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A protocol for improving the costs and outcomes of assistive reproductive technology fertility care pathways: a study using cost measurement and process mining

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Abstract

Introduction

Value-based healthcare suggests that care outcomes should be evaluated in relation to the costs of delivering that care from the perspective of the provider. However, few providers achieve this because measuring costs is considered complex and elaborate and, further, studies routinely omit cost estimates from 'value' assessments due to lacking data. Consequently, providers are currently unable to steer towards increased value despite financial and performance pressures. This protocol describes the design, methodology and data collection process of a value measurement and process improvement study in fertility care featuring complex care paths with both long and non-linear patient journeys.

Methods and analysis

We employ a sequential study design to calculate total costs of care for patients diagnosed with an ovulation disorder and undergoing infertility treatments. In doing so, we identify process improvement opportunities and cost predictors, and will reflect on the benefits of the information generated for medical leaders. Time-to-pregnancy will be viewed in relation to total costs to determine value. By combining time-driven, activity-based costing (TDABC) with observations and process mining, we trial a method for measuring care costs for large cohorts using electronic health record (EHR) data. To support this method, we create activity and process maps for all relevant treatments: ovulation induction, intra-uterine insemination, in-vitro fertilisation (IVF), in-vitro fertilisation with intracytoplasmic sperm injection (ICSI) and frozen embryo transfer after IVF. Our study design, by showing how different sources of data can be combined to enable cost and outcome measurements, can be of value to researchers and practitioners looking to measure costs for care paths or entire patient journeys in complex care settings.

Ethics and dissemination

This study was approved by the ESHPM Research Ethics Review Committee (ETH122-0355) and the Reinier de Graaf Hospital (2022-032). Results will be disseminated through seminars, conferences, and peer-reviewed publications.

Strengths and limitations of this study

- By integrating TDABC with process mining, this study will lead to the development of a method that enables large-scale cost estimations to be made that allow clinics and hospitals to routinely measure outcomes in relation to costs facilitating value-based healthcare (VBHC).
- Including medical expert input at every stage of the study will positively impact the validity of the results and enable the study to develop an approach that can lead to better care paths.
- By selecting a clinic that operates under World Health Organization guidelines and adheres to European Society of Human Reproduction and Embryology (ESHRE) and Dutch Association for Obstetrics & Gynaecology (NVOG) standards, the research results may be generalisable to other clinics that follow similar guidelines.
- The study is limited by the single-centre design, facilitating more in-depth research, but simultaneously this may impact the generalisability of the results.
- By using retrospective EHR data, the findings may have been influenced by the technological advancements made in the last decade in the field of embryology and fertility care.

Introduction

The healthcare services, policy and management literature emphasises the need to strive for 'value' in healthcare by considering both costs and outcomes at the patient level [1,2]. To improve value, providers must either deliver better outcomes, or the same outcomes more efficiently, and this requires an ability to measure costs per outcome over time [3]. Cost measurement at the patient level provides insight into the sources of costs, guidance for process improvement initiatives [4] and can inform payment policies such as bundled payment initiatives [5]. Such information would be particularly useful to medical leaders who face complex decisions and trade-offs in a world of financial pressures. In a recent consensus report of European university hospitals, 'routinely measuring costs at the patient level' was not achieved by any of the frontrunner hospitals studied [2]. Experts have stressed the need to measure costs and outcomes across full treatment cycles, and to learn how to optimise health outcomes relative to costs [6], but indicate they are currently unable to do so [2].

This difficulty is reflected in the fact that most value-based healthcare (VBHC) studies focus on reimbursement amounts as a proxy for provider costs rather than the actual costs itself, even though reimbursements have been shown to be unrelated to actual costs incurred by the care provider [7]. Reimbursements paid by insurers or patients assume global averages and do not reflect the actual costs incurred by care providers, and hide the variability in costs across patient groups [8]. As such, they do not inform clinics on their own cost variability, or where to target process quality initiatives to improve value [7,9] and should not be used for value assessments and managerial decision making.

However, some recent studies have assessed the 'true costs' of care which they define as total organisational costs incurred by care providers in delivering care [7,10]. To date, cost measurements have predominantly been successful in enabling process improvements in surgical and to an extent in orthopaedic care paths [4,7]. These areas are characterised by relatively short and linear cycles of care compared to more complex care elsewhere characterised by long patient journeys involving chronic or multiple conditions, or requiring additional care such as mental health support [11]. The reality is that little is known about whether benefits can be realised from cost measurement in complex care or medical specialties that feature long care paths with many

decision points, alternative treatment options and extensive time horizons [12]. In such cases, there is little attempt to measure costs and outcomes from the initial consultation or diagnosis through the entire care path. Instead, costs are typically estimated by using charges filed by the hospital, diagnosis-related group prices (DRGs) or length of stay as a proxy of costs [13,14]. However, these are uninformative about the actual costs paid by the care provider and these proxies hide within-treatment variability. Furthermore, proxies such as LOS are irrelevant for treatment without hospital stays. As a result, proxies used in earlier studies are too aggregated for managerial decision-making [12].

Fertility care offers a relevant opportunity to investigate the applicability and merits of cost measurement for value-based processes and quality improvements in complex care. Current knowledge is limited to reimbursement totals or hospital prices, which range from $412-$50,233 (≈ €400-€50,000) per month across treatments, countries and patient characteristics [15–19]. The costs of assistive reproductive technologies (ARTs) are largely unknown, and clinics stand to gain valuable managerial and organisational information that would be relevant for internal decision-making [12], for reimbursement negotiations with insurers [5] and for long-term planning [9,20].

This research protocol describes the study design and methods to be applied in a sequential multi-phase project in which we will measure the costs of delivering fertility care, identify potential process improvement opportunities and evaluate the value of such cost information to medical leaders when making value-based decisions. By describing the study design, analyses, and data collection in detail we hope to aid researchers and practitioners in responding to the call for sounder cost estimates to enable VBHC.

Aims, context and research questions

The broad purpose of this research project is to further the VBHC research agenda through the application of TDABC and process mining in a complex, long and non-linear carepath setting. Our research specifically assists the development of better fertility care paths by enabling clinics to measure and strive for high value care, defined by a short time-to-pregnancy relative to costs. A recent patient-centred fertility care survey confirmed previous research that the biggest contributor to patient satisfaction is time-to-pregnancy [21] which can range from months to years in some cases.

The context of fertility care and ART care pathways

After being referred by their GP, couples or individuals enter a fertility clinic wishing for a healthy pregnancy and birth. During an initial fertility assessment (IFA), diagnostic testing is conducted over a period of four to six weeks after which the clinic provides an assessment, diagnosis, and prognosis. Treatment is cyclical in nature because each treatment cycle must be timed to match the female patient's monthly menstrual cycle. Patients can be switched from one treatment to a more invasive alternative throughout the trajectory, making fertility care an example of complex care. Current guidelines suggest starting with the least invasive treatment option available for a patient's characteristics and indications, which is why it is common for patients to try ovulation induction (OI) or intra-uterine insemination (IUI) before moving on to in-vitro fertilisation (IVF) or IVF with intracytoplasmic sperm injection (IVF-ICSI). It is not unusual for a patient to try IUI for six monthly cycles before switching to IVF. Indications favouring one treatment over another can change as the patient progresses through treatment cycles because each treatment cycle provides additional information to gynaecologists and physicians. This is why per-cycle care costs are considered one of the four key factors in evaluating value in ARTs [22].

Current treatment protocols for fertility care in the Netherlands are defined by the WHO, the Dutch Association for Obstetrics & Gynaecology (NVOG), and the European Society of Human Reproduction and Embryology (ESHRE). As such, the baseline costs we will calculate will be relevant to clinics adhering to similar guidelines. We summarise treatment options and their abbreviations used in this protocol in Figure 1.

figure 1 here

Figure 1 Explanatory diagram of treatment options and treatment transfer possibilities for patients diagnosed with an ovulation disorder.

RQ1: What are the costs of delivering infertility treatment, and where are the opportunities for improved value?

In 2020, the WHO called for safe, effective and affordable fertility treatment worldwide [23]. In the past, live birth rate (LBR) has been the key outcome reported in the literature and by clinics. Recent studies urge looking beyond only the LBR when assessing the outcomes of fertility treatments. Instead, four broad factors should be considered [24,25]: live birth rate; total costs per treatment cycle; incidences of complications in mother or baby as indicators of value; and patient-reported outcome and experience measures.

Per-cycle cost measurement

In seeking to answer this research question, we will conduct a TDABC analysis in line with Kaplan and Anderson [20] as the viability of this approach has been demonstrated in other medical specialties that include chronic conditions [12]. In this approach, the costs of care are calculated using the minutes worked by care professionals as a key factor in distributing the organisational care costs incurred by the care provider across a care path. Organisational costs include salaries paid to staff, rent, infrastructure, disposable materials consumed, medications used or prescribed, and equipment used. The analysis also identifies 'cost predictors', which are variables associated with longer treatment durations and/or higher costs. Identifying cost predictors, or phases during the care path that are particularly costly, helps identify opportunities for cost reduction or quality improvement through care path redesign. Care path redesign involves shifting activities or entire processes to a more effective order, technology, or way of working.

