The IVF laboratory : from coping and workarounds to a structured and controlled model for lab processes to adhere to physiological time constraints using computer simulation

Aida Kaffel

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The IVF laboratory : from coping and workarounds to a structured and controlled model for lab processes to adhere to physiological time constraints using computer simulation

Aida Kaffel

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Faculty of Science and Engineering

Dalton Building

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DECLARATION

Excepting any statements to the contrary, the contents of this thesis are the result of my own work. No aspect of this thesis has been copied from other sources or written by others, including people and artificial intelligence sources. Collaborators and contributors to this project have been acknowledged and their contributions stated. I understand that any evidence of plagiarism and/or the use of unacknowledged third-party content will be dealt with as a very serious matter and may lead to disqualification from the award or, or withdrawal of the degree. This thesis does not exceed 80,000 words.

As part of the 5-year HSST programme in Reproductive science (MAHSE-MMU, 2023-2024) some proportion of this work referred to in the thesis has been submitted in support of another qualification of this university (MMU- Module C1 **Appendix 19** (MAHSE-MMU, 2023-2024)) and Alliance Manchester Business School Manchester University (Unit A4 PGDip programme in Leadership and Management in the Healthcare Sciences).

Preliminary work for this study was accepted and presented as an abstract and oral communication at ALPHA meeting 2024 (Kaffel *et al.*, 2024).

ABSTRACT

IVF laboratory procedures are dynamic and increasingly complex. Most procedures are manual and reliant on the IVF lab staff (embryologists and practitioners). Time spent carrying out procedures and timing in relation with oocyte retrieval are closely linked to performance (ICSI, oocyte cryopreservation, fertilisation). Labs are resourced using estimations to meet timing recommendations but they are often reliant on workarounds that are challenging to plan.

Discrete event simulation (DES) is a computer modelling simulation tool used to understand and analyse workflows in systems subject to resource constraints and random variation. It is a tool that can help in identifying problems and testing potential change ideas virtually, and so is sometimes used to support quality improvement work.

The aim of this project is to demonstrate the intricate link between staffing in the IVF lab, timing of IVF lab procedures and final IVF outcomes by examining the lab using a discrete event simulation (DES) software Simul8©.

The study was carried out at Guy's Assisted conception Unit ACU GSTT-ACU. The steps in the study were first map and model the IVF laboratory processes: replicating every touchpoint of the patient or their gametes/embryo journey in a Simul8© DES model, then validate the model by comparing retrospective data (2022) to data generated by the simulation. Following validation of the model, identify bottlenecks and deviations from optimal physiological timings, and ultimately test strategies (workload, staffing, equipment and technologies) to take to mitigate against deviations.

Key variables generated by the simulation model were Processes metrics (PM) : Number of processes completed (egg collections, transfers, egg freezing, embryos freezing) within a time period. Bottlenecks was a variable represented by both queuing times for procedures and unfinished tasks at the end of staff shifts. The simulation model generated

a variable called staff time utilisation (expressed in percentage) as a daily or yearly mean rate.

Staff utilisation and job queue were compared with timing of procedures and KPI (IVF and ICSI fertilisation rate) in comparison with targets informed by the clinical literature.

Following the validation stage, preliminary results showed a clear dynamic visualisation of processes (inputs and outputs with a timeline). Challenges and limitations with the modelling included representing deviations from set behaviours or unpredictable staff choices.

Traditionally, IVF laboratory workload/resources are measured by number of weekly egg collections per whole-time equivalent (WTE) embryologists in post. Preliminary simulation results allowed a dynamic understanding of workload and resources in real time and raised awareness with stakeholders of the IVF lab complexity for allocating resources.

The validation step focused on comparing the simulation model outputs to the 2022 real life data (egg collections, egg freezing, embryos transfers completed) using the same number of inputs and was successful delivering similar behaviour in most areas. The second validation step compared the time durations delivered by the simulation model versus real life data considering in the comparison that the model assumption allowed tasks to be carried out when the resources were available and travel time between tasks was not accounted for.

Once validated, the aim of this project was to identify bottlenecks and test "what if scenarios" to improve patient outcomes, optimise workflow and balance workload with resources in the IVF laboratory. Scenarios included removing the andrology service, adding equipment, adding staff on busy days and adding 1 hour overtime for staff. The improvements observed with the different scenarios allowed identification of staffing bottlenecks that could be resolved.

Challenges of modelling the IVF laboratory include difficulty incorporating embryologists' and practitioners' non-clinical tasks due to task difficulty to give a tangible time duration.

This project is a first simulation modelling exploring a novel method to display the complexity of the lab workflows but also to analyse the complex dynamics and give answers to make improvements. The idea is to analyse the IVF laboratory differently to what has been done so far and bring solutions to a recurrent problem : carry out the lab procedures on time. Taking this idea forward in the IVF community would benefit 3 stakeholders: patients, staff and organisations.

ACKNOWLEDGEMENTS

This doctoral thesis completes a 19-year journey from starting a career as an embryologist, to completion of my training and gaining HCPC registration as a clinical embryologist in 2009, passing the RCPath part 1 & part 2 examinations. Many people have advised and supported me along the way. I would especially like to thank Dr Pierre Jouannet for the opportunity to get into the field of clinical embryology. I would also like to thank Dr Virginia Bolton who supported me to get on the HSST course.

I wish to express my profound gratitude to my supervisor, Dr Llwyd Orton and my advisor Dr Nathan Proudlove, for their unwavering support, guidance, and invaluable feedback throughout this thesis journey. Their expertise and insights greatly enriched this study and allowed me to build new thinking pathways, more resilience, more critical thinking, better time management to meet academic objectives. Completing a doctoral thesis remotely from the academic university institution delivering the DClinSci has its challenges especially within the context of having a clinical role and responsibilities in an IVF clinic.

Alliance Manchester Business School has played an important role for inspiring me choosing the topic of my doctoral thesis as well as improvement ideas preceding the project. I'm indebted to my workplace supervisor Jon Taylor for supporting me every step of the way through all improvement project ideas for GSTT-ACU lab including this one. His support was consistent, whether I was on site or away.

I am also very grateful to all Guy's ACU embryology team who were very encouraging of this project despite all data collection challenges. They engaged with my project and supported me, gave their time to provide additional feedback for continuous quality improvement. Their openness to collaborate played an incredible role in this research. This research could not be continued without the support from the Evewell embryology team who continued supporting me when I moved from GSTT-ACU to the Evewell fertility clinic for a new clinical role.

This project is dedicated to embryologists to highlight their role in the lab and their dedication to delivering the best possible care to patients, working under pressure. One of the main objectives is make sure embryologists are delivering the best possible outcome without affecting their wellbeing by workload pressures.

Lastly, but by no means least, my heartfelt special thanks goes to my husband, my children, my family and friends for their understanding, endless patience, and encouragement when it was most needed. Their unwavering belief in me and their consistent support made a significant impact, for which I am deeply grateful.

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LIST OF ABBREVIATIONS

2PN	2 Pronuclei
AI	Artificial Intelligence
AK	Aida Kaffel
ARCS	Association of Reproductive and Clinical Scientists
ASRM	American Society for Reproductive Medicine
BC	Base Case
CI	Change Ideas
COS	Controlled Ovrian HyperStimulation
DES	Discrete event simulation
EC	Egg collection
ESHRE	the European Society of Human Reproduction and Embryology
EU	Embryologist Utilisation
EV	Embryoviewer
EVU	Embryoviewer Utilisation
FET	Frozen Embryo Transfer
FR	Fertilisation Rate
GSTT	Guy's and St Thomas NHS Trust
GSTT-ACU	Guy's and St Thomas NHS Trust Assisted Conception Unit
GV	Germinal Vesicle
HFEA	Human Fertilisation and Embrtuology Authority
HRA	Health Research Authority
HSST	Higher Specialist Scientific training
ICSI	Intra Cytoplasmic Sperm Injection

IM	Input metrics
IUI	Intra Uterine Insemination
IVF	In Vitro Fertilisation
LFH	Laminar Flow Hoods
MI	Metaphase I
MII	Metaphase II
MMU	Manchester Metropolitan University
OM	Output Metrics
PB	Polar Body
PESA	Percutaneous Sperm Aspiration
PI	Principal Investigator
PM	Process Metrics
PMS	Patient Management Software
PN	Pronuclei
PU	Practitioner Utilisation
Q	Queues
QC	Quality Checks
QI	Quality Improvement
RIW	RI Witness ™
S8	Simul8©
S8C	Simul8 Consultant
SME	Subject Matter Expert
SMT	Senior Management Team
SOP	Standard Operating Procedure
TESE	Testicular Sperm extraction

TI	Time Intervals
TLT	Time Lapse Technologies
UT	Unfinished tasks
WKS	Aida Kaffel's workplace Supervisor
WTE	Whole Time Equivalent
ZP	Zona Pellucida

LIST OF APPENDICES

1 INTRODUCTION

1.1 Background

The Higher Specialist Scientific Training (HSST) is a five-year, practice-based education and training programme supported by an underpinning part-time professional doctorate and Royal College of Pathologists qualifications. The academic component of HSST is known as the DClinSci, a Research Degree meeting QAA Level 8 criteria and FQ-EHEA for doctoral degrees illustrated in **Appendix 17**.

This project has been carried out as part of the DClinSci project in reproductive science. The starting point idea of the project was to allow the IVF laboratory to meet the physiological time constraints described below to improve the success rate of IVF treatments by using a quality improvement (QI) tool called Discrete Event Simulation (DES).

The IVF lab processes conditions and times are all inspired by the physiology of human reproduction described below. The project idea was a focus on the IVF lab processes workflows using DES software modelling tool Simul8© with the assistance from a Simul8© modelling consultant to analyse and test change ideas to meet physiological time constraints.

The project idea is a QI initiative. Those tasked with improvement often move forward from the perspective of subject matter experts' knowledge (SME=embryologists). The theory of knowledge was selected here as the most suitable improvement framework to test prediction of the activities and infrastructure necessary to achieve a desired outcome. A driver diagram (**Figure 1**(Bennett and Provost, 2015)) served as a tool for building the testable hypothesis related to process timings and outcomes. For an improvement project, a driver diagram illustrates what structures, processes and norms are believed to require change in the system as well as how these could be changed through the application of specific ideas. (Reed *et al.*, 2014; Bennett and Provost, 2015).

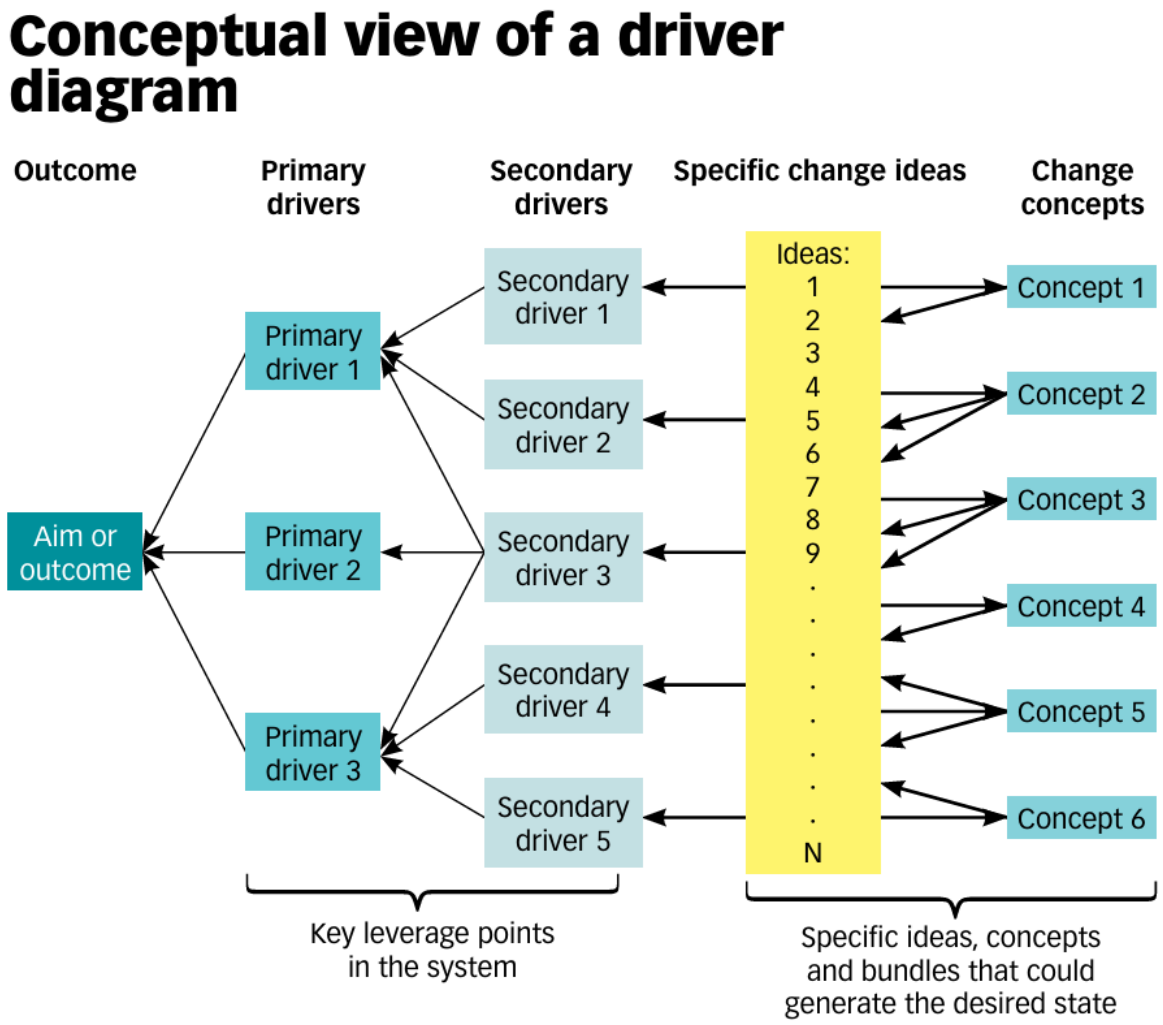

Figure 1. *Driver diagram conceptual model*

This is a driver diagram, a starting point for planning and delivery of a quality improvement initiative called action effect method, At the far left, the aim describes the objective of the improvement. Primary and secondary drivers (middle of the diagram) are the logical steps to connect interventions and concepts to the desired outcome. (Reed et al., 2014; Bennett and Provost, 2015)

In the following chapters, the literature review will build on from human physiology, the importance of time in reproductive human physiology events and how this shapes the IVF lab procedures. These concepts also represent a challenging element that can create constraints in the IVF lab workflow. A driver diagram will be used to visually represent the SME shared theory that procedures timings are one of the main contributors to IVF lab success (from research, observation and experience). A literature review of DES tools use in healthcare and IVF will be presented to explain the choice of DES using Simul8© as a tool to appreciate the system, understand variation and test change ideas (CI) using the driver diagram drawn as the project road map (**Figure 1**).

