I am willing to pay more than €30,00

In case "I am willing to pay more than €30,00" was chosen, the survey continues with question 29, otherwise question 29 was skipped.

29. You indicated that you are willing to pay more than €30,00 on an additional contribution to be able to do the blood-sampling at home. How much are you willing to pay?

_____

30. Are you willing to use this system, assuming that the costs are not higher than the additional contribution you are willing to pay? For example: If you have answered with €5,00 ; the costs of the system will not be higher than €5,00.

- ○ Yes
- ○ No

In case "No" was chosen, the survey continues with question 32.

31. How often do you want to use this system?

- ○ For all blood tests I do on a yearly basis to monitor my chronic disease
- ○ For a part of the blood tests I do on a yearly basis to monitor my chronic disease, amount:

  _____

32. Do you have any remarks?

_____
_____
_____

Thank you for your participation, your answers have been recorded.

Appendix B: Survey sample size calculation

The survey sample size (n) which was needed to acquire a valuable and reliable result was calculated with the following formula[70].

$$n = \frac{N \cdot X}{(X + N - 1)}$$

$$Where\ N{\sim}5.2\ million\ and\ X = \frac{1.96^2 \cdot 0.5 \cdot (1-0.5)}{0.05^2}$$

A 95% confidence level and a 5% margin of error were chosen for this calculation[71], resulting in a survey sample size of ~400 respondents. This means that every subgroup (DM, CVD, CKD and TD) needs at least 100 respondents to draw conclusions for the total group. However, in order to compare the subgroups, a sample size of ~400 respondents is needed per subgroup.

Appendix C: Overview of model input parameters

Table 1a. Model input probability parameters used in the model. CI = confidence interval, CKD = chronic kidney disease, CVD = cardiovascular diseases, DM = diabetes mellitus, GP = general practitioner, TD = thyroid diseases.

* Zero observations within this category. In order to draw a value from the distribution, all α's of this parameter are elevated by 1. This was considered acceptable since the probability of this parameter category was lower than 3.0%.

** Zero observations within this category. Probabilities were set to 0%, no values were drawn from a distribution. The α's of this parameter could not be elevated by 1 since the probability of the parameter category would be higher than 3.0% which was considered unacceptable.

Parameter	**Category**	**Probability**	**95% CI**	**Distribution**	**Reference**
Probability of chronic disease	DM	23.0%	23.0% to 23.1%	Dirichlet	[2, 72]
	CVD	30.5%	30.5% to 30.6%	Dirichlet	[62, 73]
	CKD	34.9%	34.8% to 34.9%	Dirichlet	[4, 74, 75]
	TD	11.6%	11.5% to 11.6%	Dirichlet	[5-8]
Male gender	DM	52.6%	52.5% to 52.7%	Beta	[61]
	CVD	52.1%	52.0% to 52.2%	Beta	[62]
	CKD	29.2%	29.1% to 29.3%	Beta	[63]
	TD	15.5%	15.3% to 15.7%	Beta	[64]
Population age distribution (male with DM)	18-24	1.0%	1.0% to 1.0%	Dirichlet	[61, 76]
	25-34	1.6%	1.6% to 1.6%	Dirichlet	[61, 76]
	35-44	3.9%	3.9% to 4.0%	Dirichlet	[61, 76]
	45-54	12.8%	12.7% to 12.9%	Dirichlet	[61, 76]
	55-64	23.6%	23.5% to 23.7%	Dirichlet	[61, 76]
	65-74	31.9%	31.8% to 32.0%	Dirichlet	[61, 76]
	75+	25.1%	25.0% to 25.2%	Dirichlet	[61, 76]