Relevance

Clinics can benefit from cost and cost predictor information because it would enable them to pursue value-based care by informing quality and process improvement initiatives and by aiding managerial decision-making [12,20]. From a theoretical perspective, cost awareness is likely to impact the decisions that medical leaders make because such information moderates the relationship between intent and behaviour [26]. Cost information provided by methods such as TDABC can be expected to aid medical professionals and leaders in their decision-making [20]. For example, revealing that a technological investment could benefit a clinic financially in the long

term by reducing per-cycle care costs may increase the likelihood of medical leaders taking value-based decisions.

In addition, reliable per-cycle cost information can be used to improve reimbursement policies for infertility treatments. This is important for three reasons. First, disproportionate reimbursements create inappropriate financial incentives. For example, IUI is currently considered a 'high earning' fertility treatment in Europe because it typically requires only a few physician hours or resources relative to the reimbursement amount. In other words, IUI treatments tend to have a positive impact on a clinic's bottom line. Conversely, IVF with ICSI is considered a 'bleeder' meaning that ICSI reimbursements are very low relative to the hours and resources involved. In some cases, clinics incur losses on ICSI treatments which are compensated for by the positive margins on IUI or OI treatments. As a consequence, under the current fee-for-service payment model used in the Netherlands, clinics or hospitals benefit from offering additional IUI or OI treatments, and even depend on these for financial stability. However, delivering additional cycles of OI or IUI treatment without achieving a pregnancy would be rated poorly in the context of VBHC. To incentivise value-based decision-making in fertility care, reimbursement amounts need to be adjusted such that the prices paid by insurers match the relative resources and hours involved. Our approach, by providing this information and making the burden on the clinics more transparent, will we hope stimulate payment renegotiations. This is particularly relevant for the future because the population's health is shifting, and the demand for IVF and IVF-ICSI treatment may increase relative to OI and IUI in Europe [27] and globally [28].

RQ2: What costs are associated with the most common patient journeys in Dutch fertility treatment?

Building on Research Question 1, we aim to devise an approach that can calculate the total cost of care across entire patient journeys taking into account the reality that patients can switch between treatment options. The cost analysis proposed under RQ1 will result in total costs of care per treatment cycle of each treatment type. RQ2 builds on this by setting out to determine the value of the care by considering outcomes in relation to costs. A short time-to-pregnancy is considered the key outcome as emphasised by patients [21], alongside process and experience measures

[21,29]. To determine value, we will consider total costs across the patient journey in relation to the time-to-pregnancy.

Patient journeys and associated costs

The costs per patient journey will be estimated using the time equations developed through TDABC with data extracted from the EHR. How we intend to combine the different sources of data is described under the heading 'study design'. Through process mining we expect to refine a model that is similar to Figure 1 but disaggregated into treatment phases. Process mining will reveal how often patients repeat certain treatments, how often patients switch between treatments, and the individual and average durations of each process. This will reveal the most common patient journeys, the costs associated with each path towards its outcome, and the time-to-pregnancy per path.

Setting

This research project is being carried out in conjunction with a fertility clinic in Voorburg, the Netherlands. The Netherlands has mandatory basic health insurance that covers GP services, mental healthcare and specialist care. Basic health insurance covers an unlimited number of cycles of OI or IUI plus three cycles of IVF, with an unlimited number of related frozen embryo transfers per IVF cycle. If a couple wish to undertake a fourth cycle of IVF this will cost €2355 for IVF and €2675 for IVF-ICSI (2022 prices) [30].

Study design and methods

We have determined a sequential study design with four phases as shown in Figure 2. The first three phases involve TDABC with multiple data collection methods. In phase 4, we will apply process mining to address the second research question. This study has been approved by the ESHPM Research Ethics Review Committee (ETH122-0355) and the Reinier de Graaf Hospital (2022-032).

figure 2 here

Figure 2 Sequential diagram indicating phases of data collection and analysis, and the associated deliverables per phase. OI: Ovulation induction, IUI: Intra-uterine insemination, IVF: In-vitro fertilisation, IVF-ICSI: IVF with intracytoplasmic sperm injection, FET: Frozen embryo transfer, IFA: Initial fertility assessment, TDABC: Time-driven activity-based costing

TDABC with observations and medical metro lines (phases 1-3)

The TDABC begins in phase 1 with a seven-step process [12]. This starts by identifying the care paths followed by patients with an ovulation disorder at the focal clinic (step 1). Care paths are defined with clear start and end points, and are further broken down into individual activities and processes (step 2). An activity is a single step in delivering care, and processes consist of several activities. These care paths will be visualised using the medical metro line visualisation tool created by *Panton designers for healthcare* for use with MS Visio. This template was created by Panton with service design experts to aid care path visualisation and shared decision-making. An important element of this mapping process is that it is iterative: as new information is shared by experts (e.g. gynaecologists, physicians, lab analysts), the activity maps will be amended until they are complete. The activity and process maps will cover all treatments offered by the clinic for patients with an ovulation disorder: OI, IUI, IVF, IVF-ICSI, FET and the IFA prior to treatment. To test the feasibility and validate this approach, we initially created one metro line using this method (Figure 3).

figure 3 here

Figure 3 Medical metro line of the initial fertility assessment prior to treatment. Patients move from left to right along the solid line. Solid circles: activities for which the patient is present, white and outlined circles: activities for which the patient is not present, circles with smaller circle in centre: consultations with patient, diamonds: decision points, dotted line: activities that may be necessary but do not apply to all patients, SST: Sperm survival test, FSH: Follicle stimulating hormone, AMH: Anti mullerian hormone, BMI: body mass index

In phase 2 we will determine the time required per activity and process identified in phase 1. In applying TDABC, one has to estimate the time (in minutes) for each activity. This involves using protocols, expert input and observations in a similar approach to Keel et al. [12]. For each metro line created in phase 1, a time equation is constructed that calculates the total process time and incorporates relevant variables that increase or decrease the time required (step 4). For activities for which treatment protocols and scheduling systems do not specify a set time, or for which care professionals cannot estimate an accurate time because the time can vary, we intend to time activities with repeated observations to determine a realistic estimate. Activities that exhibit considerable variation in duration will be observed more frequently to identify variables associated with this variation (to establish cost predictors to be incorporated in the time equations). During the observations, the researcher (ML) will ask the staff involved open-ended questions about the sources of variations, possible cost predictors and any suggestions for improvements. Personnel involved will be asked informed consent and all observational data will be anonymized.

Costs will be obtained from the clinic in the form of the clinic's total annual cost data for 2021 (step 5). Per-minute cost rates (CCRs) are calculated by pooling cost data per process, and by dividing the pooled costs by the practical capacity of the medical professional providing the care (step 6). One can anticipate more than one CCR because care paths have very different

resource requirements, thus requiring separate combinations of resource costs [20]. For example, OI does not involve the lab in any way, whereas a significant portion of the care in the IVF-ICSI care path is completed inside the lab.

In phase 3 we will calculate the costs per cycle of care. We expect to identify between 15 and 50 activities and 1 to 10 processes for each of the six care paths identified. To complete the cost calculations for such a large number of activities and processes, we have programmed a formulaic model in MS Excel using the following structure (Table 1).

Process (P)	Activity (A)	CCR1 (C1)	CCR2 (C2)	CCR*n* (C*n*)	Direct fixed costs (d)	Costs
1	1	minutes	minutes	minutes	€d	$Costs_{A1}$= $minutes_{Aa,C1}$ x C1+…+$minutes_{An,Cn}$ x C*n* + *d*
	2	minutes	minutes	minutes	€d	$Costs_{A2}$= $minutes_{Aa,C1}$ x C1+…+$minutes_{An,Cn}$ x C*n* + *d*
	n	minutes	minutes	minutes	€d	$Costs_{An}$= $minutes_{Aa,C1}$ x C1+…+$minutes_{An,Cn}$ x C*n* + *d*
n	*n*			$minutes_{An,Pn,Cn}$	$€d_{An,Pn}$	*Total costs per process:* $Costs_{P1} = Costs_{A1} +…+ Costs_{An}$ *Total costs per care path:* $Costs_{P1} +…+ Costs_{Pn}$

Table 1 Structure of the TDABC calculation programmed in MS Excel. Each row is one activity, and a process is made up of *n* activities. Each CCR identified fills one column. The number of minutes an activity takes is placed in the appropriate cell. The formula in the costs column multiplies the minutes by the given CCR to give the costs per activity. CCR: Cost capacity rate

In the cost column, the total costs per process are calculated by multiplying the minutes needed for an activity within the process by the relevant CCR and totalling these across activities. Direct fixed costs such as disposable items are allocated directly to a process if they do not vary with time (+*d*). For example, a single catheter is used with each IUI insemination: even if this procedure takes longer than usual, still only a single catheter is used. Total costs of care for a care path can then be calculated by totalling the costs per process as shown in the rightmost column (step 7).