1.1.1 The physiology of human reproduction

1.1.1.1 Physiology of the ovarian function

The human female reproductive tract consists of two ovaries, a uterus, two oviducts (commonly known as fallopian tubes), a cervix, and a vagina. Each component plays a distinct role in reproduction (Coward and Wells, 2013): production of female gametes, or oocytes, provision of an environment conducive to the fertilization of the ovulated oocyte, support for early embryo development and fetal growth and implantation until birth.

Women are born with two ovaries, located on either side of the uterus in the abdominal cavity. The mature human ovary serves as the source of all oocytes that will be ovulated throughout a woman's reproductive life. Within each ovary, follicles at various stages of development contain a single oocyte, as illustrated in **Figure 2**.

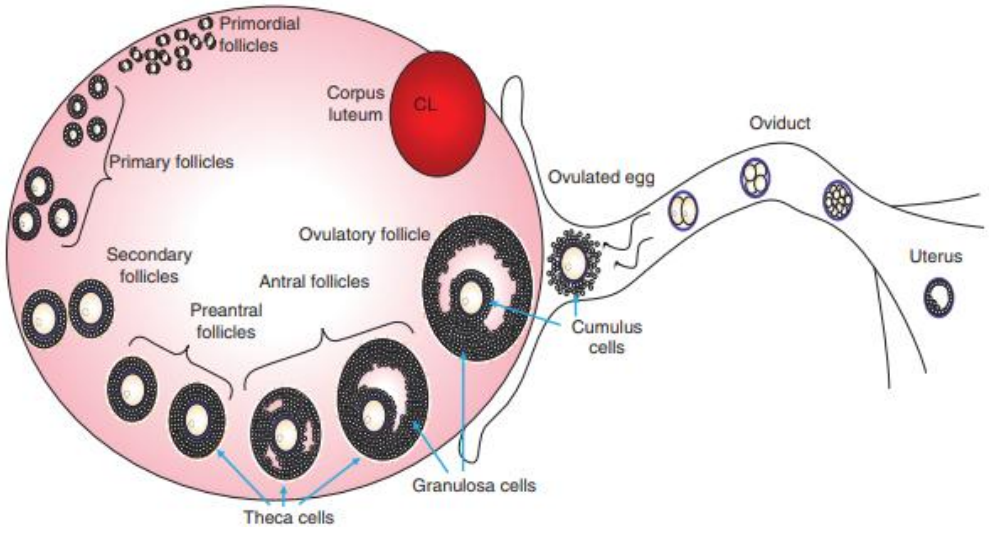

Figure 2. *Follicle development in the human ovary*
Development shown throughout a folliculogenesis cycle (Coward and Wells, 2013) page 28

Folliculogenesis begins with the formation of primordial follicles around the seventh month of embryonic development. The growth and maturation of oocytes and follicles are interdependent processes. Each oocyte is encased in a layer of flattened follicular cells, progressing through various stages: from primordial to primary, secondary, and

pre-antral follicles. This transition takes approximately six months, with an additional 85 days required for pre-antral follicles to reach the pre-ovulatory size.

During the initial stages, from primordial to pre-antral, growth and maturation occur independently of gonadotropin release. In the prenatal phase, oocytes complete the first part of meiosis, specifically meiotic prophase I. A cohort of oocytes becomes arrested in the diplotene stage toward the end of this phase. At this point, the oocyte nucleus, known as the germinal vesicle (GV), becomes distinctly visible and is characterized by the presence of a prominent nucleolus, as depicted in **Figure 3**Figure 3**.**

At puberty, oocyte maturation progresses from the meiotic prophase I arrest (GV) to the metaphase II (MII) stage in response to the mid-cycle surge of luteinizing hormone (LH), occurring approximately 24 to 36 hours before ovulation.

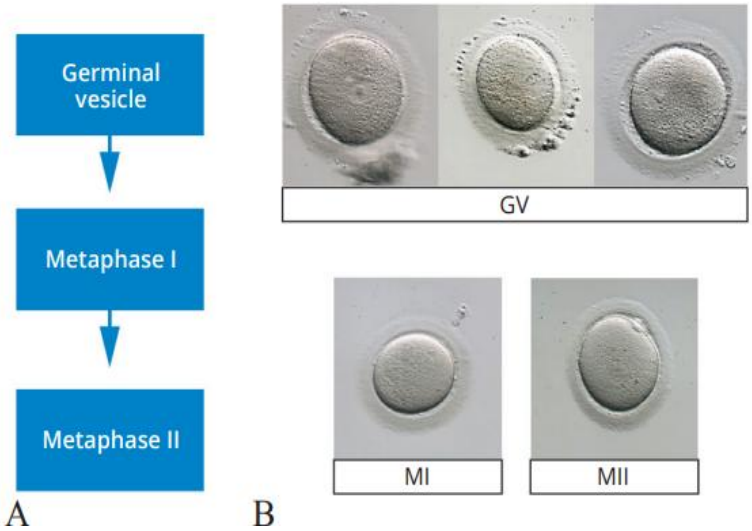

Figure 3. *key stages of oocyte maturation (Anagnostopoulou et al., 2022)*

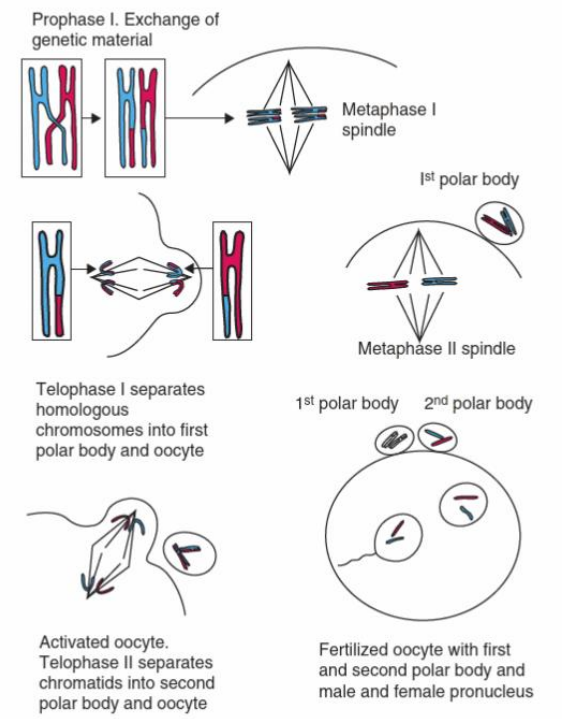

Figure 4*. Diagram of chromosome movements during female meiosis (Coward and Wells, 2013, p52)*

1.1.1.2 The oocyte

The oocyte is ovulated into the abdominal cavity while still in the arrested metaphase II (MII) stage and is subsequently directed into the fallopian tubes, where sperm migrate and fertilisation happens. The environment of the fallopian tubes is crucial for embryo development and its future health as an adult, largely due to epigenetic reprogramming. Following fertilization, the embryo progresses through distinct stages of development as it journeys to the uterus, where it will implant and develop for the next nine months (Anagnostopoulou *et al.*, 2022).

To become a fertilizable haploid egg, the diploid oocyte must extrude half of its genetic material into the first polar body (PB) and align its chromosomes along the equator of the MII spindle (**Figure 4**). In the absence of fertilization, the oocyte undergoes apoptosis, and if implantation does not occur, the endometrium is shed during each menstrual cycle. The structure and function of the endometrium are influenced by the stage of the oestrous cycle, with ovarian hormones regulating the uterine lining.

At the base of the uterus lies the cervix, which connects the uterus to the vagina. The cervix secretes mucus, the composition of which changes throughout the menstrual cycle due to hormonal regulation. During fertile periods, the mucus thins to facilitate sperm penetration, while at other times, it thickens to create a more hostile environment for sperm. The vagina is a muscular canal that links the external reproductive organs to the internal reproductive system. During intercourse, the penis ejaculates semen into the vagina. The timing and synchronization of embryo development and uterine receptivity are critical from ovulation through fertilization to implantation. These concepts play a significant role in the organization of IVF laboratories (Kol, 2021) and these are the concepts that are examined in this study.

1.1.1.3 The physiology of testicular function

The testes are responsible for producing male gametes, known as spermatozoa, as well as sexual hormones, primarily androgens. The process of spermatogenesis encompasses the production of gametes, while steroidogenesis refers specifically to the synthesis of

androgens. These two processes occur in distinct compartments that are both morphologically and functionally different. (Leung *et al.*, 2022; Nieschlag, Behre and Nieschlag, 2010). Spermatogenesis occurs within the tubular compartment of the testes. It begins with the division of stem cells and culminates in the formation of mature spermatozoa. This process can be broken down into several stages: First, spermatogoniogenesis which is a mitotic division and differentiation of diploid germ cells (spermatogonia), then the meiotic division of tetraploid germ cells (spermatocytes) resulting in haploid germ cells (spermatids) followed by transformation of spermatids into testicular sperm (spermiogenesis) leading to release of sperm from the germinal epithelium into the tubular lumen (spermiation). The process of spermatogenesis takes around 64 days for man.

Upon release from the testes, spermatozoa are not immediately capable of fertilizing oocytes. They must travel through the epididymal duct to gain full fertilization competence, a process that involves a series of membrane changes known as capacitation. These structural and metabolic alterations enable the spermatozoa to bind to the zona pellucida (ZP) and initiate the acrosome reaction. Without capacitation, spermatozoa cannot effectively bind to the ZP or fertilize the oocyte. Understanding these physiological milestones and their timing are crucial for the proper handling and processing of fresh or frozen ejaculated and surgically retrieved sperm in the IVF laboratory.

1.1.1.4 IVF treatments and laboratory layout

During IVF cycles, IVF patients undergo programmed Controlled Ovarian Hyperstimulation protocols (COS) which is an administration of a particular set of medications able to induce ovulation in anovulatory patients or to override the natural mechanisms of mono-ovulation. The growth of one or multiple follicles is then utilized for Intra Uterine Insemination (IUI) or in vitro fertilisation (IVF). A surge in gonadotropin triggers a resumption of the meiotic programme and eggs are supposed to reach the MII arrest stage within 36hours. However, oocytes retrieved from pre-ovulatory follicles often constitute an assortment of maturity stages displaying MII oocytes and immatures oocytes either at MI phase (MI) or at GV stage.

Initially, fertilization was performed using conventional IVF, where all retrieved oocytes were inseminated with a processed sperm sample. The introduction of Intra Cytoplasmic Sperm Injection (ICSI) by a Belgian team (Palermo *et al.*, 1992) has significantly improved fertilization rates and is now the preferred method for patients at risk of reduced or failed fertilization due to low sperm parameters. Only MII oocytes are subjected to freezing or ICSI, while immature oocytes are typically discarded unless they mature into the MII stage in vitro before injection. Delays in oocyte maturation may negatively impact the outcomes of IVF cycles (Anagnostopoulou *et al.*, 2022; Lin *et al.*, 2003; Yılmaz *et al.*, 2022), and improper timing of sperm injection can be a primary reason for poor developmental outcomes of late-maturing oocytes.

Sperm used for oocyte insemination is retrieved from the ejaculate (fresh or frozen sample). Sperm in semen is commonly selected based on head density or motility, parameters that could determine its ability to fertilise eggs (Leung *et al.*, 2022). During IVF (not ICSI), selection of spermatozoa by the oocyte cumulus mass and the ZP remains intact. In cases of total absence of sperm in the ejaculate, sperm may be retrieved from the epididymis through a procedure known as Percutaneous Epididymal Sperm Aspiration (PESA) or from the testis via Testicular Sperm Extraction (TESE). Sperm retrieval is one of the essential procedures conducted in IVF and andrology laboratories. This necessitates the use of ICSI for insemination, which involves directly injecting a sperm into an MII oocyte, bypassing all natural selection barriers.

Cryopreservation of embryos and oocytes (Cascante *et al.*, 2022; Rienzi *et al.*, 2017) has enabled IVF units to preserve embryos and oocytes for future use and reduced the number of embryos that need to be transferred. In humans, all developmental stages from the zygote or 2 Pronuclei (2PN) to the blastocyst can be frozen, although different cryoprotectants and freezing protocols are required for each stage (Cohen *et al.*, 1985; Lassalle, Testart and Renard, 1985; Trounson and Mohr, 1983; Zeilmaker *et al.*, 1984; Menezo, 2004). The subsequent thawing of embryos allows for their transfer in natural or stimulated cycles, necessitating synchronization between embryo thawing and endometrial receptivity (Volovsky *et al.*, 2020).

The IVF laboratory is designed to replicate physiological conditions conducive to human gamete and embryo development. The primary objective is to create a controlled environment that maximizes the potential for healthy, high-quality oocytes and embryos to develop through to implantation, ultimately leading to live births. To achieve these optimal conditions, several parameters must be carefully controlled within the laboratory, including layout, temperature, light, air quality, cleanliness, and the equipment used, such as culture media, incubators, culture vessels, and consumables to guarantee safe and optimal handling conditions of gametes and embryos: from retrieval/thaw to transfer or cryopreservation

- Light: In IVF, embryos are exposed to both microscope and ambient light. Research has shown that visible light can have detrimental effects on mammalian gametes and embryos in vitro (Hirao and Yanagimachi, 1978; Ottosen, Hindkjaer and Ingerslev, 2007). There is also evidence suggesting that human embryo blastulation (development to the blastocyst stage) rates may improve under low illumination conditions (Noda *et al.*, 1994). As a result, some IVF units opt to work under low filtered (non-UV) light and minimize the duration of observations made on gametes and embryos under the microscope.
- pH : Maintaining the pH of the embryo environment is an important factor in minimizing stress. Embryo culture formulations are buffered using bicarbonate and thus based on the Henderson-Hasselbach equation, the pH is directly affected by the bicarbonate in solution and the concentration of CO2 in the atmosphere as follows:

  $CO_2 + H_2O \quad \leftrightarrow \quad H2CO_2 \quad \leftrightarrow \quad HCO_3^- + H^+$

- Temperature: The optimal temperature for culture of human embryos is widely believed to be 37^0C, reflecting human body temperature. Routine calibration and control of equipment, such as incubators, workstations, heated stages, and tube heaters, are essential to ensure that this temperature is consistently maintained throughout embryo culture. Research indicates that fluctuations in temperature can adversely affect human oocytes; specifically, the meiotic spindle is temperature-sensitive and can be disrupted by cooling (Pickering *et al.*, 1990)

Such disruptions increase the risk of aneuploidy, a common pattern of abnormal fertilization in humans. Notably, reducing the temperature to 33°C can lead to depolymerization of spindles within just 10 minutes, and this process occurs even more rapidly at lower temperatures. The extent of recovery after rewarming is influenced by both the degree of cooling and the duration for which oocytes are kept at lower temperatures (Wang *et al.*, 2001). Conversely, spindle disruption can occur due to overheating (Sun, Wang and Keefe, 2004). The IVF and ICSI processes involve manipulating eggs, sperm, and embryos outside of incubators, which makes temperature fluctuations inevitable (Macklon *et al.*, 2021). When culture dishes are removed from incubators, rapid cooling occurs. The rate of cooling and rewarming is affected by various factors, including the culture media, the type of vessel used (with or without a lid), and the specific incubator, especially the time spent outside the incubator for observation or procedural tasks. (Cooke, Tyler and Driscoll, 2002).