Population age distribution (female with DM)	18-24	1.2%	1.2% to 1.3%	Dirichlet	[61, 76]
	25-34	1.7%	1.7% to 1.8%	Dirichlet	[61, 76]
	35-44	3.5%	3.4% to 3.5%	Dirichlet	[61, 76]
	45-54	10.8%	10.7% to 10.9%	Dirichlet	[61, 76]
	55-64	20.0%	19.8% to 20.1%	Dirichlet	[61, 76]
	65-74	27.7%	27.6% to 27.8%	Dirichlet	[61, 76]
	75+	35.1%	34.9% to 35.2%	Dirichlet	[61, 76]
Population age distribution (male with CVD)	18-24	1.3%	1.3% to 1.3%	Dirichlet	[62]
	25-34	2.1%	2.1% to 2.2%	Dirichlet	[62]
	35-44	2.1%	2.1% to 2.2%	Dirichlet	[62]
	45-54	2.5%	2.4% to 2.5%	Dirichlet	[62]
	55-64	8.6%	8.6% to 8.7%	Dirichlet	[62]
	65-74	19.1%	19.1% to 19.2%	Dirichlet	[62]
	75+	64.2%	64.1% to 64.3%	Dirichlet	[62]
Population age distribution (female with CVD)	18-24	1.7%	1.7% to 1.7%	Dirichlet	[62]
	25-34	2.8%	2.8% to 2.9%	Dirichlet	[62]
	35-44	2.8%	2.8% to 2.9%	Dirichlet	[62]
	45-54	3.4%	3.3% to 3.4%	Dirichlet	[62]
	55-64	8.7%	8.7% to 8.8%	Dirichlet	[62]
	65-74	15.4%	15.4% to 15.5%	Dirichlet	[62]
	75+	65.1%	65.0% to 65.2%	Dirichlet	[62]
Population age distribution (male with CKD)	18-24*	0.0%	0.0% to 0.0%	Dirichlet	[63, 76]
	25-34*	0.0%	0.0% to 0.0%	Dirichlet	[63, 76]
	35-44	3.5%	3.5% to 3.6%	Dirichlet	[63, 76]
	45-54	13.1%	13.0% to 13.2%	Dirichlet	[63, 76]
	55-64	19.9%	19.7% to 20.0%	Dirichlet	[63, 76]
	65-74	25.1%	25.0% to 25.2%	Dirichlet	[63, 76]
	75+	38.5%	38.3% to 38.6%	Dirichlet	[63, 76]
Population age distribution (female with CKD)	18-24	1.0%	1.0% to 1.0%	Dirichlet	[63, 76]
	25-34	3.5%	3.5% to 3.6%	Dirichlet	[63, 76]
	35-44	3.9%	3.9% to 3.9%	Dirichlet	[63, 76]
	45-54	12.5%	12.4% to 12.6%	Dirichlet	[63, 76]
	55-64	19.7%	19.6% to 19.7%	Dirichlet	[63, 76]
	65-74	26.5%	26.5% to 26.6%	Dirichlet	[63, 76]
	75+	32.9%	32.8% to 33.0%	Dirichlet	[63, 76]
Population age distribution (male with TD)	18-24	2.4%	2.2% to 2.6%	Dirichlet	[64, 76]
	25-34	5.4%	5.2% to 5.7%	Dirichlet	[64, 76]
	35-44	5.4%	5.2% to 5.7%	Dirichlet	[64, 76]
	45-54	18.6%	18.2% to 19.1%	Dirichlet	[64, 76]
	55-64	18.6%	18.2% to 19.1%	Dirichlet	[64, 76]
	65-74	27.3%	26.8% to 27.9%	Dirichlet	[64, 76]
	75+	22.1%	21.6% to 22.6%	Dirichlet	[64, 76]
Population age distribution (female with TD)	18-24	2.2%	2.2% to 2.3%	Dirichlet	[64, 76]
	25-34	8.2%	8.1% to 8.3%	Dirichlet	[64, 76]
	35-44	8.2%	8.1% to 8.3%	Dirichlet	[64, 76]
	45-54	20.1%	19.9% to 20.3%	Dirichlet	[64, 76]