Process mining (phase 4)

In phase 4, process mining will be used to analyse a retrospective cohort of patients' EHRs to reveal real patient pathways. These will be identified by extracting the relevant process start and end points and cost predictor values from the EHR alongside patient characteristics relevant to fertility care (BMI category, age category, primary vs. secondary infertility) [31]. For example, we define the IFA to start on the date of the first onsite consultation with a gynaecologist and the end

point as the date of the final IFA consultation during which the assessment results are communicated and a treatment plan discussed with the patient. The process duration is the time elapsed between these two dates. By using process mining in combination with the time equations established earlier, we can see how patients flow through the process map created in phase 1 step 2. The process mining will be conducted in line with previous research [32] in Fluxicon Disco® using the fuzzy miner algorithm. To ensure the data are unidentifiable, they will be extracted by a data scientist and supplied to us without identifiers. A detailed template of the data required will be supplied after completing phase 3 (see section 'Data' below). To validate the data gathered, and the results gained, feedback from medical professionals will be sought during each phase.

Data

Figure 4 summarises the study design in terms of the flow of raw data through to the research results.

figure 4 here

Figure 4 Explanatory sequential diagram showing the flow of data during all four phases. Labelled arrows are referred to in the text. Bold outlined rectangle: data source, rounded rectangles: analyses performed on data, solid arrows: data flow, dotted arrows: data validation, CCR; Cost capacity rate, EHR: Electronic Health Record, OI: Ovulation induction, IUI: Intra-uterine insemination, IVF: In-vitro fertilisation, IVF-ICSI: IVF with intracytoplasmic sperm injection, FET: Frozen embryo transfer, IFA: Initial fertility assessment, TDABC: Time-driven activity-based costing, VBHC: Value-based healthcare.

The treatment protocols form the basis of the medical metro lines (A). The medical metro lines will be established iteratively, with rounds of feedback from experts (B) and adjustments. The metro lines should reflect the activities and processes involved in delivering care (C). Both the metro lines and the lists of activities and processes will be validated through observations (E&F) although an initial list of anticipated activities has been prepared to enable observations to be planned (G) since these involve the timing of activities defined for the TDABC (H).

The observations will also be used to elicit staff members' opinions on processes (I&J). To complete the TDABC, cost data will be combined with the observational data and the medical metro lines. The cost data are used to calculate CCRs (L) and non-variable direct materials costs (K) [10]. Through the TDABC analysis, cost predictors will be established for each care path once the time equations are specified. The time equations identify the total minutes required for a process and will include variables that impact the time required in the form of multipliers or if-then statements [20]. This will inform the data requirements for the process mining analysis (M&N). The EHR data retrieved will consist of time stamps of key activities that define the start and end points of processes in each of the care paths identified in the medical metro lines (C), as well as the variables identified in the TDABC analysis (P). The process mining will enable the time equations to be completed through the EHR inputs on patient journeys (O).

Research Question 1 will be answered by the TDABC analysis (Q), and Research Question 2 through the process mining analysis (R) which is dependent on the TDABC analysis. An additional outcome is that the cost and outcome data will be used at the focal clinic in a VBHC dashboard.

Patient and public involvement

There is no *direct* patient or public involvement in this study. The research questions and some of the outcome measures have been informed by patient preferences reported in recent publications. The clinic's staff will be involved in the study through observations and providing expert input. The results of the research will be disseminated to the clinic's staff throughout the research phases, and to the public through conference presentations and publications. The data gathered and the medical metro lines created will inform the clinic's VBHC dashboard. Once published, the results will be used in the education programmes of bachelor and master students.

Discussion

Our aim is to contribute the VBHC literature by demonstrating how TDABC and process mining can be combined to enable realistic cost measurement on a large scale, an aspect which practitioners currently consider both urgent and a major challenge [2]. Further, by trialling this method in a complex care context we will contribute to the currently sparse literature on cost

measurement and process improvements in complex care with long time horizons and non-linear care paths [12].

We further aim to contribute to the patient-centred fertility care literature [21,29,33] by introducing TDABC to the field and by reporting real patient journey costs and outcomes (in a baseline value assessment) that can serve as a benchmark for other clinics. Other clinics will be able to input their annual costs into the model while assuming the same time-based equations. The time equations can also be adjusted as technologies change or processes modified, for example by introducing AI embryo selection [34] or vitrification [35]. Through this research, we hope to enable internal, longitudinal benchmarking as well as across-clinic benchmarking. In addition, we believe that the outcomes of this research could aid clinics in predicting future costs as populations age and change, and in their organisational decision-making [12]. This approach could contribute to improve quality and efficacy to keep healthcare affordable in the future decades.

Patients have repeatedly indicated that expectation management and information sharing are important aspects of patient satisfaction [21,29,36,37]. By incorporating patient journey information in a value-based dashboard, we aim to provide gynaecologists with the tools to better discuss likelihoods and time-to-pregnancy with patients. We see the medical metro lines created in this project as a tool with which clinics can visually communicate and redesign care paths.

This research has several methodological limitations. First, the single-centre focus of this study will potentially limit the generalisability of the results because all the data are gathered from one clinic. Nevertheless, we consider this single-centre design realistic since we are covering several care paths and anticipate a high volume of manual data collection (observations). To partially mitigate this shortcoming, we have compared the treatment protocols followed by the clinic concerned with the guidelines and standards published by the NVOG [38,39] and ESHRE and did not find any discrepancies. Furthermore, our findings are likely to be applicable in clinics that work according to WHO standards. To further improve the generalisability and benchmarking potential, we aim to measure the duration of activities that involve alternative technologies or ways of working. For example, multiple methods for freezing and thawing embryos will be observed and measured (vitrification and cryopreservation).

Second, the process mining will have limitations related to incomplete cases [40]. For patients that have started but not yet finished treatment, an outcome state cannot be defined. We will address this limitation by restricting the sample to cases with known outcome states in robustness checks, which limits the size of the cohort. An associated issue is that, by using retrospective data (especially if only completed cases), the study will be impacted by technological advancements in fertility care, with earlier cohorts treated under different technological conditions than those observed during our observations.

Third, TDABC studies can suffer from subjectivity because the cost calculations are heavily dependent on the time measures used, and these are typically estimated based on expert interviews. To address this limitation and improve the generalisability of our results given different staff experience levels, daily circumstances and patient characteristics, we will use time measurements during repeated observations to reach an average time per activity and process. This will also enable us to identify cost predictors associated with activities with variable durations as described previously.

Ethics and dissemination

This study was approved by the ESHPM Research Ethics Review Committee (ETH122-0355) and the Reinier de Graaf Hospital (2022-032). We will acquire informed consent from every participant observed during the data collection. We intend to publish the research in peer-reviewed journals and present it at relevant conferences and seminars.

Contributors

ML, HvE and KA conceptualised the project described in this proposal. ML drafted this protocol with input from HvE and KA. CH obtained funding. EvS and CH provided feedback on the proposed study. EvS and CH provided medical and regulatory input on this protocol.

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Competing interests

None declared.