- Low O2 environment. Physiological conditions in vivo suggest that the ideal environment for culturing human embryos includes a temperature of 37°C, a CO_2 concentration of 5% to 6%, and an O_2 concentration of around 5%. This is particularly important when extending culture to the blastocyst stage (Kovacic and Vlaisavljević, 2008).

Time duration of procedures is an important concept in the IVF lab linked to reduction of variations around temperature, pH or light exposure (which can impact the outcome for patients going through IVF). This concept will be explored further in the project. As displayed in **Figure** 5, all parameters listed above in addition to resources (equipment, staff and consumables) can influence embryo development. Maintaining gametes and embryos in an environment where physical and chemical parameters are kept within optimal levels is heavily dependent on one resource which the embryologist as the time spent carrying out various procedures will influence temperature, pH, and culture conditions.

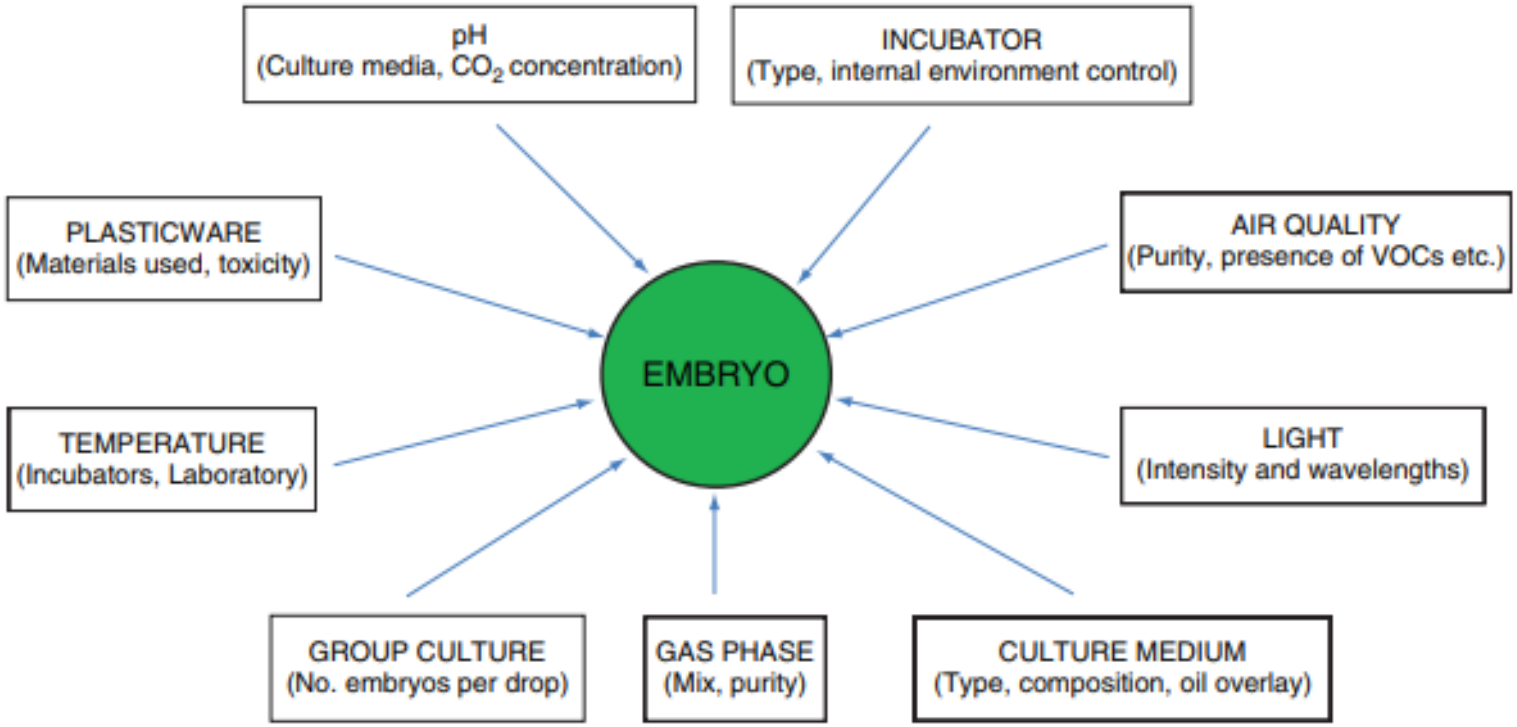

Figure 5. *Environmental, physical and chemical influences on the human embryo in vitro.*

(Coward and Wells, 2013), page 276. The environmental, physical and chemical influences can come from resources used (plasticware, incubators) but also from chemical influences (pH, temperature), environmental (light air quality, culture medium, gas) but also procedures carried out on the embryo (embryo group culture for example).

1.1.2 IVF laboratory processes, workload and impact on embryo development parameters

In the IVF laboratory, oocytes are retrieved after COS. They are then frozen (egg freezing) or inseminated (conventional IVF or ICSI). After insemination, embryos are cultured up for 5 days before a fresh transfer or 6 to 7 days before freezing. Since the inception of IVF, assessments of egg maturity and embryo development have primarily relied on morphological criteria. Morphology has been the main method used by embryologists to evaluate and select embryos for transfer (Anagnostopoulou *et al.*, 2022) even though there is an element of variability and subjectivity around it. Research has demonstrated a connection between morphological characteristics and developmental outcomes. Over time, grading systems have been established to standardize the assessment of embryo development, with observations made at specific times of development post insemination. However, this can be challenging, as embryos are dynamic entities; an embryo may appear different when observed in the morning versus the afternoon of day 5, and staff may not always be available at critical times (Liu *et al.*, 2022). All ideal morphological features expected to see embryos developed into on Day 1 to day 7 post egg collection and insemination are shown on **Figure 6**. Recently, a consensus has been published by the European Society of Human Reproduction and Embryology (ESHRE) and ALPHA scientists in reproductive science working group (Coticchio *et al.*, 2025) for oocyte and embryo observations and gradings as an update to the 2011 version of the same consensus (Embryology, 2011). The consensus highlighted the variability in embryo grading and distinguished between static versus time lapse technology (TLT) assessments. The consensus specified recommended times of embryo observations on each day of development (16-15h for day 1, 25-26h for day 2, 43-45h for day 3, 63-65h for day 3, 93-95h for day 4, 108-111h for day 5). Most laboratories use the ideal morphology described in **Figure 6** as a reference for each day of development (day 1 to day 4), so embryos are scored as ideal when they fit all the ideal descriptions and scored lower when they deviate from the ideal features (fragmentation, multinucleation, uniformity of cells, nuclei). The Gardner grading system or a modified version of it (Gardner and Schoolcraft, 1999; Coticchio *et al.*, 2025) is the most used scoring system for blastocyst stage embryos (day 5 to 7 of development post insemaintion).

The introduction of time-lapse incubators (Meseguer et al., 2011; Apter et al., 2020) has addressed the challenges associated with removing embryos from incubators for observation, particularly concerning the effects of temperature and pH fluctuations on embryo culture. This innovation has alleviated time pressures during observations and introduced the concept of morphokinetics (Meseguer et al., 2011), which focuses on the timing of embryonic developmental events rather than ideal morphology on a certain day. **Figure 7** shows the timeline of embryo growth and development seen through the lens of conventional embryo grading and time-lapse imaging. This allowed embryologists to identify critical milestones in embryo development, such as fertilization, early cleavage, blastulation, and hatching. Consequently, new algorithms for embryo selection and de-selection have been developed (Apter *et al.*, 2020; Basile *et al.*, 2015; Valera *et al.*, 2023; Giménez *et al.*, 2023; Coticchio *et al.*, 2025) and new practices have been introduced such as introduction of quality controls for embryo annotation (Sundvall et al., 2013). Time-lapse technologies (TLT) also enabled embryologists to explore the significance of timing in embryo development and its impact on IVF outcomes and sometime its association with ploidy status (Mumusoglu *et al.*, 2017). Artificial intelligence tools have been introduced recently in addition to time-lapse selection tools to overcome variation in assessments (Coticchio *et al.*, 2024b; Yang *et al.*, 2024; Bamford *et al.*, 2023). The overall aim was to improve outcomes by reducing variations.

Despite these advancements, most procedures in the IVF laboratory remain manual, relying on the expertise of embryologists (egg collection, egg freezing, embryo freezing, ICSI, embryo biopsy). Most of the IVF lab procedures involve using timers to minimize the exposure of embryos and gametes to variations in temperature, pH, light, ambient air, and potentially toxic components. There are still gaps in knowledge regarding the optimal timing between the induction of ovulation and insemination, as well as the timing of oocyte denudation and ICSI (Maggiulli *et al.*, 2020). Given the critical role of procedures' timing, staffing and hands-on experience are essential factors contributing to the success rates of IVF laboratories.

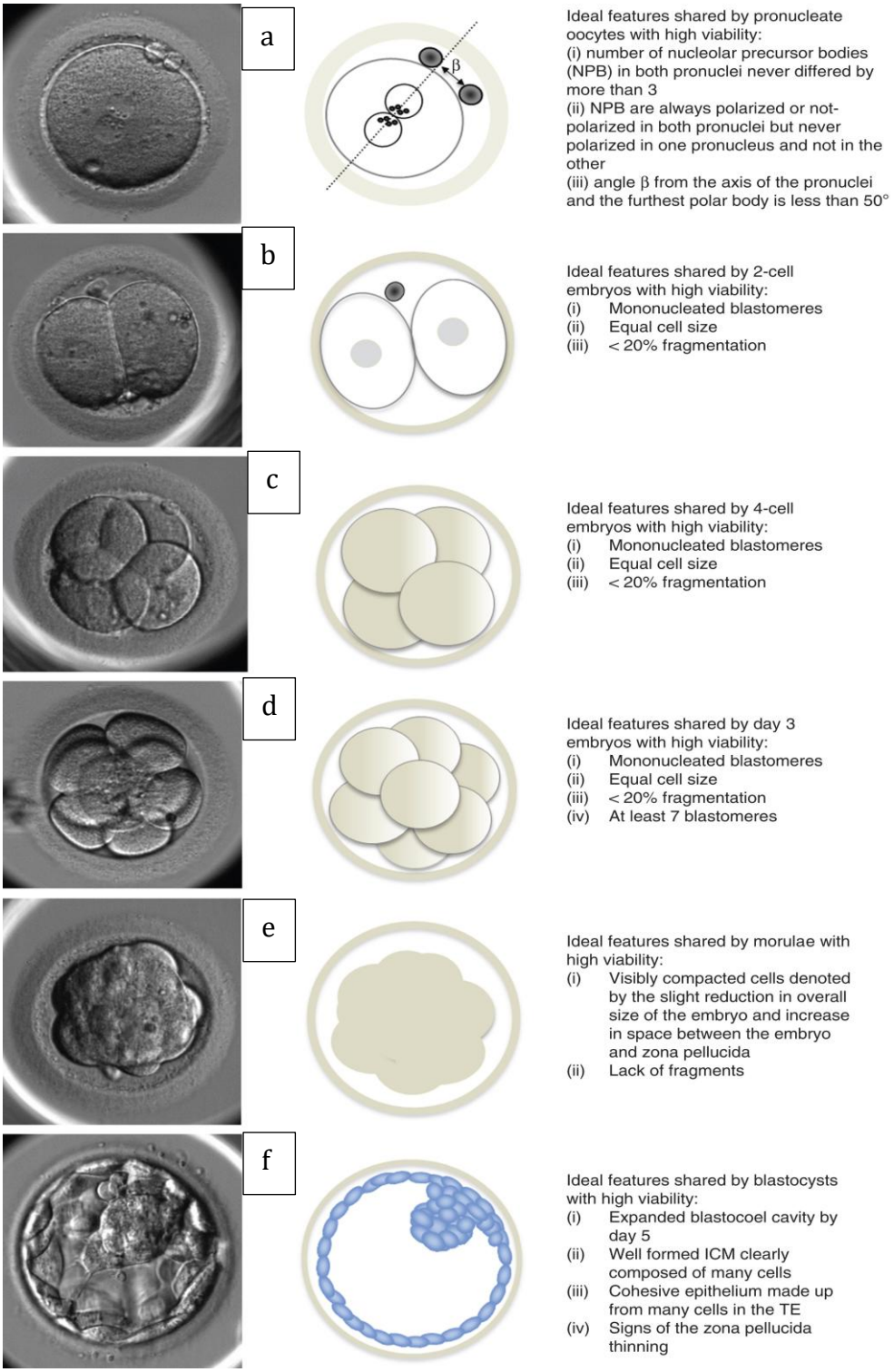

***Figure 6**. Key morphological features of human embryos with high viability*

(Gardner and Balaban, 2016) The diagram shows (a) the pronucleate stage observed Day 1 post EC (b & c) 2 and 4 cell stages observed on Day 2, (d) 8 cell stage observed on Day 3 (e) morula stage observed on Day 4 and (f) blastocyst stage observed on Day 5, 6 or 7.