	55-64	20.1%	19.9% to 20.3%	Dirichlet	[64, 76]
	65-74	22.6%	22.4% to 22.8%	Dirichlet	[64, 76]
	75+	18.6%	18.4% to 18.8%	Dirichlet	[64, 76]
Location for DM 18-24	Hospital	75.0%	63.2% to 86.8%	Dirichlet	Survey
	Service phlebotomy center	25.0%	13.2% to 36.8%	Dirichlet	Survey
	GP's office*	0.0%	0.0% to 0.0%	Dirichlet	Survey
	At home*	0.0%	0.0% to 0.0%	Dirichlet	Survey
Location for DM 25-34	Hospital	72.3%	60.1% to 84.6%	Dirichlet	Survey
	Service phlebotomy center	25.5%	13.6% to 37.5%	Dirichlet	Survey
	GP's office	2.1%	0.0% to 6.1%	Dirichlet	Survey
	At home*	0.0%	0.0% to 0.0%	Dirichlet	Survey
Location for DM 35-44	Hospital	61.8%	46.3% to 77.2%	Dirichlet	Survey
	Service phlebotomy center	35.3%	20.1% to 50.5%	Dirichlet	Survey
	GP's office	2.9%	0.0% to 8.3%	Dirichlet	Survey
	At home*	0.0%	0.0% to 0.0%	Dirichlet	Survey
Location for DM 45-54	Hospital	61.5%	49.7% to 73.4%	Dirichlet	Survey
	Service phlebotomy center	32.3%	20.9% to 43.7%	Dirichlet	Survey
	GP's office	3.1%	0.0% to 7.3%	Dirichlet	Survey
	At home	3.1%	0.0% to 7.3%	Dirichlet	Survey
Location for DM 55-64	Hospital	55.1%	43.3% to 66.8%	Dirichlet	Survey
	Service phlebotomy center	33.3%	22.2% to 44.5%	Dirichlet	Survey
	GP's office	10.1%	3.0% to 17.3%	Dirichlet	Survey
	At home	1.4%	0.0% to 4.3%	Dirichlet	Survey
Location for DM 65-74	Hospital	32.6%	23.0% to 42.2%	Dirichlet	Survey
	Service phlebotomy center	57.6%	47.5% to 67.7%	Dirichlet	Survey
	GP's office	6.5%	1.5% to 11.6%	Dirichlet	Survey
	At home	3.3%	0.0% to 6.9%	Dirichlet	Survey
Location for DM 75+	Hospital	33.3%	17.2% to 49.4%	Dirichlet	Survey
	Service phlebotomy center	51.5%	34.5% to 68.6%	Dirichlet	Survey
	GP's office	6.1%	0.0% to 14.2%	Dirichlet	Survey
	At home	9.1%	0.0% to 18.9%	Dirichlet	Survey
Location for CVD 18-44	Hospital	42.1%	19.9% to 64.3%	Dirichlet	Survey
	Service phlebotomy center	42.1%	19.9% to 64.3%	Dirichlet	Survey
	GP's office	10.5%	0.0% to 24.3%	Dirichlet	Survey
	At home	5.3%	0.0% to 15.3%	Dirichlet	Survey

Location for CVD 45-54	Hospital	45.0%	34.1% to 55.9%	Dirichlet	Survey
	Service phlebotomy center	45.0%	34.1% to 55.9%	Dirichlet	Survey
	GP's office	8.8%	2.6% to 14.9%	Dirichlet	Survey
	At home	1.3%	0.0% to 3.7%	Dirichlet	Survey
Location for CVD 55-64	Hospital	46.8%	38.5% to 55.1%	Dirichlet	Survey
	Service phlebotomy center	38.8%	30.7% to 47.0%	Dirichlet	Survey
	GP's office	10.1%	5.1% to 15.1%	Dirichlet	Survey
	At home	4.3%	0.9% to 7.7%	Dirichlet	Survey
Location for CVD 65-74	Hospital	38.1%	31.6% to 44.6%	Dirichlet	Survey
	Service phlebotomy center	51.2%	44.5% to 57.8%	Dirichlet	Survey
	GP's office	7.9%	4.3% to 11.5%	Dirichlet	Survey
	At home	2.8%	0.6% to 5.0%	Dirichlet	Survey
Location for CVD 75+	Hospital	31.5%	22.0% to 41.0%	Dirichlet	Survey
	Service phlebotomy center	43.5%	33.3% to 53.6%	Dirichlet	Survey
	GP's office	8.7%	2.9% to 14.5%	Dirichlet	Survey
	At home	16.3%	8.8% to 23.9%	Dirichlet	Survey
Location for CKD 18-24	Hospital	100.0%	100.0% to 100.0%		Survey
	Service phlebotomy center**	0.0%	0.0% to 0.0%		Survey
	GP's office**	0.0%	0.0% to 0.0%		Survey
	At home**	0.0%	0.0% to 0.0%		Survey
Location for CKD 25-34	Hospital	92.6%	82.7% to 100.0%	Dirichlet	Survey
	Service phlebotomy center	3.7%	0.0% to 10.8%	Dirichlet	Survey
	GP's office	3.7%	0.0% to 10.8%	Dirichlet	Survey
	At home**	0.0%	0.0% to 0.0%		Survey
Location for CKD 35-44	Hospital	79.3%	64.6% to 94.1%	Dirichlet	Survey
	Service phlebotomy center	20.7%	5.9% to 35.4%	Dirichlet	Survey
	GP's office**	0.0%	0.0% to 0.0%		Survey
	At home**	0.0%	0.0% to 0.0%		Survey
Location for CKD 45-54	Hospital	76.2%	63.9% to 88.5%	Dirichlet	Survey
	Service phlebotomy center	21.4%	9.6% to 33.3%	Dirichlet	Survey
	GP's office	2.4%	0.0% to 6.8%	Dirichlet	Survey
	At home*	0.0%	0.0% to 0.0%	Dirichlet	Survey
Location for CKD 55-64	Hospital	71.7%	58.7% to 84.8%	Dirichlet	Survey