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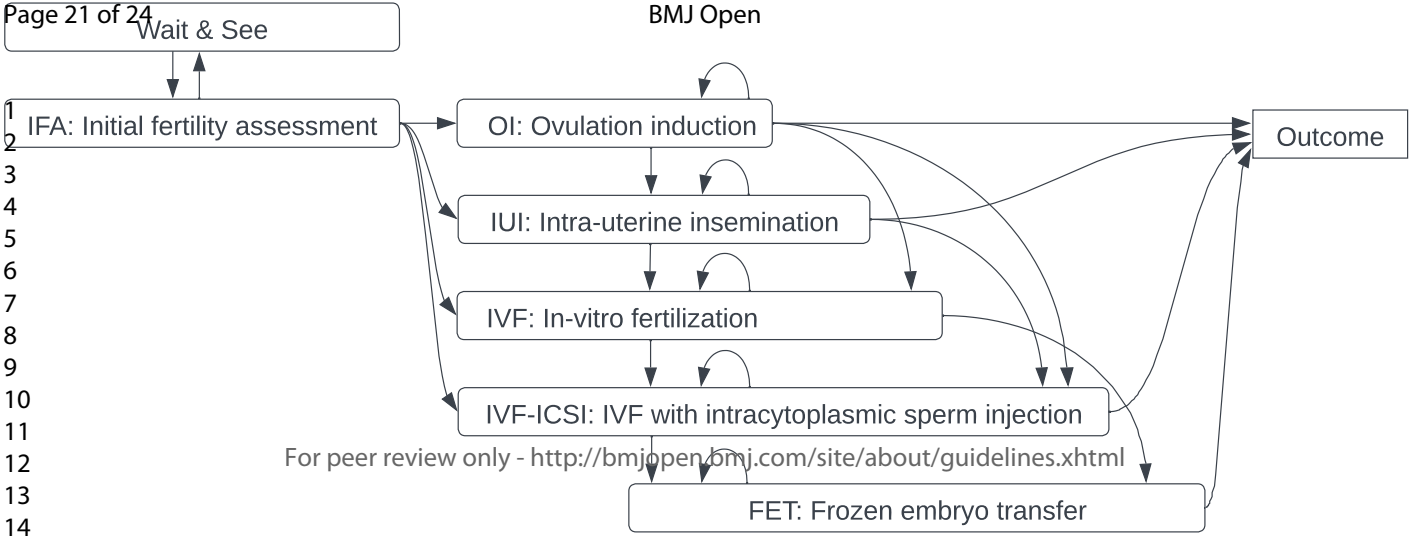
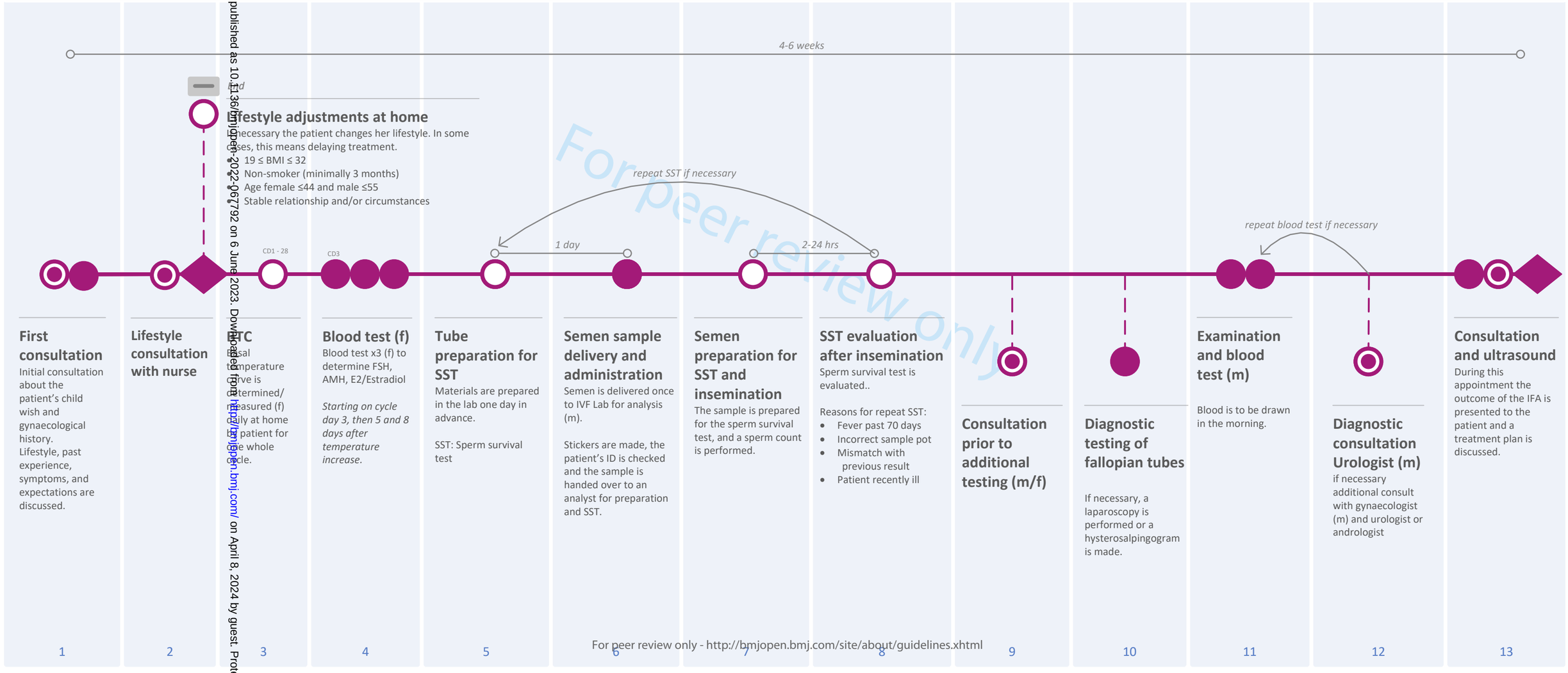


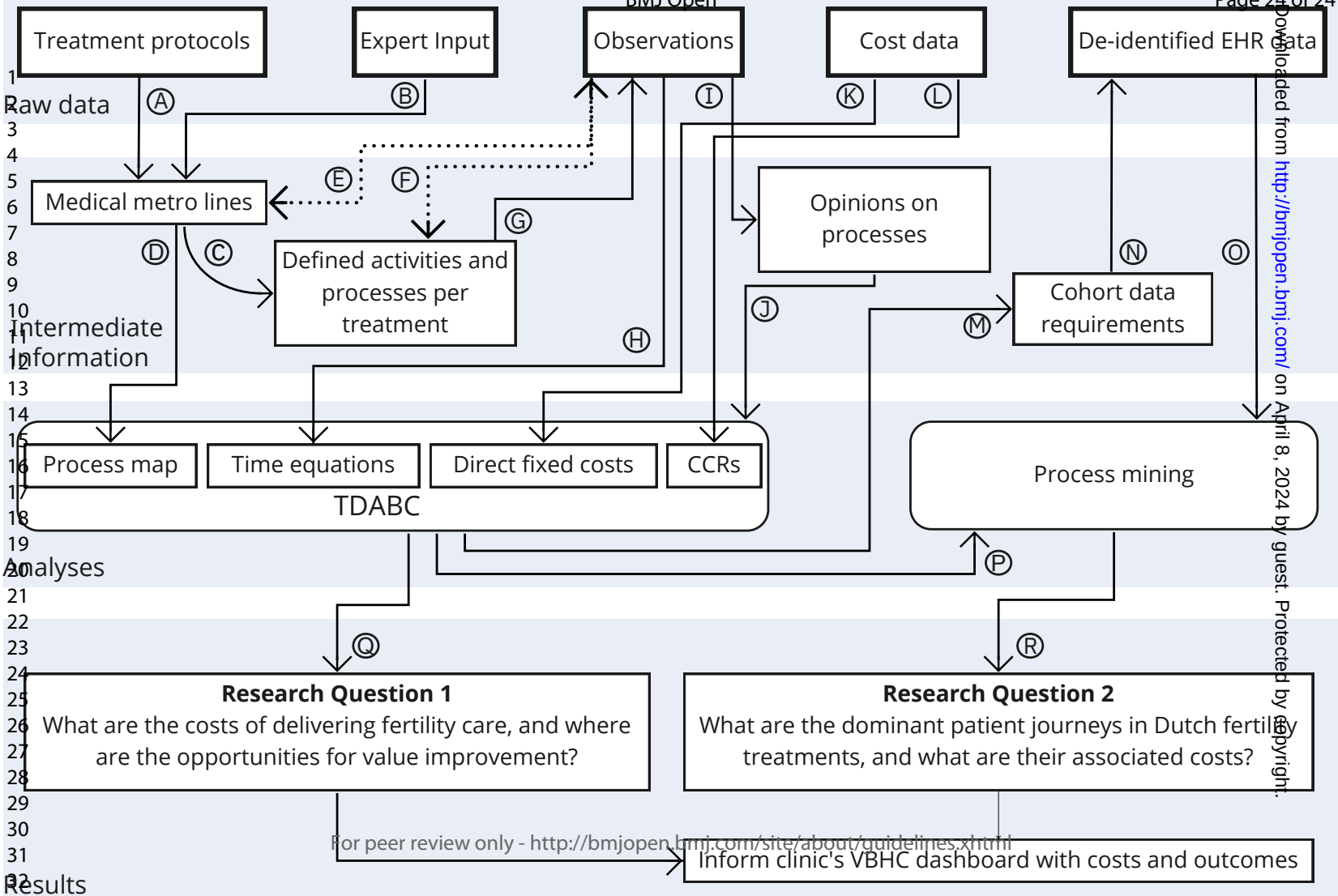
	Phase 1	Phase 2	Phase 3	Phase 4
Data collection and/or analysis	Document analysis (protocols)	Document analysis (financial), observations with time measures, build model	Cost calculation and internal communication of results, informal interviews	Process mining of EHR data, and modelling costs using cohort
Method	TDABC	TDABC	TDABC	Process mining
Deliverables	Medical metro line and process maps for OI, IUI, IVF, IVF-ICSI, FET and IFA	Time equations, and determination of EHR data requirements	Per-cycle costs for OI, IUI, IVF, FET, and IFA	Patient journey outcomes and costs from initial consultation to pregnancy

Initial Fertility Assessment

From initial consultation to diagnosis and treatment plan

Initial Fertility Assessment (IFA)





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A protocol for improving the costs and outcomes of assistive reproductive technology fertility care pathways: a study using cost measurement and process mining

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A protocol for improving the costs and outcomes of assistive reproductive technology fertility care pathways: a study using cost measurement and process mining

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Abstract

Introduction

Value-based healthcare suggests that care outcomes should be evaluated in relation to the costs of delivering that care from the perspective of the provider. However, few providers achieve this because measuring costs is considered complex and elaborate and, further, studies routinely omit cost estimates from 'value' assessments due to lacking data. Consequently, providers are currently unable to steer towards increased value despite financial and performance pressures. This protocol describes the design, methodology and data collection process of a value measurement and process improvement study in fertility care featuring complex care paths with both long and non-linear patient journeys.