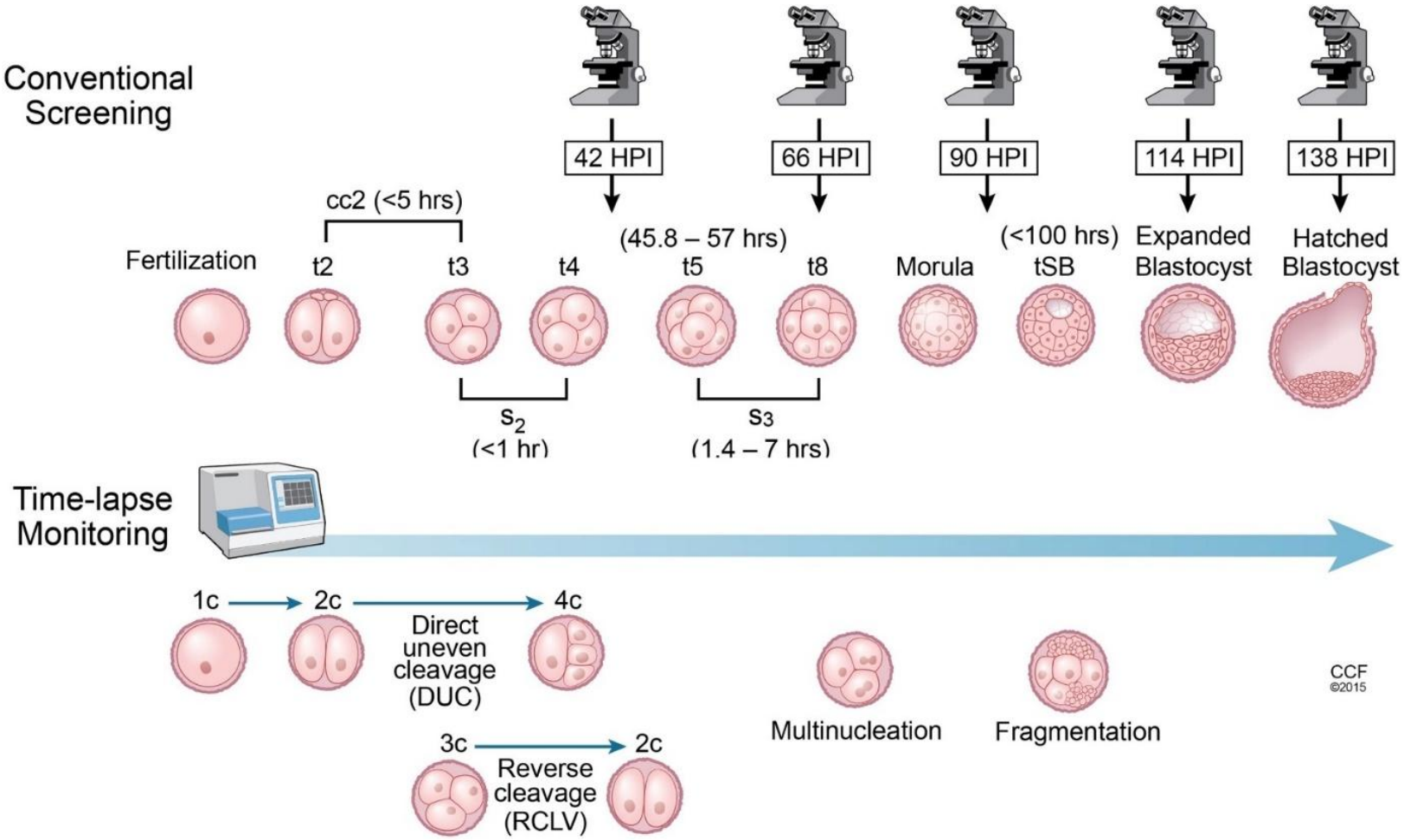

Figure 7. *Embryo growth and development*

The top part of the figure displays embryo grading as determined by conventional microscopy and the bottom part shows cell divisions and features discovered through time-lapse imaging. (Goodman et al., 2016).

1.1.3 Procedures' timings in IVF

With the advent of time-lapse imaging, there has been a change in embryo assessments (Gardner and Balaban, 2016) and an increasing interest in the timing of procedures (Coticchio *et al.*, 2024a) within IVF as summarized in **Table 1**. These timings encompass clinical procedures (such as stimulation and trigger) as well as witnessing, but primarily there was a focus on laboratory procedures (denudation or stripping, ICSI, fertilization check, PN formation, and PN fading), in relation to embryo developmental morphokinetics and IVF outcomes. All publications referenced in **Table 1** examine the timing of individual procedures or the time elapsed between two procedures (e.g., from egg retrieval to denudation). While timing is critical for the outcomes of IVF lab procedures, no consensus has emerged regarding any specific process. Furthermore, none of the studies investigated all laboratory processes collectively, likely due to the complexity and multitude of parameters involved.

Many time duration parameters in the IVF lab were investigated but the following three were the most mentioned and are followed more frequently than others in relation to IVF outcomes: OM1: time between egg collection and egg freezing, OM2, time between egg collection and ICSI, and OM3, time between IVF insemination and fertilisation check. The time durations were coded OM1, OM2, OM3 in this study for easiness of recollection. Even with the introduction of time-lapse technologies discussed above, time durations between procedures remain dependant on the presence of embryologists because they are linked to manual procedures (ICSI, egg freezing, IVF fertilisation check). Attempts to remove the variability linked to these processes are still experimental (Zhu *et al.*, 2023; Costa-Borges *et al.*, 2023; Bayram *et al.*; Bayram *et al.*, 2024) and time-lapse technologies did not alleviate the time pressure around these parameters.

***Table 1**. IVF process timings researched and published*

Process timing investigated	References
Stimulation	(Inaudi *et al.*, 1995; Detti *et al.*, 2008; Setti *et al.*, 2022b; Kol, 2021; Robertson, Chmiel and Cheong, 2021)
Witnessing	(Holmes *et al.*, 2021)
Testicular sperm retrieval	(Levran *et al.*, 2001; Topuz *et al.*, 2021)
IUI	(Bahadur et al., 2017; Cohlen et al., 2018)
Trigger and oocyte retrieval	(Pérez-Padilla *et al.*, 2024; Cimadomo *et al.*, 2022; Droesch *et al.*, 1988; Falagario *et al.*, 2017; Bodri *et al.*, 2014; Bodri *et al.*, 2015; Chen *et al.*, 2014; Fenwick *et al.*, 2002; Huang *et al.*, 2020; Hariton *et al.*, 2021; Helmer *et al.*, 2022)
Oocyte handling time	(Garor *et al.*, 2015)
Oocyte vitrification (OM1) **Oocyte warming**	(An *et al.*, 2022; Chen *et al.*, 2003; Rienzi *et al.*, 2010; Gürtin *et al.*, 2019; Parmegiani *et al.*, 2008; Song *et al.*, 2010)
In Vitro Maturation of oocytes	(Garor *et al.*, 2015; Funahashi, 2013)
Stripping	(Mizuno *et al.*, 2019; Patrat *et al.*, 2012; Naji *et al.*, 2018; Carvalho *et al.*, 2020)
IVF insemination **ICSI insemination (OM2)**	(Wang *et al.*, 2021; Garor *et al.*, 2015; Pujol *et al.*, 2018; Maggiulli *et al.*, 2020; Vandenberghe *et al.*, 2021; Azizi *et al.*, 2020; Ranganath *et al.*, 2021; Shiraiwa *et al.*, 2021; Patrat *et al.*, 2012; Esiso *et al.*, 2021; Smith *et al.*, 2021)
Fertilisation check (OM3)	(Embryology, 2011; Barrie *et al.*, 2021; Kobayashi *et al.*, 2021; Santella, Limatola and Chun, 2020)
PN formation and PN breakdown	(Kobayashi *et al.*, 2021)
Freezing at PN stage (IVF/ICSI)	(Damario *et al.*, 1999; Makieva *et al.*, 2023)
Embryo morphokinetics	(Almaslami and Aljunid, 2020; Akhter and Shahab, 2017; Blais *et al.*, 2021; Cruz *et al.*, 2013; Fenwick

	et al., 2002; Setti *et al.*, 2022a; Bamford *et al.*, 2023; Valera *et al.*, 2023)
Blastulation and embryo grading	(Thang *et al.*, 2024; Franasiak *et al.*, 2018; Liu *et al.*, 2022; Soukhov *et al.*, 2022)
Embryos' morphokinetics (sperm characteristics)	(Borges *et al.*, 2024; Eastick *et al.*, 2017; Karavani *et al.*, 2021)
Embryo transfer	(An *et al.*, 2022; Bergenheim *et al.*, 2021; Gajjar *et al.*, 2024; Weissman *et al.*, 2009)
Embryo warming	(Bartels *et al.*, 2019)
Endometrial receptivity for frozen embryo transfer	(Connell *et al.*, 2015; Gajjar *et al.*, 2024; Chen *et al.*, 2023; Mizrachi *et al.*, 2022)
Embryo freezing	(Makieva *et al.*, 2023; Sparks, 2015)
Embryo biopsy	(Harton *et al.*, 2011; Aizer *et al.*, 2020; Akhter and Shahab, 2017)

1.1.4 Challenges in the IVF laboratory and impact on results

Since the birth of the first IVF baby, where a mature oocyte was retrieved from a naturally growing follicle, current IVF treatments have evolved to include the use of medications that recruit multiple follicles and control ovulation timing. Initially, GnRH agonists were employed to down-regulate the secretion of gonadotropins, specifically luteinizing hormone (LH) and follicle-stimulating hormone (FSH). This down-regulation suppressed endogenous gonadotropin production and prevented the LH surge, allowing for planned egg retrieval following an injection of human chorionic gonadotropin (hCG) (Fleming *et al.*, 1982). Stimulation protocols designed to recruit multiple fertilizable oocytes for IVF have been continually refined, now tailored to each patient's medical history and condition. Additionally, new AI algorithms and models are being explored to enhance outcomes (Hariton *et al.*, 2021; Curchoe, 2022; Canon *et al.*, 2024; Muasher, Abdallah and Hubayter, 2006). The response to ovarian stimulation and its duration can vary significantly among patients, making the timeline from the start of stimulation to egg collection often unpredictable (Muasher, Abdallah and Hubayter, 2006). Consequently,

the number of eggs retrieved for each patient, which determines the workload in the laboratory, can also be variable and unpredictable.

In the IVF laboratory, embryologists are responsible for the safe handling and observation of gametes and embryos whether using conventional microscopy or time-lapse technologies. Other critical tasks include lab maintenance, equipment standardization, and meticulous record-keeping in addition to train junior members. Most procedures in the IVF lab are manual and depend heavily on the expertise of embryologists (Go, 2015b; Wyns *et al.*, 2022; Cohen *et al.*, 2018a). Over the past decade, IVF laboratories have become increasingly complex, integrating advanced equipment, technologies, and processes. While automation and AI have been applied to some tasks (Holmes *et al.*, 2021; Gardner and Balaban, 2016; Campbell *et al.*, 2022; Wikland and Sjöblom, 2000; Montjean *et al.*, 2024), most automations remain in development and have yet to be widely implemented (Zhu *et al.*, 2023; Costa-Borges *et al.*, 2023; Montjean *et al.*, 2024; Campbell *et al.*, 2022). The time taken to perform procedures is influenced by staff competencies, availability, and workstation readiness, all of which can fluctuate due to unpredictable workloads (Hickman *et al.*, 2020). As the complexity of procedures has increased, the demand for a greater number of embryologists to maintain safe and efficient laboratory conditions has increased as well (Basar, Unsal and Ergun, 2024; Kasraie and Kennedy, 2024; Alikani et al., 2014; Campbell et al., 2022; Veiga et al., 2022). As per the driver diagram used in **Figure 8**, staff as a resource in the IVF lab can affect outcomes (**Figure 9**). From the literature, it has been established that staff shortages can create environments prone to errors (Toft and Mascie-Taylor, 2005; Kennedy and Mortimer, 2007) and can influence outcomes. Additionally, the duration of carrying out certain procedures, such as ICSI, has shown that less experienced operators may contribute to longer times and affect outcomes, likely due to the sensitivity of oocytes to temperature variations (Maggiulli *et al.*, 2020). Overall, there is uncertainty regarding workload in the IVF lab, particularly in relation with the number and complexity of procedures. The success of these procedures relies heavily on staff availability, competency, and efficiency, as they are closely tied to embryo developmental milestones and the duration that gametes and embryos are outside incubators.

The literature review shows that many parameters can affect embryo development (**Figure 5**) and hence the IVF cycle outcome. These parameters (pH, temperature, light exposure) are themselves influenced by the time the eggs or embryos are exposed to an environment with physico-chemical variations. The duration of exposure is dependent on the time spent by embryologists carrying out procedures. Published articles also demonstrated that an egg and embryo competence and development are dependent on when procedures happen (egg collection 36h after trigger, inseminations on Day 0 , freezing eggs on Day 0). To improve quality and outcomes and reduce variations in processes, there has been growing interest in applying Artificial Intelligence (AI) modelling in IVF clinics , both in the laboratory settings and during stimulation protocols (Pérez-Padilla et al., 2024; Pavlovic, Jiang and Hariton, 2024; Canon et al., 2024; Yang et al., 2024) but AI is still being validated and the embryologist remains the main IVF lab actor.

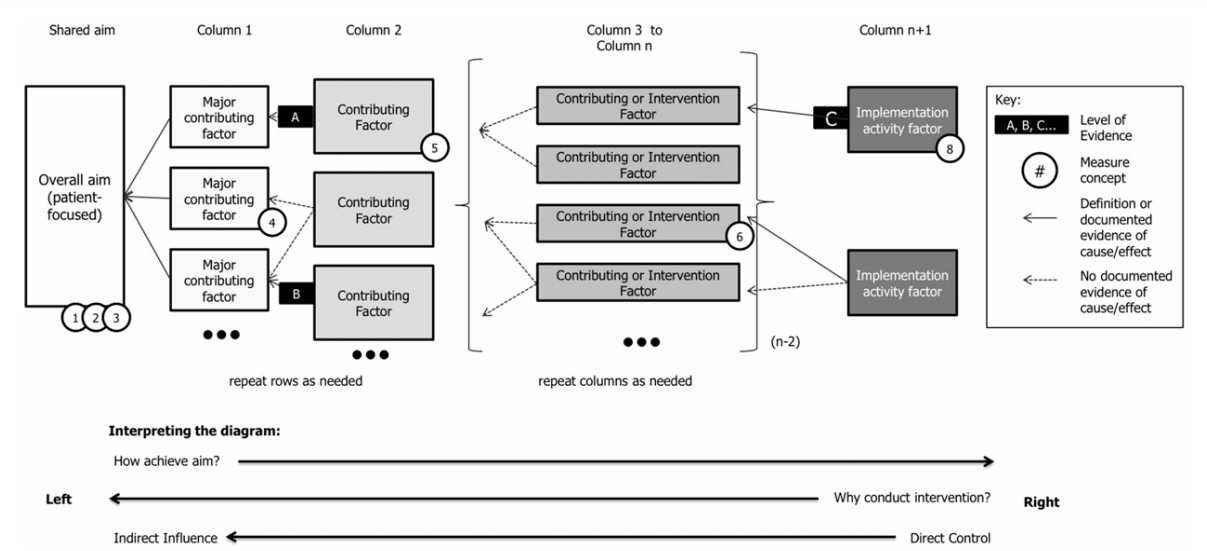

Figure 8*. Schematic action effect diagram*

Guide to interpreting the components and overall structure of a typical action effect diagram (Reed et al., 2014)

Despite the critical role of timing in embryo development, published data typically focused on individual parameters rather than the entire process (**Table 1**). Very few QI projects have been published in the IVF field (Veiga *et al.*, 2022; Wood and Proudlove, 2022; Woodland and Carroll, 2022). The focus in this project was driven by an interest in developing a QI project that could integrate all parameters reported in the literature (from the lab perspective) confirmed as contributing to the outcomes for IVF patients.

The theory of knowledge-Action effect method (AEM) diagram framework as shown on **Figure 9** was used as a road map to start the QI project. **Figure 8** was adapted to the situation we were looking to improve outcomes as displayed on **Figure 9**. The AEM start by the shared aim which is to have the best outcome possible for patients having IVF treatments. The major contributing factors in the IVF lab outcomes are believed to be the time durations between procedures and the length of time the procedures are carried out. The primary drivers for procedures timings and durations are workload, resources (staff and equipment) and processes involved. To act on primary drivers, we can act on secondary drivers such as planned procedures, staff and resources available, procedures duration. Time durations between IVF lab procedures and timing of procedures are very important factors that can affect success rates, themselves linked to staffing. This study aimed to use a QI initiative to make improvements in the outcomes by acting on the IVF lab processes and demonstrating the link between timing of procedures, workload and staffing capacity.