	Service phlebotomy center	21.7%	9.8% to 33.7%	Dirichlet	Survey
	GP's office	4.3%	0.0% to 10.2%	Dirichlet	Survey
	At home	2.2%	0.0% to 6.4%	Dirichlet	Survey
Location for CKD 65-74	Hospital	56.7%	40.0% to 73.3%	Dirichlet	Survey
	Service phlebotomy center	36.7%	20.5% to 52.9%	Dirichlet	Survey
	GP's office	6.7%	0.0% to 15.1%	Dirichlet	Survey
	At home*	0.0%	0.0% to 0.0%	Dirichlet	Survey
Location for CKD 75+	Hospital	30.8%	5.7% to 55.9%	Dirichlet	Survey
	Service phlebotomy center	46.2%	19.1% to 73.3%	Dirichlet	Survey
	GP's office	7.7%	0.0% to 22.2%	Dirichlet	Survey
	At home	15.4%	0.0% to 35.0%	Dirichlet	Survey
Location for TD all ages	Hospital	49.9%	45.3% to 54.4%	Dirichlet	Survey
	Service phlebotomy center	41.9%	37.4% to 46.4%	Dirichlet	Survey
	GP's office	8.0%	5.5% to 10.5%	Dirichlet	Survey
	At home	0.2%	0.0% to 0.6%	Dirichlet	Survey
Dependency on others	DM	18.3%	14.5% to 22.1%	Beta	Survey
	CKD	17.1%	11.9% to 22.3%	Beta	Survey
	TD	16.8%	13.4% to 20.3%	Beta	Survey
Dependency on others for CVD	18-44	36.8%	15.2% to 58.5%	Beta	Survey
	45-54	20.0%	11.2% to 28.8%	Beta	Survey
	55-64	17.3%	11.0% to 23.5%	Beta	Survey
	65-74	11.2%	7.0% to 15.4%	Beta	Survey
	75+	16.3%	8.8% to 23.9%	Beta	Survey
Willing to use hem-col DM	18-24	85.4%	75.4% to 95.4%	Beta	Survey
	25-34	83.0%	72.2% to 93.7%	Beta	Survey
	35-44	85.3%	73.4% to 97.2%	Beta	Survey
	45-54	81.5%	72.1% to 91.0%	Beta	Survey
	55-64	82.6%	73.7% to 91.6%	Beta	Survey
	65-74	67.4%	57.8% to 77.0%	Beta	Survey
	75+	54.5%	37.6% to 71.5%	Beta	Survey
Willing to use hem-col CVD	18-44	73.7%	53.9% to 93.5%	Beta	Survey
	45-54	71.3%	61.3% to 81.2%	Beta	Survey
	55-64	74.8%	67.6% to 82.0%	Beta	Survey
	65-74	57.7%	51.1% to 64.3%	Beta	Survey
	75+	48.9%	38.7% to 59.1%	Beta	Survey
Willing to use hem-col CKD	18-24	66.7%	40.0% to 93.3%	Beta	Survey
	25-34	81.5%	66.8% to 96.1%	Beta	Survey
	35-44	82.8%	69.0% to 96.5%	Beta	Survey
	45-54	73.8%	60.5% to 87.1%	Beta	Survey
	55-64	78.3%	66.3% to 90.2%	Beta	Survey

	65-74	50.0%	32.1% to 67.9%	Beta	Survey
	75+	23.1%	0.2% to 46.0%	Beta	Survey
Willing to use hem-col TD	All ages	75.2%	71.2% to 79.1%	Beta	Survey

Table 1b. Model input cost parameters used in the model. GP = general practitioner.

* 95% CI is based on an assumed standard error of 25%, except for the costs of venous sampling.