Methods and analysis

We employ a sequential study design to calculate total costs of care for patients undergoing non-surgical fertility care treatments. In doing so, we identify process improvement opportunities and cost predictors, and will reflect on the benefits of the information generated for medical leaders. Time-to-pregnancy will be viewed in relation to total costs to determine value. By combining time-driven, activity-based costing (TDABC) with observations and process mining, we trial a method for measuring care costs for large cohorts using electronic health record (EHR) data. To support this method, we create activity and process maps for all relevant treatments: ovulation induction (OI), intra-uterine insemination, in-vitro fertilisation (IVF), in-vitro fertilisation with intracytoplasmic sperm injection (ICSI) and frozen embryo transfer after IVF. Our study design, by showing how different sources of data can be combined to enable cost and outcome measurements, can be of value to researchers and practitioners looking to measure costs for care paths or entire patient journeys in complex care settings.

Ethics and dissemination

This study was approved by the ESHPM Research Ethics Review Committee (ETH122-0355) and the Reinier de Graaf Hospital (2022-032). Results will be disseminated through seminars, conferences, and peer-reviewed publications.

Strengths and limitations of this study

- This method accounts for patient level cost variation by incorporating time equations and cost predictors.
- This method enables large-scale patient level cost estimation in complex care by combining time-driven activity-based costing with process mining.
- Including medical expert input at every stage of the study design enables care path comparison and redesign.
- The study design is limited by a single-centre set-up, facilitating more in-depth research, but simultaneously this may impact the generalisability of the results gained with such methods.
- By using retrospective electronic health record data, the method may be influenced by the technological advancements or treatment protocol adjustments over time.

Introduction

The healthcare services, policy and management literature emphasises the need to strive for 'value' in healthcare by considering both costs and outcomes at the patient level [1,2]. To improve value, providers must either deliver better outcomes, or the same outcomes more efficiently, and this requires an ability to measure costs per outcome over time [3]. Cost measurement at the patient level provides insight into the sources of costs, guidance for process improvement initiatives [4] and can inform payment policies such as bundled payment initiatives [5]. Such information would be particularly useful to medical leaders who face complex decisions and trade-offs in a world of financial pressures. In a recent consensus report of European university hospitals, 'routinely measuring costs at the patient level' was not achieved by any of the frontrunner hospitals studied [2]. Experts have stressed the need to measure costs and outcomes across full treatment cycles, and to learn how to optimise health outcomes relative to costs [6], but indicate they are currently unable to do so [2].

This difficulty is reflected in the fact that most value-based healthcare (VBHC) studies focus on reimbursement amounts as a proxy for provider costs rather than the actual costs itself, even though reimbursements have been shown to be unrelated to actual costs incurred by the care provider [7]. Reimbursements paid by insurers or patients assume global averages and do not reflect the actual costs incurred by care providers, and hide the variability in costs across patient groups [8]. As such, they do not inform clinics on their own cost variability, or where to target process quality initiatives to improve value [7,9,10] and should not be used for value assessments and managerial decision making.

However, some recent studies have assessed the 'true costs' of care which they define as total organisational costs incurred by care providers in delivering care [7,11]. To date, cost measurements have predominantly been successful in enabling process improvements in surgical and to an extent in orthopaedic care paths [4,7]. These areas are characterised by relatively short and linear cycles of care compared to more complex care elsewhere characterised by long patient journeys involving chronic or multiple conditions or requiring additional care such as mental health support [12]. The reality is that little is known about whether benefits can be realised from cost measurement in complex care or medical specialties that feature long care paths with many

decision points, alternative treatment options and extensive time horizons [13]. In such cases, there is little attempt to measure costs and outcomes from the initial consultation or diagnosis through the entire care path. Instead, costs are typically estimated by using charges filed by the hospital, diagnosis-related group prices (DRGs) or length of stay as a proxy of costs [14,15]. In this case, length of stay refers to the duration for which patients were admitted to a ward or department with overnight stays. However, these are uninformative about the actual costs paid by the care provider and these proxies hide within-treatment variability. Furthermore, proxies such as length of stay are irrelevant for treatments without hospital stays (i.e., outpatient treatments). As a result, proxies used in earlier studies are too aggregated for managerial decision-making [13].

Fertility care offers a relevant opportunity to investigate the applicability and merits of cost measurement for value-based processes and quality improvements in complex care. Current knowledge is limited to reimbursement totals or hospital prices, which range from $412-$50,233 (≈ €400-€50,000) per month across treatments, countries and patient characteristics [16–20]. The costs of assistive reproductive technologies (ARTs) are largely unknown, and clinics stand to gain valuable managerial and organisational information that would be relevant for internal decision-making [10, 13], for reimbursement negotiations with insurers [5] and for long-term planning [9,21].

This research protocol describes the study design and methods to be applied in a sequential multi-phase project in which we will measure the costs of delivering fertility care, identify potential process improvement opportunities and evaluate the value of such cost information to medical leaders when making value-based decisions. By describing the study design, analyses, and data collection in detail we hope to aid researchers and practitioners in responding to the call for sounder cost estimates to enable VBHC.

Aims, context and research questions

The broad purpose of this research project is to further the value-based care research agenda through the application of TDABC and process mining in a complex, long and non-linear care path setting. Our research specifically assists the development of better fertility care paths by enabling clinics to measure and strive for high value care, defined by a short time-to-pregnancy relative to costs. A recent patient-centred fertility care survey confirmed previous research that the biggest

contributor to patient satisfaction is time-to-pregnancy [22] which can range from months to years in some cases.

The context of fertility care and ART care pathways

After being referred by their general practitioner, couples or individuals enter a fertility clinic wishing for a healthy pregnancy and birth. During an initial fertility assessment (IFA), diagnostic testing is conducted over a period of four to six weeks after which the clinic provides an assessment, diagnosis, and prognosis. Treatment is cyclical in nature because each treatment cycle must be timed to match the female patient's monthly menstrual cycle. Patients can be switched from one treatment to a more invasive alternative throughout the trajectory, making fertility care an example of complex care. Current guidelines suggest starting with the least invasive treatment option available for a patient's characteristics and indications, which is why it is common for patients to try ovulation induction (OI) or intra-uterine insemination (IUI) before moving on to in-vitro fertilisation (IVF) or IVF with intracytoplasmic sperm injection (IVF-ICSI). It is not unusual for a patient to try IUI for six monthly cycles before switching to IVF. Indications favouring one treatment over another can change as the patient progresses through treatment cycles because each treatment cycle provides additional information to gynaecologists and physicians. This is why per-cycle care costs are considered one of the four key factors in evaluating value in ARTs [23].

Current treatment protocols for fertility care in the Netherlands are defined by the WHO, the Dutch Association for Obstetrics & Gynaecology (NVOG), and the European Society of Human Reproduction and Embryology (ESHRE). As such, the baseline costs we will calculate will be relevant to clinics adhering to similar guidelines. We summarise treatment options and their abbreviations used in this protocol in Figure 1.

figure 1 here

Figure 1 Explanatory diagram of non-surgical treatment options and treatment transfer possibilities for patients diagnosed with subfertility.

RQ1: What are the costs of delivering subfertility treatments, and where are the opportunities for improved value?

In 2020, the WHO called for safe, effective and affordable fertility treatment worldwide [24]. In the past, live birth rate (LBR) has been the key outcome reported in the literature and by clinics. Recent studies urge looking beyond only the LBR when assessing the outcomes of fertility treatments. Instead, four broad factors should be considered [25,26]: live birth rate; total costs per treatment cycle; incidences of complications in mother or baby as indicators of value; and patient-reported outcome and experience measures.

Per-cycle cost measurement

In seeking to answer this research question, we will conduct a TDABC analysis in line with Kaplan and Anderson [21] as the viability of this approach has been demonstrated in other medical specialties that include chronic conditions [13]. In this approach, the costs of care are calculated using the minutes worked by care professionals as a key factor in distributing the organisational care costs incurred by the care provider across a care path. Organisational costs include salaries paid to staff, rent, infrastructure, disposable materials consumed, medications used or prescribed, and equipment used. The analysis also identifies 'cost predictors', which are variables associated with longer treatment durations and/or higher costs. Identifying cost predictors, or phases during the care path that are particularly costly, helps identify opportunities for cost reduction or quality improvement through care path redesign. Care path redesign involves shifting activities or entire processes to a more effective order, technology, or way of working.

Relevance

Clinics can benefit from cost and cost predictor information because it would enable them to pursue value-based care by informing quality and process improvement initiatives and by aiding managerial decision-making [13,21]. From a theoretical perspective, cost awareness is likely to impact the decisions that medical leaders make because such information moderates the relationship between intent and behaviour [27]. Cost information provided by methods such as TDABC can be expected to aid medical professionals and leaders in their decision-making [21]. For example, revealing that a technological investment could benefit a clinic financially in the long

term by reducing per-cycle care costs may increase the likelihood of medical leaders taking value-based decisions.

In addition, reliable per-cycle cost information can be used to improve reimbursement policies for infertility treatments. This is important for three reasons. First, disproportionate reimbursements create inappropriate financial incentives. For example, IUI is currently considered a 'high earning' fertility treatment in Europe because it typically requires only a few physician hours or resources relative to the reimbursement amount. In other words, IUI treatments tend to have a positive impact on a clinic's bottom line. Conversely, IVF with ICSI is considered a 'bleeder' meaning that ICSI reimbursements are very low relative to the hours and resources involved. In some cases, clinics incur losses on ICSI treatments which are compensated for by the positive margins on IUI or OI treatments. As a consequence, under the current fee-for-service payment model used in the Netherlands, clinics or hospitals benefit from offering additional IUI or OI treatments, and even depend on these for financial stability. However, delivering additional cycles of OI or IUI treatment without achieving a pregnancy would be rated poorly in the context of VBHC. To incentivise value-based decision-making in fertility care, reimbursement amounts need to be adjusted such that the prices paid by insurers match the relative resources and hours involved. Our approach, by providing this information and making the burden on the clinics more transparent, will we hope stimulate payment renegotiations. This is particularly relevant for the future because the population's health is shifting, and the demand for IVF and IVF-ICSI treatment may increase relative to OI and IUI in Europe [28] and globally [29].