For this initiative, it was necessary to have a QI tool that could integrates the following parameters, high variability, interconnection and high dynamic. Amongst the QI-operations management tools used in healthcare and published, DES modelling was the tool that met all criteria listed above : variability, interconnection and complexity (Brazil, Purdy and Bajaj, 2019; Ramwadhdoebe *et al.*, 2009): The literature review will list all the advantages of this tool in the next section.

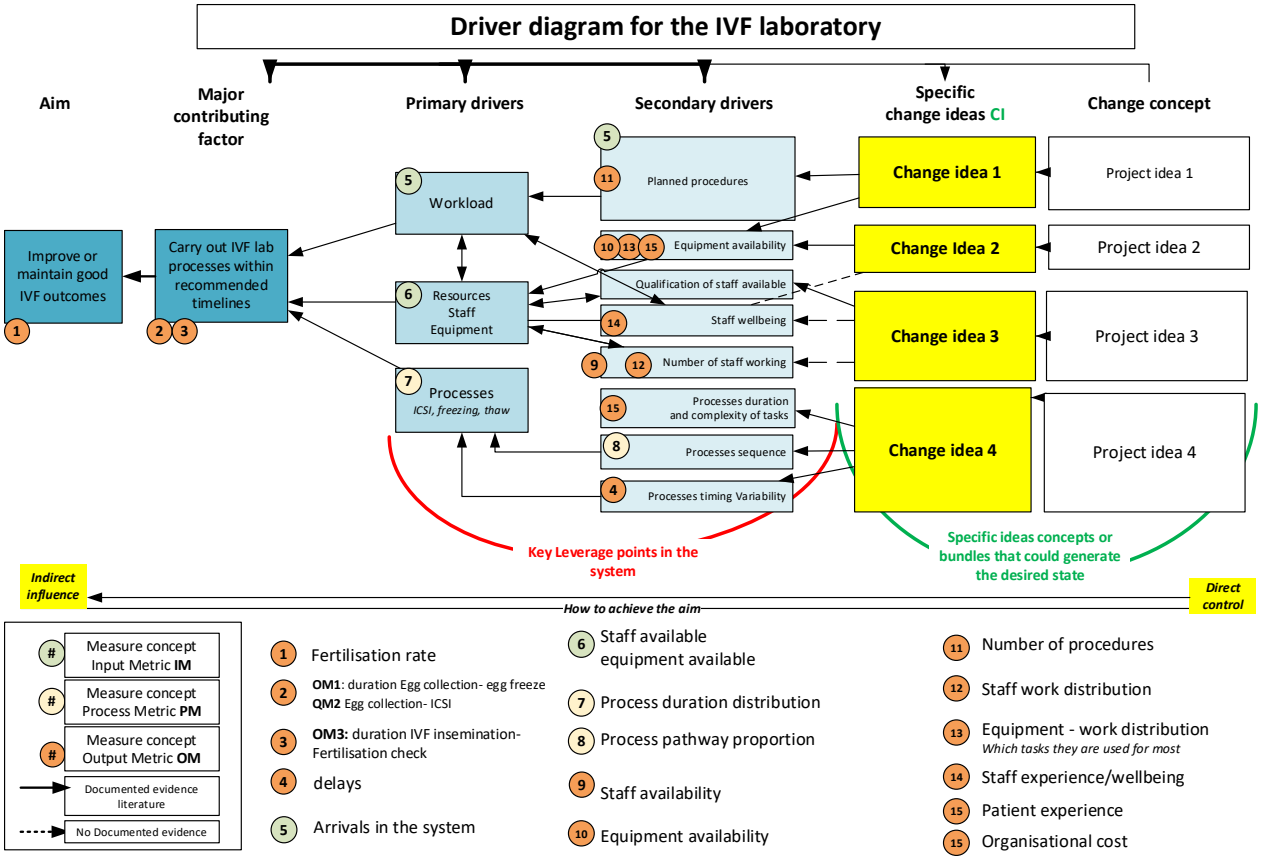

Figure 9. *AEM diagram adapted for IVF lab QI initiative*

The AEM diagram shown on Figure 8 was adapted to the IVF lab situation to start a QI project. The diagram goes from left to right from what we are trying to achieve and what the contributing factors to this, then the primary drivers who are influenced by secondary drivers. The diagram allows linking all concepts involved to know how to act on the system with change ideas (right of the diagram)to change the outcomes. The coloured circles are the concepts that we can measure to assess the drivers of change whether they are input metrics, process metrics or output metrics.

1.2 Discrete event simulation in healthcare and IVF- Literature review

1.2.1 Discrete event simulation in healthcare

Healthcare systems are inherently complex and unpredictable, often operating with limited resources and facilities, such as staff and premises. These systems face constant pressure to ensure safety, efficiency, and cost savings.

What is simulation modelling

Simulation imitates a system that progresses through time. It can be static or dynamic. One of the best examples used daily is the weather forecast simulation or display where we can see a simulation movement of weather fronts over days ahead such as movement of rainy clouds over time or visualisation of rain prediction. The IVF lab is a dynamic system that progresses through time with all three elements where simulation can be helpful: **interconnection, complexity and variability**. There are different techniques of simulation modelling : Monte Carlo simulation, system dynamics, agent-based simulation and DES (Robinson *et al.*, 2004). The latter is widely used across healthcare systems because it models queuing systems. DES is represented by entities flowing from one activity to another and activities are separated by queues. Queues result when activities arrive at a faster rate than processed by the next activity. Computer simulations serve as valuable modelling tools to address the dynamics of such complex environments. They provide a visual representation of how real-world systems operate over time, helping to identify critical points and bottlenecks while enabling the exploration of "what if" scenarios without any practical or financial implications (Vázquez-Serrano, Peimbert-García and Cárdenas-Barrón, 2021).

DES is a tool to **visualise, measure and improve** complex and interconnected systems such as the IVF lab. DES as a QI tool, has been used in healthcare (Simul8, 2024; Ramwadhdoebe *et al.*, 2009; Proudlove *et al.*, 2017; Vázquez-Serrano, Peimbert-García and Cárdenas-Barrón, 2021). Simulations can estimate the consequences of various interventions in healthcare, allowing identification of the optimal scenario based on desired outcomes (Marshall *et al.*, 2015; Jahn *et al.*, 2010; Ramwadhdoebe *et al.*, 2009). A

recent review of 231 papers focusing on simulation modelling in healthcare (Vázquez-Serrano, Peimbert-García and Cárdenas-Barrón, 2021) highlighted a growing trend from 1994 to 2021 in using this methodology to tackle operational challenges in healthcare settings. The same review identified that the most used simulation software in healthcare were Arena® (Rockwell Automation, Milwaukee, WI, USA)(35%) (Automation, 2025) and Simul8© (Simul8 Corporation, Boston, MA, USA)(21%). However, 32% of the publications did not mention the software utilized. Both Arena® and Simul8© allow the modeler to develop hybrid simulation models in the same interface environment and both have been used in healthcare. There is no peer reviewed published comparison of both software on a same model but software comparisons are available online. In comparison websites such as Capterra(Inc, 2025) and SalesForge (media, 2025), Simul8© has been recognised as a user friendly interface, accessible for new and experienced users allowing a quick model building and easy interpretation of results. Simul8© is recognized as one the fastest simulation engines allowing users to create and test models rapidly for easy decision- making. The limitation of Simul8© comes from the fact that it is not a multi complex simulation tool and does not give 3D visualisations as its competitors. Arena® has a detailed approach for DES, which makes it powerful but might involve a complex and long curve for learning. Users have noted that Arena® can be clunky and may require more steps to accomplish tasks compared to Simul8©, which could slow down the modelling process. Both tools are applicable across various industries, but Arena® has a stronger foothold in manufacturing and logistics, while Simul8© is versatile across multiple sectors including healthcare and logistics.

Outcomes measured by simulations in healthcare can encompass various factors, including time efficiency, resources utilisation, time spent in the system, financial savings, resource allocation and scheduling, quality and defect rates, as well as patient health and safety. Most studies reviewed were conducted within hospital emergency departments, primarily led by academics for research purposes. Notably, only 10% of these studies demonstrated evidence of implementation. Barriers to implementation have been identified as the following (Brailsford *et al.*, 2013; Brailsford, 2005; Vázquez-Serrano, Peimbert-García and Cárdenas-Barrón, 2021; Johnson, Burgess and Sethi, 2020): First the culture in healthcare, professionals often create workarounds in response to pressure to

solve problems immediately instead of taking the time to do a root cause analysis. Second is the infrastructure that lacks access to accurate data. Data recording in healthcare suffers from inefficient routines for administrative tasks. The next challenge is the scale, complexity, and healthcare intricate systems. Healthcare systems are grouped under the same umbrella but there is a huge diversity and variations across the system that can complicate implementation. Another identified challenge to implementation is the buy-in and credibility: In fact, there is often distrust for QI initiatives in healthcare due to a lack of knowledge and training in such disciplines by healthcare practitioners. The conflicting objectives in initiating this type of project is a major barrier. The reason is a difference in priorities between managers and medical personnel and that can hinder alignment for the same purpose using a tool that is introduced by management. Hospital managers often see the operational models as a tool to influence change driven by government performance targets. Many healthcare workers resist to yet more changes introduced by management as they struggle to cope with every day's workload already in addition to feeling that models brought in by management are trying to reduce human beings to widgets in a production line to meet targets and agenda. (Brailsford *et al.*, 2013; Brailsford, 2005). Managers focus is perceived to be political objectives and healthcare workers focus is manageable workload and patient's care.

1.2.2 Simulation in IVF and embryology

Before the project was started, recent literature was explored to research computer simulation in IVF/embryology in relation to procedures' timings and staffing. A literature review using PubMed Database was conducted on 21/09/2022 and updated on 29/09/2024 using the following keywords in different combinations, IVF, timing, simulation and staffing. The review showed the publications numbers shown in **Table 2**.

Table 2. *Literature review search results with different wording combinations*

	IVF	***Timing***	***Simulation***	***Staffing***	***Embryology***
	X	*656*	*171*	*19*	*1970*
Timing	*X*	*X*	*7983*	*1660*	*5081*
Simulation	*X*	*X*	*x*	*1578*	*3033*
Staffing	*X*	*x*	*x*	*x*	*42*
Embryology	*X*	*x*	*x*	*x*	*x*

After filtering through titles and abstracts for relevance to the subject and removing duplicates, we obtained the following number of publications shown in **Table 3**.

Table 3. *Literature review search after removing non relevant/duplicate articles*

	IVF	***Timing***	***Simulation***	***Staffing***	***Embryology***
IVF	*X*	*147*	*154*	*10*	*0*
Timing	*X*	*x*	*0*	*41*	*35*
Simulation	*X*	*x*	*x*	*0*	*3*
Staffing	*X*	*x*	*x*	*X*	*10*
Embryology	*X*	*X*	*x*	*X*	*x*

Simulation and modelling in embryology articles were primarily focused on embryo development (Briscoe, 2019; Sugita, 1966; Rosado-Olivieri and Brivanlou, 2021). This confirms that simulation has an established role in education and training of healthcare professionals. (Brazil, Purdy and Bajaj, 2019). It has been employed in training contexts (Chase *et al.*, 2020; Heitmann *et al.*, 2017; Mo *et al.*, 2020), including the simulation of ovulation and the creation of developmental models (Leung *et al.*, 2022). Research on simulation modelling in IVF has largely concentrated on the cost-effectiveness of various protocols (Almaslami and Aljunid, 2020 Cassettari *et al.*, 2016; Al-Inany *et al.*, 2006)), the

application of mathematical modelling for quality control (Awadalla, Ingles and Ahmady, 2021; Abbara *et al.*, 2018), and decision-making processes (Babigumira, Sharara and Garrison, 2018).

Staffing in embryology and IVF laboratories has been addressed in the literature through various guidelines (Kasraie and Kennedy, 2024; De los Santos *et al.*, 2016; Veiga *et al.*, 2022; Lee *et al.*, 2023). While several articles emphasized the importance of training and competency among embryologists (Keck *et al.*, 2005; Veiga *et al.*, 2022; Go, 2015b), there remains to be a lack of consensus or a defined model regarding the optimal number of embryologists needed to ensure safe, high-quality care and manageable workloads (Alikani *et al.*, 2014; Cohen *et al.*, 2018a).

Studies have highlighted variability in IVF laboratory practices, especially that many tasks remain manual (Paternot *et al.*, 2011; Mains and Van Voorhis, 2010) and introduction of new technologies is dependent on budgets allocated. The timing of the IVF lab tasks, crucial to success rates is influenced by workload and staffing levels (Expósito *et al.*, 2010; Priddle, Pickup and Hayes, 2022). With timings being key for success, there is a lot of pressure in the IVF laboratory and currently a growing concern regarding work pressure on embryologists and their wellbeing (Murphy *et al.*, 2023; Fitzgerald, Legge and Frank, 2013; López-Lería *et al.*, 2014; Campbell *et al.*, 2022; Priddle, Pickup and Hayes, 2022). Embryologists are the main resource of the IVF lab and their wellbeing (mental, physical) is crucial for the service delivered to patients.

The literature review in PubMed using the word combinations IVF, Timing, Simulation, staffing, embryology has shown that this QI concept (simulation modelling) has never been used to analyse workflows and constraints in assisted conception units or the IVF laboratory. Workflows in the IVF laboratory have been reported as major contributing factor to procedures' timing and hence final outcomes.

1.3 Summary of introduction and literature review

The literature review served as a knowledge base to build a driver diagram for a QI initiative to evaluate, support effective design, execution and evaluation of DES as a QI

method for analysing and trialling change ideas. (Reed *et al.*, 2014). The shared knowledge was highlighted by the literature review that the time spent on procedures involving gametes and embryos, as well as the timing of these procedures in the IVF lab, are critical parameters that can significantly influence success rates. Both factors are contingent on the available laboratory resources—staff and equipment—alongside the workload that must be managed. Despite the importance of this topic, published literature assessing staffing resources necessary to meet the required timings in IVF laboratories has primarily relied on approximations (Campbell *et al.*, 2022; De los Santos *et al.*, 2016; Expósito *et al.*, 2010; Keck *et al.*, 2005; Veiga *et al.*, 2022; Alikani *et al.*, 2014; Lee *et al.*, 2023).

1.4 Relevance of this research and innovation

The literature review has revealed a significant gap in knowledge in QI initiatives linking workload, resources and processes in the IVF lab. The application of DES for IVF laboratory workflows was also a concept that has never been used in the field as an improvement tool. None of the articles reviewed focusing on simulation in healthcare specifically addressed IVF laboratory processes, highlighting a potential area for further exploration. Additionally, most articles about simulation are mostly carried out by simulation experts and less by healthcare professionals. DES can effectively model complex healthcare environments characterized by unpredictable workloads, emphasizing the importance of timing and procedural durations like emergency departments. DES among other QI tools offers the ability to analyse, identify, and trial various scenarios without any real-world repercussions. Utilizing this technique to support QI could help identify bottlenecks in the IVF workflow and evaluate whether staffing levels affect the timing and execution of procedures. Additionally, it may assist in determining optimal staffing levels necessary to perform procedures within the required timeframes, ultimately to achieve the best outcomes for patients.