Parameter	**Category**	**Costs**	**95% CI***	**Distribution**	**Reference**
Costs venous sampling	Hospital	€ 9.04	€8.08 to €9.99	Gamma	[44-48]
	Service phlebotomy center	€ 15.34	€14.09 to €16.60	Gamma	[41-43, 49-55]
	GP's office	€ 18.13	€17.92 to €18.34	Gamma	[41-43, 49-55]
	At home	€ 25.16	€19.36 to €30.96	Gamma	[41-43, 49-55]
Costs Hem-col	Hem-col	€ 20.42	€10.42 to €30.43	Gamma	[77-79]
	Extra tube	€ 1.95	€0.99 to €2.91	Gamma	[77]
Waste processing per tube	Venous	€ 0.01	€0.01 to €0.02	Gamma	[80-84]
	Hem-col	€ 0.01	€0.00 to €0.01	Gamma	[59, 80-84]
Travel costs	Hospital	€ 6.08	€3.10 to €9.07	Gamma	[58]
	Service phlebotomy center	€ 1.02	€0.52 to €1.52	Gamma	[58]
	GP's office	€ 0.45	€0.23 to €0.67	Gamma	[58]
	Hem-col	€ 1.02	€0.52 to €1.52	Gamma	[56, 58, 85]
Production loss costs per hour per male patient	18-24	€ 40.74	€20.78 to €60.70	Gamma	[58]
	25-34	€ 40.74	€20.78 to €60.70	Gamma	[58]
	35-44	€ 40.74	€20.78 to €60.70	Gamma	[58]
	45-54	€ 40.74	€20.78 to €60.70	Gamma	[58]
	55-64	€ 40.74	€20.78 to €60.70	Gamma	[58]
	65-74	€ 4.91	€2.51 to €7.32	Gamma	[57, 58]
	75+	€ 0.73	€0.37 to €1.09	Gamma	[57, 58]
Production loss costs per hour per female patient	18-24	€ 33.97	€17.32 to €50.61	Gamma	[58]
	25-34	€ 33.97	€17.32 to €50.61	Gamma	[58]
	35-44	€ 33.97	€17.32 to €50.61	Gamma	[58]
	45-54	€ 33.97	€17.32 to €50.61	Gamma	[58]
	55-64	€ 33.97	€17.32 to €50.61	Gamma	[58]
	65-74	€ 4.10	€2.09 to €6.10	Gamma	[57, 58]
	75+	€ 0.61	€0.31 to €0.91	Gamma	[57, 58]
Costs informal care giver per hour		€ 15.05	€7.68 to €22.42	Gamma	[58]

Table 1c. Model input parameters used in the model. CI = confidence interval, CKD = chronic kidney disease, CVD = cardiovascular diseases, DM = diabetes mellitus, GP = general practitioner, TD = thyroid diseases.

Parameter	**Category**	**Value**	**95% CI**	**Distribution**	**References**
Amount of phlebotomy appointments per year	DM	4.3	3.6 to 5.0	Gamma	Survey
	CKD	6.2	5.5 to 6.9	Gamma	Survey
	TD	4.5	4.1 to 4.8	Gamma	Survey
Amount of phlebotomy appointments per year for CVD	18-44	4.4	1.9 to 6.8	Gamma	Survey
	45-54	4.4	1.8 to 7.0	Gamma	Survey

	55-64	4.0	3.0 to 5.1	Gamma	Survey
	65-74	3.8	3.0 to 4.6	Gamma	Survey
	75+	6.9	4.0 to 9.8	Gamma	Survey
Time spent at the hospital in hours	DM	2.4	2.3 to 2.5	Gamma	Survey
	CVD	2.3	2.2 to 2.4	Gamma	Survey
	CKD	2.9	2.7 to 3.0	Gamma	Survey
	TD	2.2	2.1 to 2.3	Gamma	Survey
Time spent at the service phlebotomy center in hours	DM	1.7	1.6 to 1.8	Gamma	Survey
	CVD	1.7	1.6 to 1.8	Gamma	Survey
	CKD	1.6	1.4 to 1.8	Gamma	Survey
	TD	1.7	1.6 to 1.8	Gamma	Survey
Time spent at the GP's office in hours	DM	1.7	1.4 to 2.0	Gamma	Survey
	CVD	1.4	1.3 to 1.6	Gamma	Survey
	CKD	1.7	1.4 to 2.1	Gamma	Survey
	TD	1.6	1.3 to 1.8	Gamma	Survey
Time spent at home in hours	DM	1.2	0.5 to 1.9	Gamma	Survey
	CVD	0.9	0.7 to 1.1	Gamma	Survey
	CKD	1.0	0.8 to 1.3	Gamma	Survey
	TD	1.0	0.8 to 1.3	Gamma	Survey
Time spent with hem-col in hours		0.5	0.3 to 0.8	Gamma	[77]