RQ2: What costs are associated with the most common patient journeys in Dutch fertility treatments?

Building on Research Question 1, we aim to devise an approach that can calculate the total cost of care across entire patient journeys taking into account the reality that patients can switch between treatment options. The cost analysis proposed under RQ1 will result in total costs of care per treatment cycle of each treatment type. RQ2 builds on this by setting out to determine the value of the care by considering outcomes in relation to costs. A short time-to-pregnancy is considered the key outcome as emphasised by patients [22], alongside process and experience measures

[22,30]. To determine value, we will consider total costs across the patient journey in relation to the time-to-pregnancy.

Patient journeys and associated costs

The costs per patient journey will be estimated using the time equations developed through TDABC with data extracted from the electronic health record (EHR). How we intend to combine the different sources of data is described under the heading 'study design'. Through process mining we expect to refine a model that is similar to Figure 1 but disaggregated into treatment phases. Process mining will reveal how often patients repeat certain treatments, how often patients switch between treatments, and the individual and average durations of each process. This will reveal the most common patient journeys, the costs associated with each path towards its outcome, and the time-to-pregnancy per path.

Setting

This research project is being carried out in conjunction with a fertility clinic in Voorburg, the Netherlands. The Netherlands has mandatory basic health insurance that covers GP services, mental healthcare and specialist care. Basic health insurance covers an unlimited number of cycles of OI or IUI plus three cycles of IVF, with an unlimited number of related frozen embryo transfers sett €2675 for IVF-ICSI (2022 prices) [31].

Study design and methods

We have determined a sequential study design with four phases as shown in Figure 2. The first three phases involve TDABC with multiple data collection methods. In phase 4, we will apply process mining to address the second research question. This study has been approved by the ESHPM Research Ethics Review Committee (ETH122-0355) and the Reinier de Graaf Hospital (2022-032). To limit the research burden associated with the manual collection of activity durations using a stopwatch in phase 2, we focus on patients receiving non-surgical treatment options, as also shown in figure 1.

figure 2 here

Figure 2 Sequential diagram indicating phases of data collection and analysis, and the associated deliverables per phase. OI: Ovulation induction, IUI: Intra-uterine insemination, IVF: In-vitro fertilisation, IVF-ICSI: IVF with intracytoplasmic sperm injection, FET: Frozen embryo transfer, IFA: Initial fertility assessment, TDABC: Time-driven activity-based costing

TDABC with observations and medical metro lines (phases 1-3)

The TDABC begins in phase 1 with a seven-step process [13]. This starts by identifying the care paths followed by patients with subfertility at the focal clinic (step 1). Care paths are defined with clear start and end points, and are further broken down into individual activities and processes (step 2). An activity is a single step in delivering care, and processes consist of several activities. These care paths will be visualised using the medical metro line visualisation tool created by *Panton designers for healthcare* for use with MS Visio. This template was created by Panton with service design experts to aid care path visualisation and shared decision-making. An important element of this mapping process is that it is iterative: as new information is shared by experts (e.g. gynaecologists, physicians, lab analysts), the activity maps will be amended until they are complete. The activity and process maps will cover all treatments offered by the clinic for patients with subfertility diagnoses: OI, IUI, IVF, IVF-ICSI, FET and the IFA prior to treatment. To test the feasibility and validate this approach, we initially created one metro line using this method (Figure 3).

figure 3 here

Figure 3 Medical metro line of the initial fertility assessment prior to treatment. Patients move from left to right along the solid line. Solid circles: activities for which the patient is present, white and outlined circles: activities for which the patient is not present, circles with smaller circle in centre: consultations with patient, diamonds: decision points, dotted line: activities that may be necessary but do not apply to all patients, SST: Sperm survival test, FSH: Follicle stimulating hormone, AMH: Anti mullerian hormone, BMI: body mass index

In phase 2 we will determine the time required per activity and process identified in phase 1. In applying TDABC, one has to estimate the time (in minutes) for each activity. This involves using protocols, expert input and observations in a similar approach to Keel et al. [13]. For each metro line created in phase 1, a time equation is constructed that calculates the total process time and incorporates relevant variables that increase or decrease the time required (step 4). For activities for which treatment protocols and scheduling systems do not specify a set time, or for which care professionals cannot estimate an accurate time because the time can vary, we intend to time activities with repeated observations to determine a realistic estimate. Activities that exhibit considerable variation in duration will be observed more frequently to identify variables associated with this variation (to establish cost predictors to be incorporated in the time equations). During the observations, the researcher (ML) will ask the staff involved open-ended questions about the sources of variations, possible cost predictors and any suggestions for improvements. Personnel involved will be asked informed consent and all observational data will be anonymized.

Costs will be obtained from the clinic in the form of the clinic's total annual cost data for 2021 (step 5). Per-minute cost rates (CCRs) are calculated by pooling cost data per process, and by dividing the pooled costs by the practical capacity of the medical professional providing the care (step 6). One can anticipate more than one CCR because care paths have very different

resource requirements, thus requiring separate combinations of resource costs [21]. For example, OI does not involve the lab in any way, whereas a significant portion of the care in the IVF-ICSI care path is completed inside the lab.

In phase 3 we will calculate the costs per cycle of care. We expect to identify between 15 and 50 activities and 1 to 10 processes for each of the six care paths identified. To complete the cost calculations for such a large number of activities and processes, we have programmed a formulaic model in MS Excel using the following structure (Table 1).

Process (P)	Activity (A)	CCR1 (C1)	CCR2 (C2)	CCR*n* (C*n*)	Direct fixed costs (d)	Costs
1	1	minutes	minutes	minutes	€d	$Costs_{A1}$= $minutes_{A1,C1}$ x C1+…+$minutes_{An,Cn}$ x C*n* + *d*
	2	minutes	minutes	minutes	€d	$Costs_{A2}$= $minutes_{A2,C1}$ x C1+…+$minutes_{An,Cn}$ x C*n* + *d*
	n	minutes	minutes	minutes	€d	$Costs_{An}$= $minutes_{An,C1}$ x C1+…+$minutes_{An,Cn}$ x C*n* + *d*
n	*n*			$minutes_{An,Pn,Cn}$	$€d_{An,Pn}$	*Total costs per process:* $Costs_{P1} = Costs_{A1} + ... + Costs_{An}$ *Total costs per care path:* $Costs_{P1} + ... + Costs_{Pn}$

Table 1 Structure of the TDABC calculation programmed in MS Excel. Each row is one activity, and a process is made up of *n* activities. Each CCR identified fills one column. The number of minutes an activity takes is placed in the appropriate cell. The formula in the 'costs' column multiplies the minutes by the given CCR to give the costs per activity. CCR: Cost capacity rate

In the cost column, the total costs per process are calculated by multiplying the minutes needed for an activity within the process by the relevant CCR and totalling these across activities. Direct fixed costs such as disposable items are allocated directly to a process if they do not vary with time (+*d*). For example, a single catheter is used with each IUI insemination: even if this procedure takes longer than usual, still only a single catheter is used. Total costs of care for a care path can then be calculated by totalling the costs per process as shown in the rightmost column (step 7).

Process mining (phase 4)

In phase 4, process mining will be used to analyse a retrospective cohort of patients' electronic health records (EHRs) to reveal real patient pathways. These will be identified by extracting the relevant process start and end points and cost predictor values from the EHRs alongside patient characteristics relevant to fertility care (BMI category, age category, primary vs. secondary infertility) [32]. For example, we define the IFA to start on the date of the first onsite

consultation with a gynaecologist and the end point as the date of the final IFA consultation during which the assessment results are communicated and a treatment plan discussed with the patient. The process duration is the time elapsed between these two dates. By using process mining in combination with the time equations established earlier, we can see how patients flow through the process map created in phase 1 step 2. The process mining will be conducted in line with previous research [33] in Fluxicon Disco® and R using the fuzzy miner algorithm. To ensure the data are unidentifiable, they will be extracted by a data scientist and supplied to us without identifiers. Additionally, data will be categorical where possible. A detailed template of the data required will be supplied after completing phase 3 (see section 'Data' below). To validate the data gathered, and the results gained, feedback from medical professionals will be sought during each phase.

Data

Figure 4 summarises the study design in terms of the flow of raw data through to the research results.

figure 4 here

Figure 4 Explanatory sequential diagram showing the flow of data during all four phases. Labelled arrows are referred to in the text. Bold outlined rectangle: data source, rounded rectangles: analyses performed on data, solid arrows: data flow, dotted arrows: data validation, CCR; Cost capacity rate, EHR: Electronic Health Record, OI: Ovulation induction, IUI: Intra-uterine insemination, IVF: In-vitro fertilisation, IVF-ICSI: IVF with intracytoplasmic sperm injection, FET: Frozen embryo transfer, IFA: Initial fertility assessment, TDABC: Time-driven activity-based costing, VBHC: Value-based healthcare.