Simulation and IVF laboratory

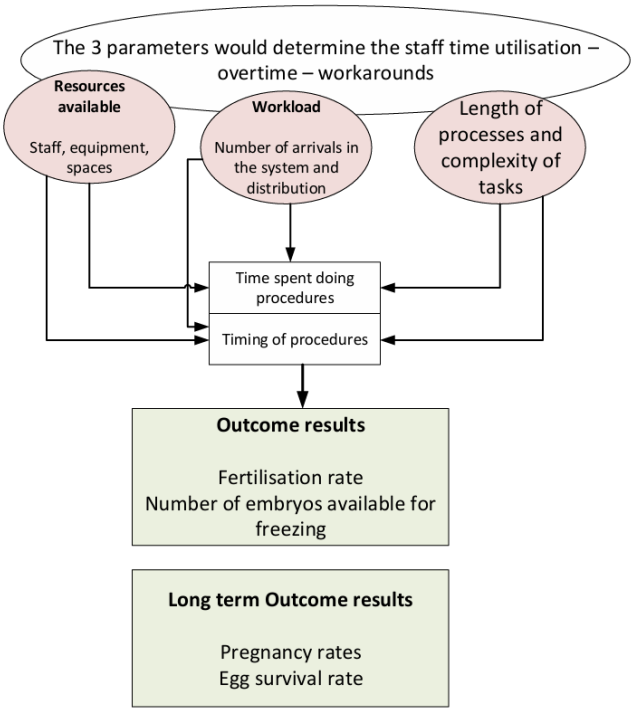

Figure 10. *IVF lab processes*

The diagram shows the link between the 3 secondary drivers: resources, workload and time length of procedures. The 3 drivers will determine staff utilisation during a workday, which then influences timing of procedures and finally outcome results

The link shown here linked between staffing-workload-timings to influence outcomes suggest that staff time utilisation can be a proxy for outcome results

The IVF laboratory operates as an operational system that is subject to 3 parameters linking to time and timings (duration between two tasks) : Firstly. **Variability that is** predictable such as staff and unpredictable such as length of processes. Secondly **interconnection,** where none of the processes work in isolation but rather affect one another; any change in one part can affect the other (ie: delay in egg collection can delay insemination or egg freezing). The third parameter is the complexity of the tasks requiring hand eye coordination and scientific knowledge. The IVF lab is an operations system that is variable, complex and has many interconnected processes. It is a system that includes human activity and is a result of a physical system that progresses through time. To understand the influence of each parameter that affects timing in the IVF lab in its complexity and variability (**Figure 10**), we investigated QI techniques published in healthcare settings and determined that simulation modelling responded to the 3

parameters named above, especially with regards to modelling requirements for staff resources.

Simulation modelling in IVF

The literature review showed an increase in interest in healthcare simulation modelling publications and one of the most used software in healthcare DES studies is Simul8© (Vázquez-Serrano, Peimbert-García and Cárdenas-Barrón, 2021). According to the literature review, the challenge in healthcare remains the implementation phase that stems from simulation analysis studies even though the final purpose is improving results, patient experience and staff time utilisation.

The objective of this research was to use the driver diagram described above for the study (**Figure 11**) to **firstly** use DES to map the IVF lab workflows and create a dynamic simulation model that mimics the lab workflows on Simul8© software. The second part of the project was to validate the model created. **The third part was to** use the simulation model to analyse if staffing levels are affecting workflows and hence patients' outcome results and identify bottlenecks in processes. **The fourth part** of the project was to use the simulation model created and validated to try "what if scenarios" and suggest effective improvements. Assisted conception services could potentially benefit greatly from DES use and application, firstly to understand the dynamics of the system by using a different tool that has never been used so far. This could lead to marginal improvements in practice or not at all but still adds a learning from the process of trialling a new tool used in other dynamic systems such as A&E and airports. This should result in a worldwide learning experience to share with practitioners and researcher in the IVF community.

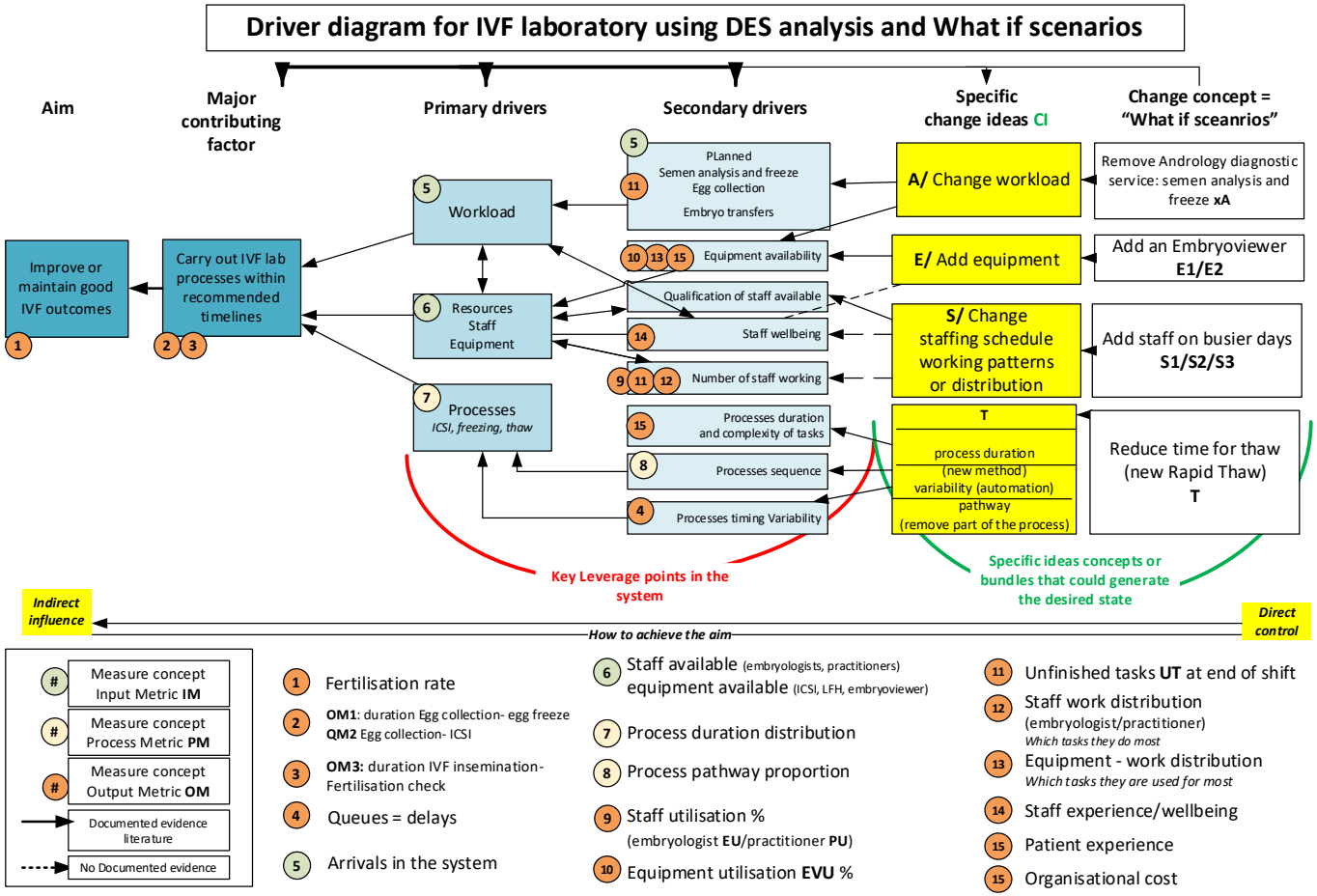

Figure 11. *Driver diagram for the IVF lab using DES analysis (simul8©)*

The driver diagram created in Figure 9 adapted for the project analysing the IVF lab dynamics and introducing change ideas using DES. The IM, PM and OM (circles in green, yellow and orange) are the specific measures used and detailed later in the project. The change ideas come from the identified issues with the secondary drivers

2 AIMS AND OBJECTIVES

2.1 Aims

The aims of this study were to demonstrate the intricate link between staffing in the IVF lab, timing of IVF lab procedures and the final IVF outcomes. The long-term aim was to use this project as a resource for forward planning.

2.2 Objectives

The first objective of this study was to create a computer simulation model using Simul8© software, a model that covers most clinical tasks carried out by embryologists. The second objective was to validate this model to confidently confirm that it is a "digital twin"- high computer representation of the real system running in close-to-real-time. (Salehnejad and Proudlove, 2023) for the real-world IVF lab to reproduce its most important features despite its complexities. The third objective was to have some metrics from the base case model created that allow to analyse the IVF lab workflows. The final objective was to compare the data from the base case model created to the results from different scenarios experimented on the model (change ideas) applied to resources (staff and equipment) workflows and planning.

2.3 Research questions

- Can the IVF lab be modelled into a DES "digital twin" as defined in the literature?
- Can the model created in Simul8© give usefully accurate results and be validated?
- Does the analysis of the model data show any link between staffing levels – duration of procedures and clinical outcomes?
- Can the scenarios tested point towards the answer of what the optimum working conditions are to carry out all the IVF tasks on time ?

2.4 Hypothesis

The hypothesis posits that an IVF laboratory can be effectively modelled using DES in Simul8© software and that the model can be validated and used to confirm correlations

between staffing, timing of procedures and clinical outcomes for experimenting different scenarios and forward planning for staffing and workflows to improve outcomes.

2.5 Rationale for the project

The IVF community and especially embryologists have been trying to address the embryology lab staffing issue using approximations and building recommendations (Alikani *et al.*, 2014; Kasraie and Kennedy, 2024; De los Santos *et al.*, 2016). Staffing in the embryology lab is a pressing concern especially with the complexity of tasks, strain to deliver tasks on time and safety concerns such as errors risk, serious incidents, staff burnout (Priddle, Pickup and Hayes, 2022). This project used a driver diagram and the AEM in an attempt first time ever to deploy a QI tool: simulation modelling using the software Simul8© to model the IVF lab as accurately as possible incorporating all procedures carried out by embryologists and have a more detailed view on the staffing and the lab processes incorporating resources and workload with dynamic timing. Simulation models are capable of imitating dynamic and complex interconnected systems characterized by significant variability as they evolve over time. The healthcare sector, and specifically the IVF laboratory, embodies all three elements that make it an excellent candidate for DES especially that it has never been used in IVF laboratory as per literature review.

2.6 Stakeholder engagement

The project aligns closely with the strategic objectives and requirements of Guy's and St Thomas' NHS Trust- GSTT (Trust, 2024) and its regulator, the Human Fertilisation and Embryology Authority (HFEA, 2020). Specifically, it emphasizes the use of data for continuous improvement, for the best patient outcomes, and supports responsible innovation to promote new and more effective ways of working. This approach also contributes positively to the Trust's financial position.

Ultimately, the project seeks to enhance patient experience and outcomes while improving staff experiences and utilization, potentially leading to cost savings. This aligns with the Trust's new values of providing "better, faster, and fairer healthcare."(Trust, 2024). This project is particularly relevant, as it is expected to directly benefit the IVF clinic and its patients, resonating with the interests of all stakeholders involved.

Stakeholder engagement has been actively initiated through various channels:

1. Presentation of the preliminary project outline: The initial project was presented to the GSTT-ACU team in December 2022.
2. Sharing preliminary results: The preliminary findings were shared with the wider IVF community at the Alpha Meeting Conference in June 2024 (Kaffel *et al.*, 2024), as well as with the Evewell clinic's embryology team in London in July 2024 where the HSST trainee was employed as a lab manager from April 2023.
3. Final project outcomes presentation: The final outcomes of the project were presented to GSTT-ACU embryology team in September 2024. Stakeholder engagement was measured through a questionnaire distributed via Google Forms (Kaffel, 2024b) as outlined in Appendix 4.

Engaging a healthcare team (here the embryology team) is a critical contributor of the model validation process and its overall viability. (Proudlove *et al.*, 2017)

2.7 Innovation

A new concept is investigated in this project: looking at IVF lab processes and staffing in a different way and with a different tool that encompasses all tasks involved rather than each one in isolation. The embryologist must carry out tasks manually and all pathways and tasks are complex and interconnected with time being the main pressure. The literature review highlighted a notable absence of publications regarding the use of DES in IVF workflows. The innovation of this project lies in its pioneering application of this concept to analyse process flows within the IVF laboratory. Most simulation examples are reported in simulation journals, with simulation expert authors, rather than institutional QI teams (Brazil, Purdy and Bajaj, 2019). This project of simulation modelling has been initiated and developed by an embryologist seeking to improve outcome through a QI approach by involving a collaboration effort with: An embryologist (SME) who possesses expertise in the workflows and has a comprehensive knowledge of all relevant processes. A Simul8© consultant with extensive experience in DES and proficiency in the Simul8© software. This project examines the IVF lab staffing issue in a different new approach that was never used in the past and is driven by a clinical need rather than merely academic interest, emphasizing its practical relevance and potential to address real-world challenges in the IVF setting.

3 METHODOLOGY

The use of DES as a QI initiative needs to link into an underlying QI theory. The QI theory enforces the ability to demonstrate causality, allows a strategy of implementation and it also contributes to understand the effectiveness of DES in the context studied. The AEM connects potential interventions and implementation activities with an overall improvement objective through a diagrammatic representation of hypothesised and evidenced cause/effect relationships. A driver diagram was created to lay out the use of DES in the IVF lab as a QI initiative.

This DES research approach is grounded in Robinson's Discrete Event Simulation (DES) framework (Robinson, 2014) to address complex problems by virtually replicating real-world scenarios. Key stages of this process are illustrated in **Figure 12** below.

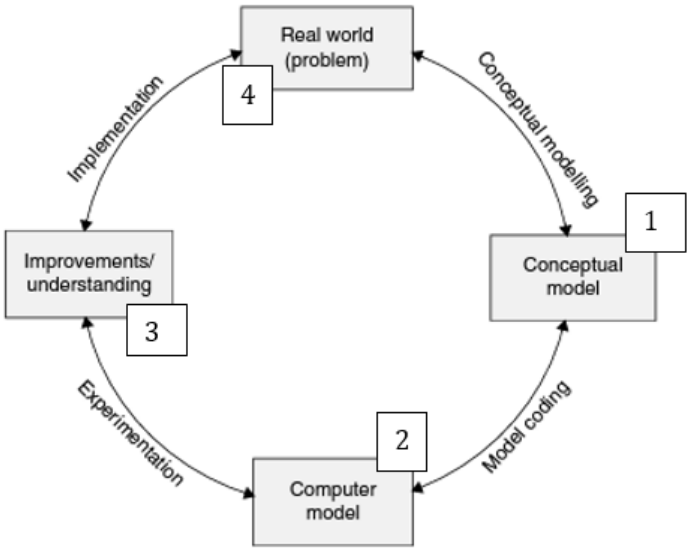

Figure 12. *Simulation studies key stages and activities.*
The figure shows an outline of a simulation study (Robinson, 2014b). It starts and comes back to the real-world problem. The boxes represent the key stages and important deliverables in a study: (1) conceptual model : description of the model to be developed (2) computer model: the simulation model implemented on a computer (3)Improvement/understanding derived from the results of experimentation (4) The real-world problem that is the starting point and can be improved by implementing the understandings gained from the previous step

3.1 Ethics

This project has been categorized as a service improvement initiative and did not require approval from the Health Research Authority (HRA), as confirmed by completing the NHS HRA questionnaire and discussing the project with the Research and Development department at GSTT (**Appendix 8**).

An application for service improvement at GSTT was authorized (Appendix 6, Appendix 7) as Audit No. 16169 and an EthOS application with Manchester Metropolitan University (MMU) was also approved (EthOS reference number 69416, **Appendix 5**).

3.2 Study design: Driver diagram

A driver diagram was used to map the QI initiative (**Figure 9**, **Figure 11**). It described the overall objective of the improvement. Contributing factors are boxes representing the logical steps required to connect the interventions and the objective. They are caused by the intervention(s) and the achievement of the objective is caused by them. The methodology used is also described in **Figure 13**.

3.3 Conceptual model

Creating a conceptual model that accurately represents the real system was essential before conducting further analysis. The fundamental principle behind developing an accurate conceptual model using DES is to thoroughly understand all processes, activities, and resources involved (Law and Winter Simulation; Robinson, 2014a). The information required to construct the model includes details about the activities involved in lab processes and their pathways (sequences), the rate of arrivals into the system, the duration of each activity, and the availability of resources needed for each task (such as equipment, space, and staff).

3.4 Computer model

Simul8© was the simulation software chosen to build the computer model using the process map designed in the conceptual model phase. The simulation design first step was to translate the conceptual model (**Figure 27**) into its computer model copy on Simul8© Software in a step-by-step approach adding all input data that came from the

real-world setting (Process metrics: pathways, proportions in each pathway, timing distributions, resources used). The translation of the conceptual model into a computer model consisted of having consecutive activities, queues and endpoints to mimic the workflow. Adding input metrics into the model (arrivals) should result in the model generating output metrics that can be compared to real life. Before the model can be used for analysis, it must be continuously verified by the team and validated by comparing the output results from the simulation to the output results from the real model. Validation makes sure that the model accurately represents the behaviour of the actual real-life system.

3.5 Output metrics - Validation

The most important in using simulation data is to obtain accurate Output Metrics (OM) after entering input data or Input Metrics (IM). The key in obtaining accurate results is dealing with initialisation bias and obtaining sufficient output data to have an accurate measurement of performance (Robinson, 2014a). Obtaining sufficient output data is obtained by carrying out multiple replications or runs of the model to reduce the variance. The recommendation in literature is to run 3-5 replications (Law and Winter Simulation, 2022). Simul8© software as well as many simulation packages can provide an experimentation option that allows the user to have a suggested number of replications for each output parameter and provides then a confidence interval. A significance level of 5% has been selected to determine the number of runs necessary for each output parameter which means there a 95% probability that mean is obtained within the confidence interval.

3.6 Experimentation analysis

Experimentation analysis or "what if scenarios" analysis can be generated from the model created by changing the model settings: changing input metrics (number of staff available, number of equipment), changing process metrics (change of pathways or pathway duration for example) to observe how the output metrics change. Simulation does not give a ready answer or solution but offers to vary metrics in a simulation and observe if that resolves an issue that was identified.

3.7 Data and statistical analysis

Before starting to analyse any simulation data, an empirical data statistical analysis was conducted on retrospective 2022 data parameters OM1, OM2 and OM3 link to fertilisation rate (FR) outcome. This was used to demonstrate the link between time durations of some lab processes (OM1, OM2 and OM3) and clinical outcomes. The statistical link between both parameters was investigated using first chi square test for comparing FR in each category then a linear regression improved by a logistic regression test linking OM2 and OM3 to FR.

White box validation for process metrics (PM) and black box validation statistical analysis compared the data distribution delivered by the model for PM (egg collection, embryo transfers, sperm freezing) to 2022 data. OM1, OM2 and OM3 versus 2022 real-life distribution using an independent t-test with a *p value <= 0.05* indicating strong evidence of statistical significance. No statistical analysis was used to compare scenarios to BC for the distribution of OM1, OM2, OM3.

Using t-student independent test for comparing distributions between the simulation model and real-life data assumes that a simulation model behaves exactly the same as real-life which is controversial but it is the closest statistical test to use to validate the model in a tangible format (Law and Winter Simulation, 2022). It also assumes that the data from 2022 is the true value but it is only a year of workload. We have chosen to plot 2022 data into 110 simulation runs for PM. For OM parameters, only 5 simulation runs were tested against 2022 data.

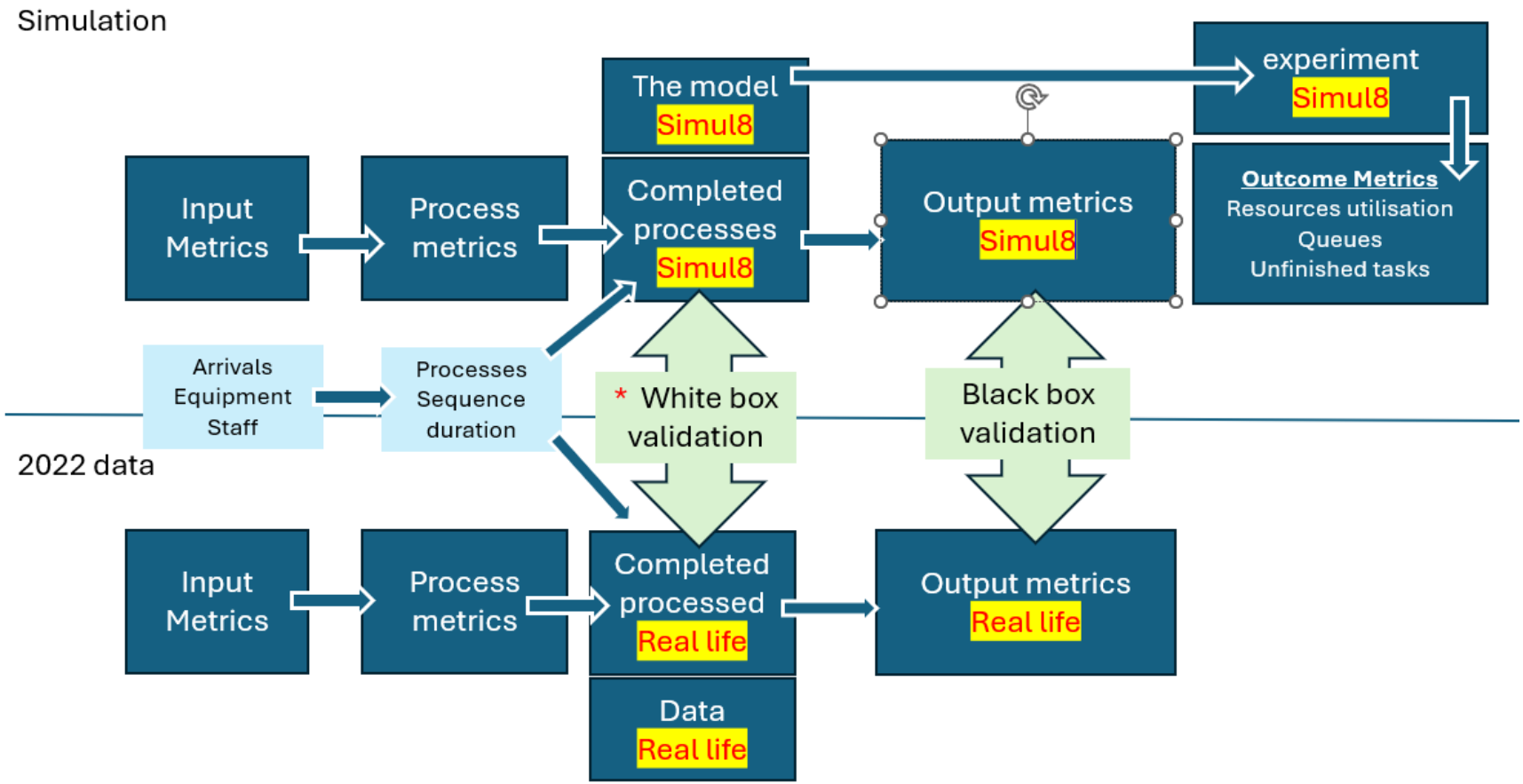

Figure 13. *Methodology of computer simulation design, validation and scenario testing*

It includes collecting input metrics IM (arrivals, equipment and staff), process metrics PM (sequence proportions, durations) to create a model that can be compared to real life data by using a white box validation. The model produces output metrics OM used to do a black box validation and then analyse the system. The model can then be used to experiment new strategies and analyse their effect on the OM.

4 EMPIRICAL STUDY

The study was carried out using GSTT-ACU IVF lab model utilizing a one-year dataset gathered from GSTT-ACU from January to December 2022. GSTT-ACU is the largest NHS and Preimplantation Genetic Testing (PGT) fertility centre in the UK. This centre handles on a yearly basis approximately 1,500 fresh cycles (egg collections including egg freezing), 400 PGT cycles, and 1,500 frozen embryo transfers (FET), offering services such as IVF, ICSI, egg freezing, embryo freezing and thawing, and fertility preservation. The year 2022 was chosen as the base of the model as it was the closest complete up to date data before the start of the project (March 2023). The IVF lab at GSTT-ACU is divided into 5 working areas as per the floorplan (**Appendix 25**). In 2022, the embryology team was composed of 19 embryologists and 5 reproductive science practitioners contracted on full time and part time basis. The number of Whole Time Equivalent (WTE) staff members per month will be detailed later in the study.

As per the driver diagram (**Figure 11**), the fertilisation rate (FR) link to the time durations OM1, OM2 and OM3 in 2022 retrospective data at GSTT-ACU was explored first. Once the link was demonstrated through the retrospective data, OM1, OM2 and OM3 were used as proxy to success in the remainder part of the simulation project. OM1: Time between egg collection and egg freezing, OM2, time between egg collection and ICSI and OM3 time between IVF insemination and fertilisation check (**Figure 14**).

A conceptual model for the IVF lab was developed using previously created workflow diagrams (**Appendix 26**). This conceptual framework was then translated into a computer model utilizing Simul8© professional software (desktop version), with a weekly support from a Simul8© consultant (S8C).Both AK and the Simul8 consultant (S8C) collaborated through weekly Microsoft Teams meetings for over a year (April 2023 to May 2024), as outlined in a contract between AK, GSTT and Simul8© Corporation (**Appendix 11**, **Appendix 12**, **Appendix 13**, **Appendix 14**). All necessary data for constructing the model was extracted from GSTT-ACU databases by AK. The Simul8©

consultant contributed by applying their expertise in using the Simul8© software, while the underlying idea and conceptualization of the project were solely the work of AK.

4.1 Retrospective data analysis

Using the driver diagram as a roadmap for the project (**Figure 11**), focusing on maintaining good IVF outcomes (FR), the major contributing factors as described below and shown on **Figure 14** were : OM1, OM2 and OM3 as described in the literature review section above. OM1. time between egg collection and egg freezing, OM2, time between egg collection and ICSI and OM3, time between IVF insemination and fertilisation check. The primary measurable outcome from OM2 and OM3 chosen for our focus is the (FR= number of 2PN observed on day1/ number eggs inseminated x 100). OM1 success rate cannot be measured immediately and can take more than 10 years to measure as this involves egg freezing. When eggs are frozen, they can sometimes be stored for more than 10 years at the end of which they are not necessarily used by patients to allow measuring success. The reason why the time durations linked to these processes were chosen is that they are still manual, relying on embryologists' availability.

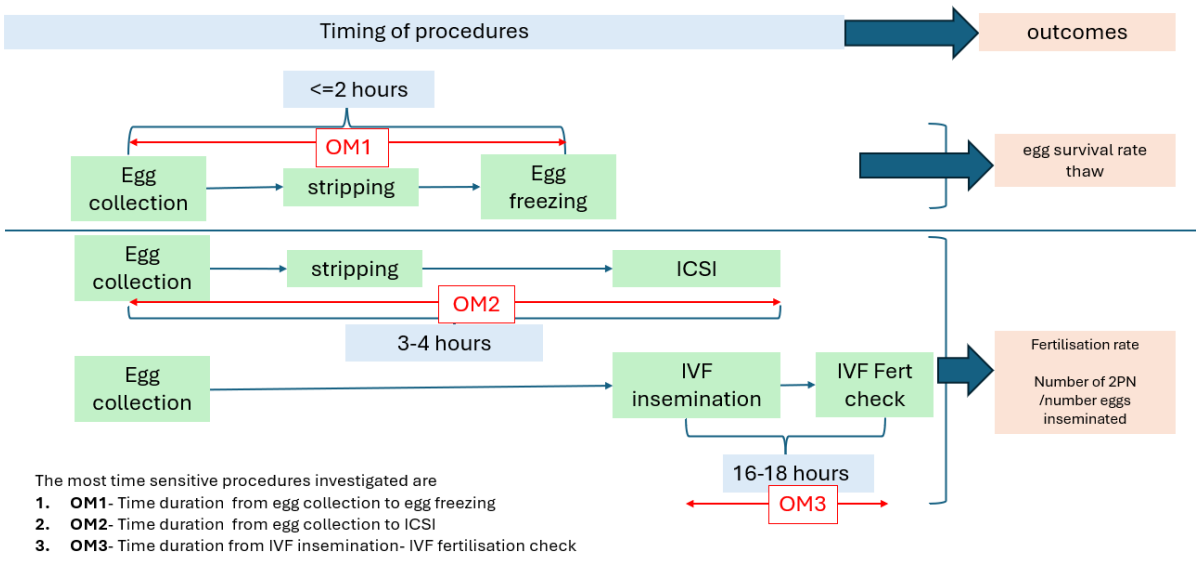

Figure 14. *Process duration OM1, OM2, OM3*

OM1, OM2 and OM3 were the 3-time durations in the IVF lab chosen as contributing factors to success. Parameters distributions during 2022 at GSTT-ACU were assessed in addition to their correlatiopn to fertilisation rate outcome for OM2 and OM3.