The treatment protocols form the basis of the medical metro lines (A). The medical metro lines will be established iteratively, with rounds of feedback from experts (B) and adjustments. The metro lines should reflect the activities and processes involved in delivering care (C). Both the metro lines and the lists of activities and processes will be validated through observations (E&F) although an initial list of anticipated activities has been prepared to enable observations to be planned (G) since these involve the timing of activities defined for the TDABC (H).

The observations will also be used to elicit staff members' opinions on processes (I&J). To complete the TDABC, cost data will be combined with the observational data and the medical metro lines. The cost data are used to calculate CCRs (L) and non-variable direct materials costs (K) [11]. Through the TDABC analysis, cost predictors will be established for each care path once the time equations are specified. The time equations identify the total minutes required for a process and will include variables that impact the time required in the form of multipliers or if-then statements [21]. This will inform the data requirements for the process mining analysis (M&N). The EHR data retrieved will consist of time stamps of key activities that define the start and end points of processes in each of the care paths identified in the medical metro lines (C), as well as the variables identified in the TDABC analysis (P). The process mining will enable the time equations to be completed through the EHR inputs on patient journeys (O).

Research Question 1 will be answered by the TDABC analysis (Q), and Research Question 2 through the process mining analysis (R) which is dependent on the TDABC analysis. An additional outcome is that the cost and outcome data will be used at the focal clinic in a VBHC dashboard. The study project, including design and coordination, is scheduled to run from 01/01/2021 to 01/11/2024. Data collection is ongoing and planned to be completed by 01/01/2024 including potential data cleaning in preparation for the process mining analysis.

Patient and public involvement

There is no *direct* patient or public involvement in this study. The research questions and some of the outcome measures have been informed by patient preferences reported in recent publications. The clinic's staff will be involved in the study through the observations and providing expert input. The results of the research will be disseminated to the clinic's staff throughout the research phases, and to the public through conference presentations and publications. The data gathered and the medical metro lines created will inform the clinic's VBHC dashboard. Once published, the results will be used in the education programmes of bachelor and master students.

Discussion

Our aim is to contribute the VBHC literature by demonstrating how TDABC and process mining can be combined to enable realistic cost measurement on a large scale, an aspect which practitioners currently consider both urgent and a major challenge [2]. Further, by trialling this

method in a complex care context we will contribute to the currently sparse literature on cost measurement and process improvements in complex care with long time horizons and non-linear care paths [13].

We further aim to contribute to the patient-centred fertility care literature [22,30,34] by introducing TDABC to the field and by reporting real patient journey costs and outcomes (in a baseline value assessment) that can serve as a benchmark for other clinics. Other clinics will be able to input their annual costs into the model while assuming the same time-based equations. The time equations can also be adjusted as technologies change or processes modified, for example by introducing AI embryo selection [35] or vitrification [36]. Through this research, we hope to enable internal, longitudinal benchmarking as well as across-clinic benchmarking. In addition, we believe that the outcomes of this research could aid clinics in predicting future costs as populations age and change, and in their organisational decision-making [13]. This approach could contribute to improve quality and efficacy to keep healthcare affordable in the future decades.

Patients have repeatedly indicated that expectation management and information sharing are important aspects of patient satisfaction [22,30,37,38]. By incorporating patient journey information in a value-based dashboard, we aim to provide gynaecologists with the tools to better discuss likelihoods and time-to-pregnancy with patients. We see the medical metro lines created in this project as a tool with which clinics can visually communicate and redesign care paths.

This research has several methodological limitations. First, the single-centre focus of this study will potentially limit the generalisability of the results because all the data are gathered from one clinic. Nevertheless, we consider this single-centre design realistic since we are covering several care paths and anticipate a high volume of manual data collection (observations). To partially mitigate this shortcoming, we have chosen a focal clinic that adheres to European guidelines, meaning that the standard operating procedures and ways of working are comparable to other European clinics governed by the NVOG [39,40] and ESHRE. These treatment protocols are publicly available for comparison purposes [41]. The treatment modalities we cover in this research project are described in detail in prior consensus statements issued by ESHRE [41-49]. Furthermore, our findings are likely to be applicable in clinics that work according to WHO standards. To further improve the generalisability and benchmarking potential, we aim to measure

the duration of activities that involve alternative technologies or ways of working. For example, multiple methods for freezing and thawing embryos will be observed and measured (vitrification and cryopreservation).

Second, the process mining will have limitations related to incomplete cases [50]. For patients that have started but not yet finished treatment, an outcome state cannot be defined. We will address this limitation by restricting the sample to cases with known outcome states in robustness checks, which limits the size of the cohort. An associated issue is that, by using retrospective data (especially if only completed cases), the study will be impacted by technological advancements in fertility care, with earlier cohorts treated under different technological conditions than those observed during our observations.

Third, TDABC studies can suffer from subjectivity because the cost calculations are heavily dependent on the time measures used, and these are typically estimated based on expert interviews. To address this limitation and improve the generalisability of our results given different staff experience levels, daily circumstances and patient characteristics, we will use time measurements during repeated observations to reach an average time per activity and process. This will also enable us to identify cost predictors associated with activities with variable durations as described previously.

Ethics and dissemination

This study was approved by the ESHPM Research Ethics Review Committee (ETH122-0355) and the Reinier de Graaf Hospital (2022-032). We will acquire informed consent from every participant observed during the data collection. We intend to publish the research in peer-reviewed journals and present it at relevant conferences and seminars.

Contributors

ML, HvE and KA conceptualised the project described in this proposal. ML drafted this protocol with input from HvE and KA. CH obtained funding. EvS and CH provided feedback on the proposed study. EvS and CH provided medical and regulatory input on this protocol.

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Competing interests

None declared.

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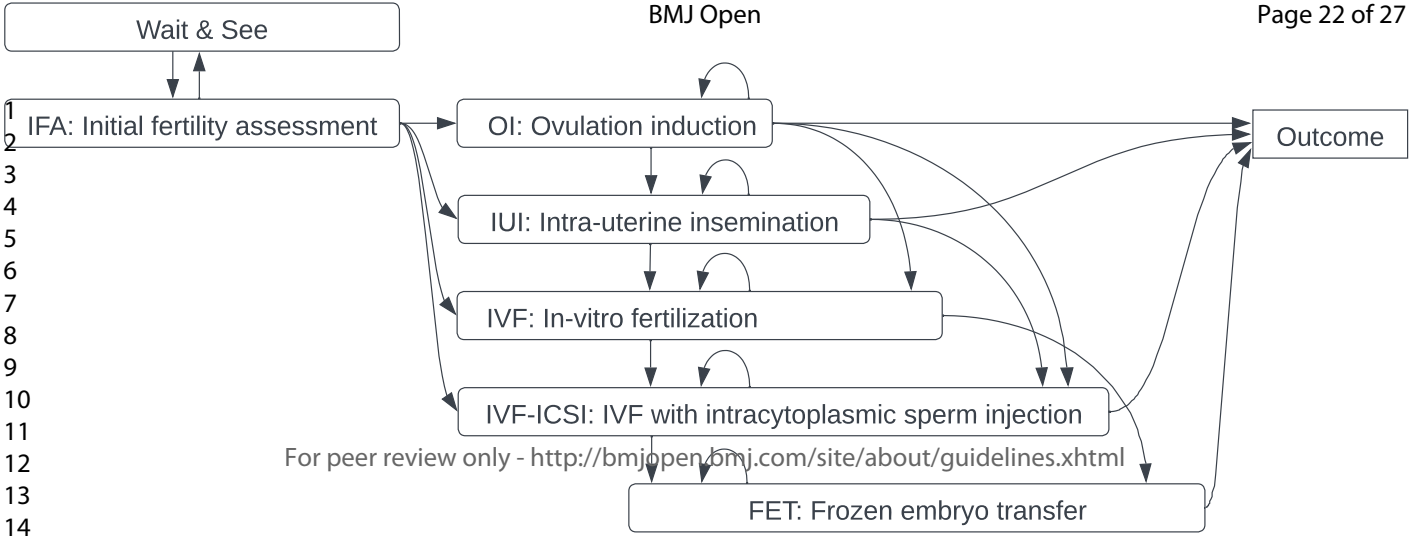
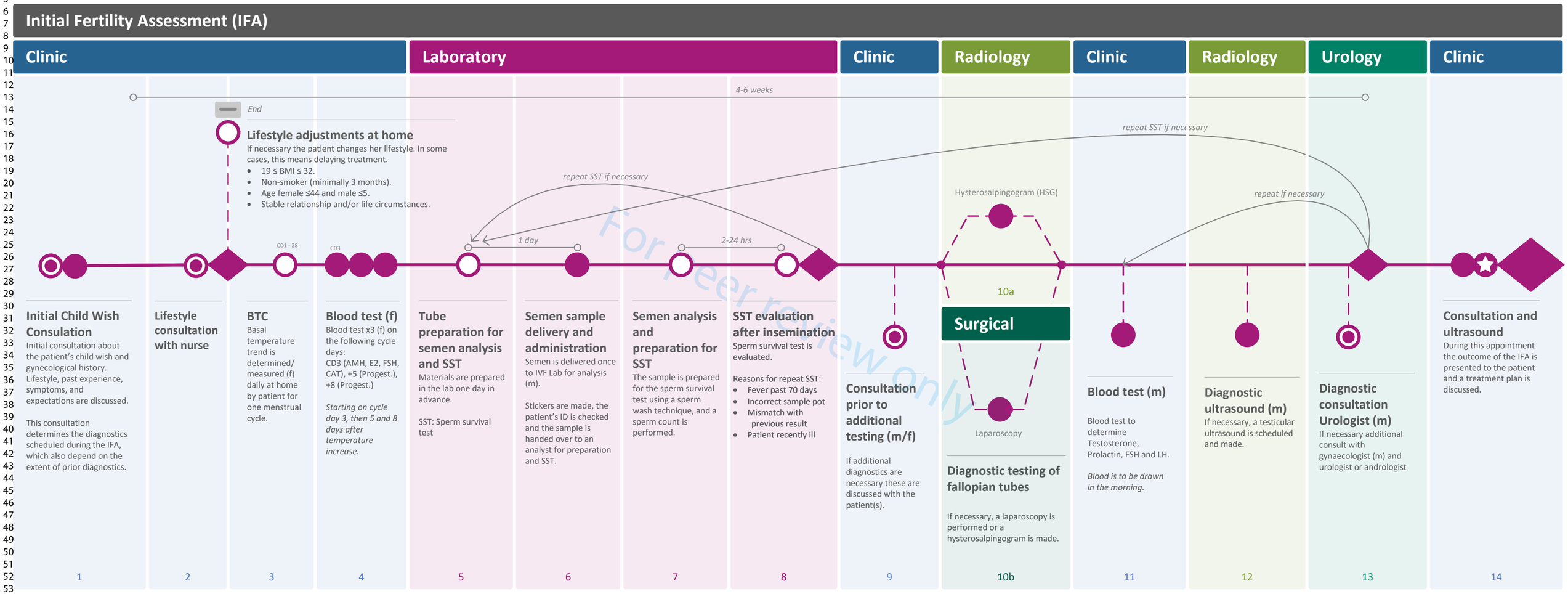


	Phase 1	Phase 2	Phase 3	Phase 4
Data collection and/or analysis	Document analysis (protocols)	Document analysis (financial), observations with time measures, build model	Cost calculation and internal communication of results, informal interviews	Process mining of EHR data, and modelling costs using cohort
Method	TDABC	TDABC	TDABC	Process mining
Deliverables	Medical metro line and process maps for OI, IUI, IVF, IVF-ICSI, FET and IFA	Time equations, and determination of EHR data requirements	Per-cycle costs for OI, IUI, IVF, FET, and IFA	Patient journey outcomes and costs from initial consultation to pregnancy

METRO MAPPING

Initial Fertility Assessment

From initial consultation to diagnosis and treatment plan



Legend

Drop-down step with dotted line. Optional step, required under certain conditions. Does not apply to all patients.

Consultation with patient.

CD Menstrual cycle day.

Treatment or step for which the patient is present.

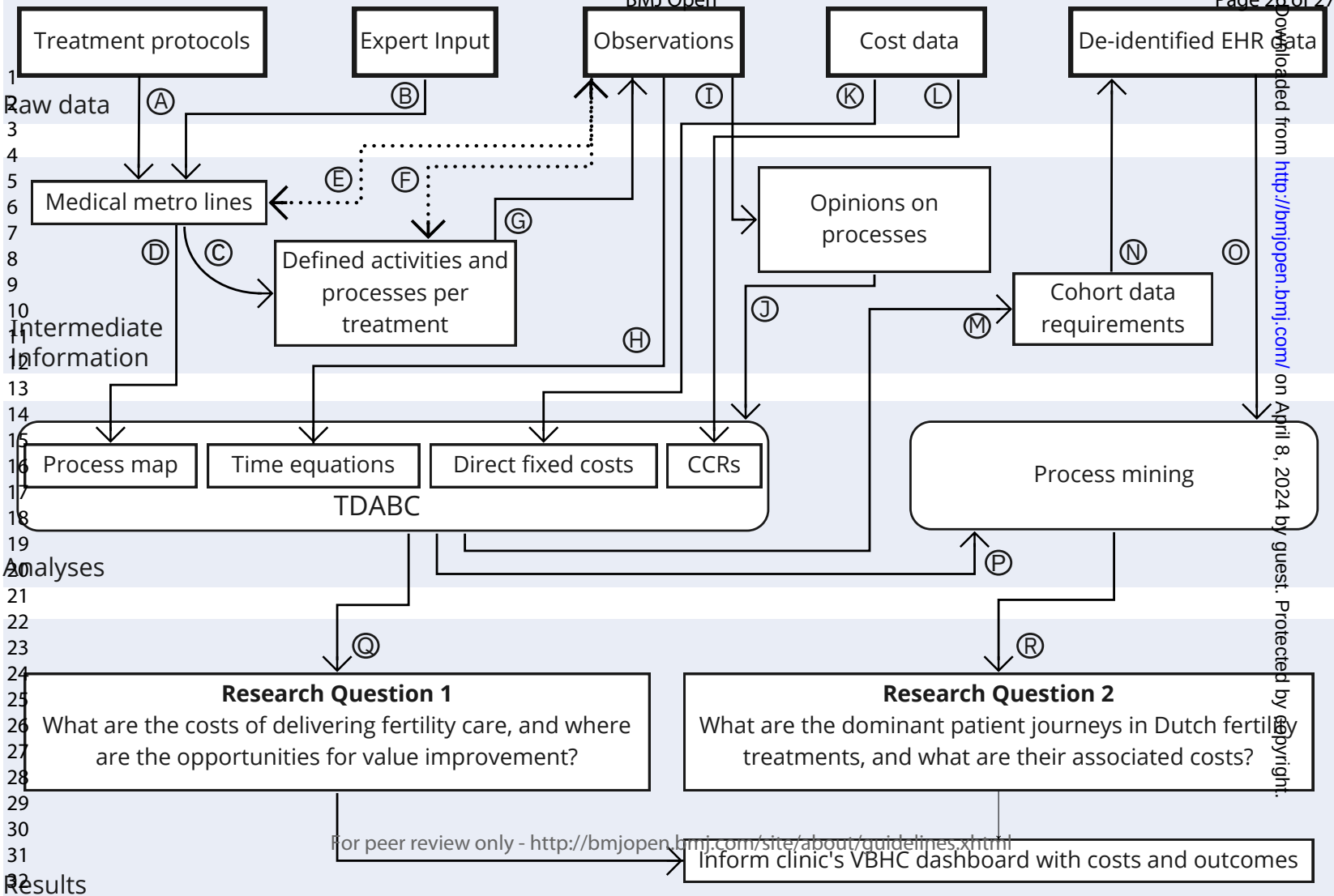
Arrow back; repeat step under certain conditions

Treatment or step for which the patient is not present (patient at home).

Arrow forward; skip step under certain conditions

Decision point; multiple routes possible

Consultation with patient involving shared decision making.



CHEERS 2022 Checklist

	Item	Guidance for Reporting	Reported in section
TITLE			
Title	1	Identify the study as an economic evaluation and specify the interventions being compared.	n/a
ABSTRACT			
Abstract	2	Provide a structured summary that highlights context, key methods, results and alternative analyses.	abstract
INTRODUCTION			
Background and objectives	3	Give the context for the study, the study question and its practical relevance for decision making in policy or practice.	introduction, page 5-9
METHODS			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	n/a
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	n/a
Setting and location	6	Provide relevant contextual information that may influence findings.	setting, discussion
Comparators	7	Describe the interventions or strategies being compared and why chosen.	n/a
Perspective	8	State the perspective(s) adopted by the study and why chosen.	n/a
Time horizon	9	State the time horizon for the study and why appropriate.	methods
Discount rate	10	Report the discount rate(s) and reason chosen.	n/a
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Aims, Relevance, Discussion
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Data, Aims, Research question 1 & 2
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Aims, context and research questions
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Study design and methods
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	n/a
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	n/a
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	n/a
Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for sub-groups.	n/a
Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	n/a
Characterizing uncertainty	20	Describe methods to characterize any sources of uncertainty in the analysis.	n/a
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (e.g., clinicians or payers) in the design of the study.	patient and public involvement
RESULTS			
Study parameters	22	Report all analytic inputs (e.g., values, ranges, references) including uncertainty or distributional assumptions.	n/a
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	n/a
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	n/a
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	n/a
DISCUSSION			
Study findings, limitations, generalizability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could impact patients, policy, or practice.	Discussion
OTHER RELEVANT INFORMATION			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Funding statement
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Competing interests

Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, Caulley L, Chaiyakunapruk N, Greenberg D, Loder E, Mauskopf J, Mullins CD, Petrou S, Pwu RF, Staniszewska S; CHEERS 2022 ISPOR Good Research Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. BMJ. 2022;376:e067975.