4.1.1 OM1 distribution - 2022 data

Following the Standard Operating Procedure (SOP) of egg freezing at GSTT-ACU (**Appendix 20**), the time separating egg collection and stripping is recommended to be up to one hour which is followed directly by the egg freezing process. According to the SOP, the egg freezing process can theoretically range take from 16 minutes to over one hour depending on how many oocytes are collected and how many straws are loaded with oocytes to freeze. According to the SOP at GSTT-ACU, OM1 should theoretically range from 1h16 to over 2 hours from the egg collection. The data from 2022 (**Figure 15**) shows a mean value of OM1 as 92 minutes ranging from 30 minutes to 394 minutes. Having set the target value at 120 minutes, 83% of OM1 values are within the target of 120 minutes. The literature confirms that eggs age through time and recommend egg freezing as soon as possible after egg collection but there is no general consensus on the best timing.

The SOP states that egg freezing should be 38-39 h post hCG which represents a mean of 2h post egg collection. Most studies report freezing eggs within 2 hours of egg collection which is why the target was set at 120 minutes (Parmegiani *et al.*, 2008; Gürtin *et al.*, 2019; Song *et al.*, 2010; Rienzi *et al.*, 2010) on the assumption that egg collection is scheduled 36h post hCG trigger. This time duration is important to allow thawing eggs in the future and allow them to recover before ICSI where ICSI is recommended to be done 2-4 h (OM2) post egg retrieval. The physiological background to the timing requirements has been described above : In vivo, oocytes are ovulated 36-38h post LH surge and 36-38h post trigger in an IVF cycle. Oocytes are then mostly arrested at the MII stage (called mature stage). If the oocytes are not mature at that point, a delayed maturation can negatively impact the outcomes of IVF cycles (Anagnostopoulou *et al.*, 2022; Lin *et al.*, 2003; Yılmaz *et al.*, 2022), and improper timing of sperm injection can be a primary reason for poor developmental outcomes of late-maturing oocytes (Yılmaz *et al.*, 2022). Oocyte ageing by incubating oocytes for a long time after their collection and before their insemination could be a cause for poor outcome (Santella, Limatola and Chun, 2020; Carvalho *et al.*, 2020).

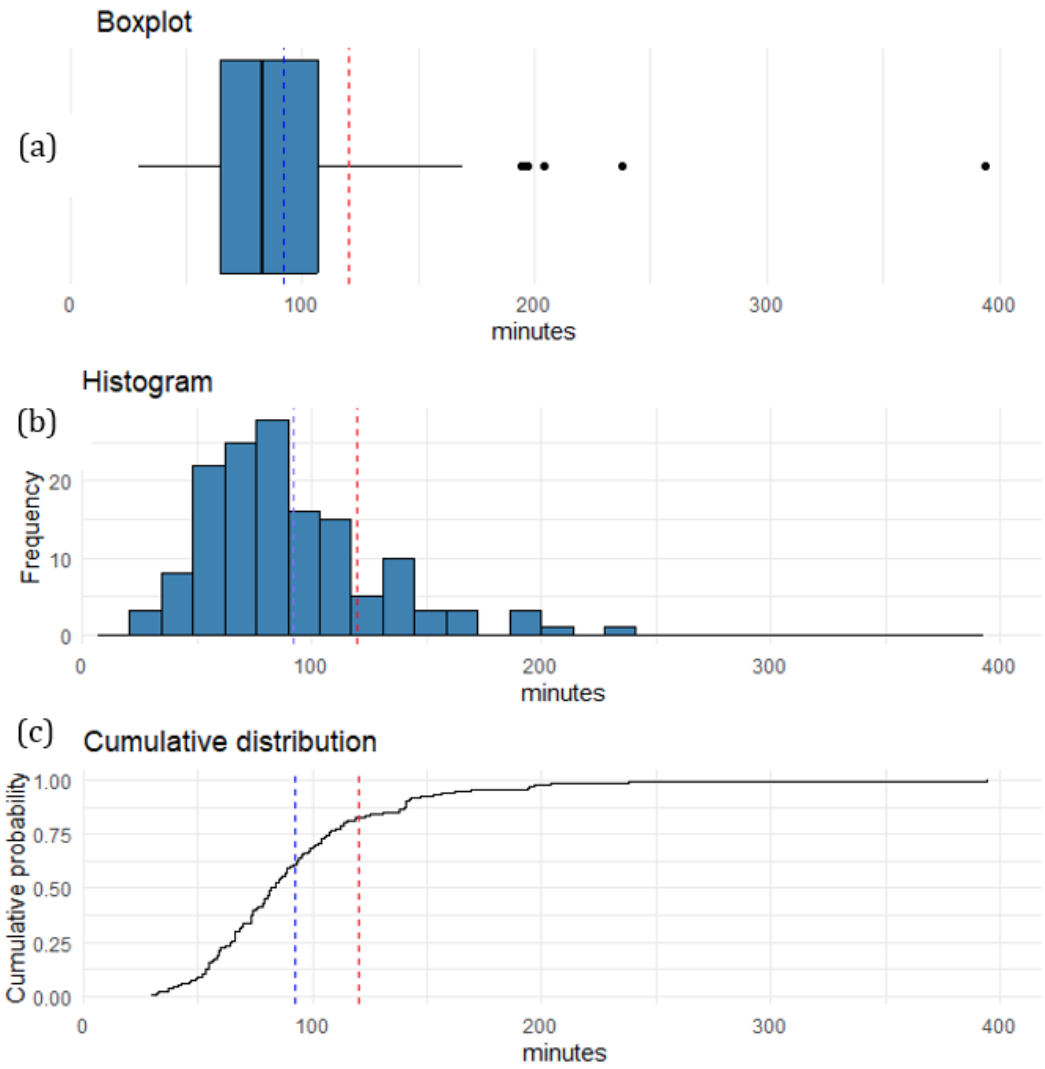

***Figure 15**. Distribution of OM1 at GSTT-ACU- 2022 data*

The dataset is represented by n=144. The distribution is presented in 3 different formats (a) boxplots (b) histograms and (c) cumulative distribution.

The mean value of OM1 is represented by the blue dotted vertical line and the target value of OM1 is represented by the red dotted line.

Observing the data from the day of egg collection's perspective (**Error! Reference s ource not found.Figure 16**), Mondays and Wednesdays have the highest number of egg-freezing procedures and Saturday the lowest. OM1 had a high variation across all days. Apart from Saturday where OM1 was over the 120 minutes target, the remaining days, most values were under the 120 minutes target. The median value during each day was lower than the mean 92 minutes with the median being closest to the mean on Mondays. Mondays and Wednesdays have the most outliers. The median was skewed towards the lower range for Thursdays and Fridays which means that OM1 tended to have a shorter timeframe.

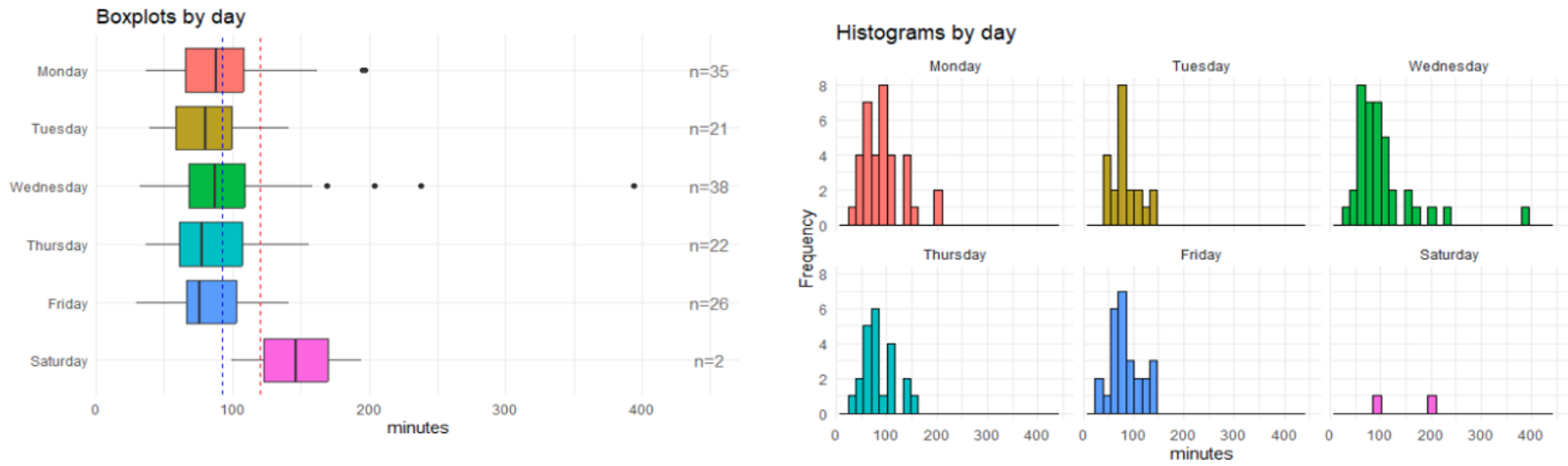

Figure 16. *OM1 distribution per day of EC- GSTT ACU -2022 data*

The data set (n=144) is shown as boxplot distribution (Left) depending on the day of the week where EC is carried out. This allows a visual understanding of values per day of procedure. The blue line shows the mean value of OM1 from the 2022 dataset, the red line showing the target line of 120 minutes. The n number on the right of the figure indicates the number of values in the set.

The same Data set is also shown as histograms (Right) depending on the day of the week where EC is carried out. It visually shows the distribution of the values on each day

OM1 first effect outcome could be measured by the survival rate of eggs post thaw (after defrosting). Unfortunately, this outcome is difficult to assess as a very low number of patients return to defrost their eggs and use them for treatment (Cascante *et al.*, 2022; Loreti *et al.*, 2024; Chang, Shapiro and Nagy, 2022). Eggs can remain frozen more than 10 years before being used. In fact a study at GSTT-ACU revealed that only 16% of patient returned for using their eggs (Kakkar *et al.*, 2023). In our data set, we could not study this effect as very few patients returned to defrost their eggs frozen in 2022.

4.1.2 OM2 distribution and link to outcomes - 2022 data

The SOP at GSTT-ACU recommends that ICSI is carried out after 12pm on day of EC, 38-41h post HCG (**Appendix 21**), ICSI being within 1h of stripping. Knowing that egg collections at GSTT-ACU are planned 36h post trigger (Kakkar *et al.*, 2023), the SOP recommendations mean that ICSI must be done 2-5h post egg collection where stripping is done immediately before ICSI. In reality, ICSI procedures are carried out as soon as staff and equipment are available but there is also a prioritisation according to the procedure difficulty and number of eggs to inject. We must also note that egg collections can be scheduled for up to 3:30pm and due to accumulated delay from the day, the 36h is not necessarily accurate. Delays in egg collections are not accounted for in ICSI time management. The literature review shows variable results with different durations of OM2, some in favour of OM2 being around 2-3 hours and some stating that there is no influence. It is accepted that it shouldn't be too prolonged as it affects the eggs' ability to fertilise (Wang *et al.*, 2021). There are many variabilities in the literature with OM2 timing as it is composed of two-time durations added to each other (egg collection to stripping and stripping to ICSI) in addition to time of egg collection being linked to different hCG trigger times. Considering the published literature, we have set a target as 3 hours for OM2.

GSTT retrospective data collected from RIW system (n=921) has shown that the distribution of OM2 for 2022 has a mean of 169 minutes (between 2.5 and 3 hours) and if we consider 180 minutes (3 hours) as a target, 57% of values were within the target value of 3h **Figure 17**. In fact, looking at the boxplot distribution, we can see a few outliers

on the histogram OM2 data from 2022 (n=921) showed a high variability in timing, 57% within 3 hours.

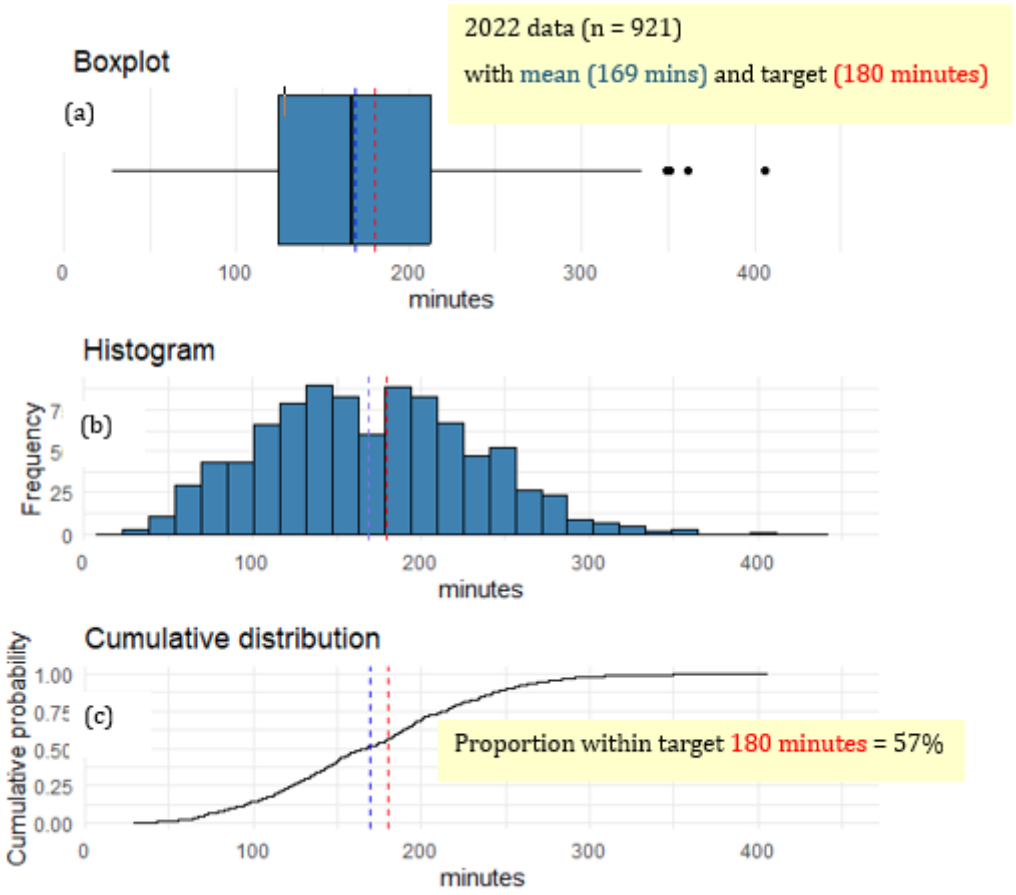

Figure 17*. OM2 distribution in boxplots, histograms and cumulative distribution*

The dataset is represented by n=921. The distribution is presented in 3 different formats (a) boxplots (b) histograms and (c) cumulative distribution. The mean value of OM2 is 169 minutes and if we consider the target as 180 minutes, 57% of OM2 are within the target

Observing the data from the perspective of the day the egg collection (**Figure 18**), Mondays and Fridays have the highest number of ICSI procedures and Saturday the lowest. **OM2** had a high variation across all days, apart from Saturday which is only represented by 2 values. The mean OM2 is lower than the target and is, on the busiest two days over 3 hours for the Tuesday to Thursdays.

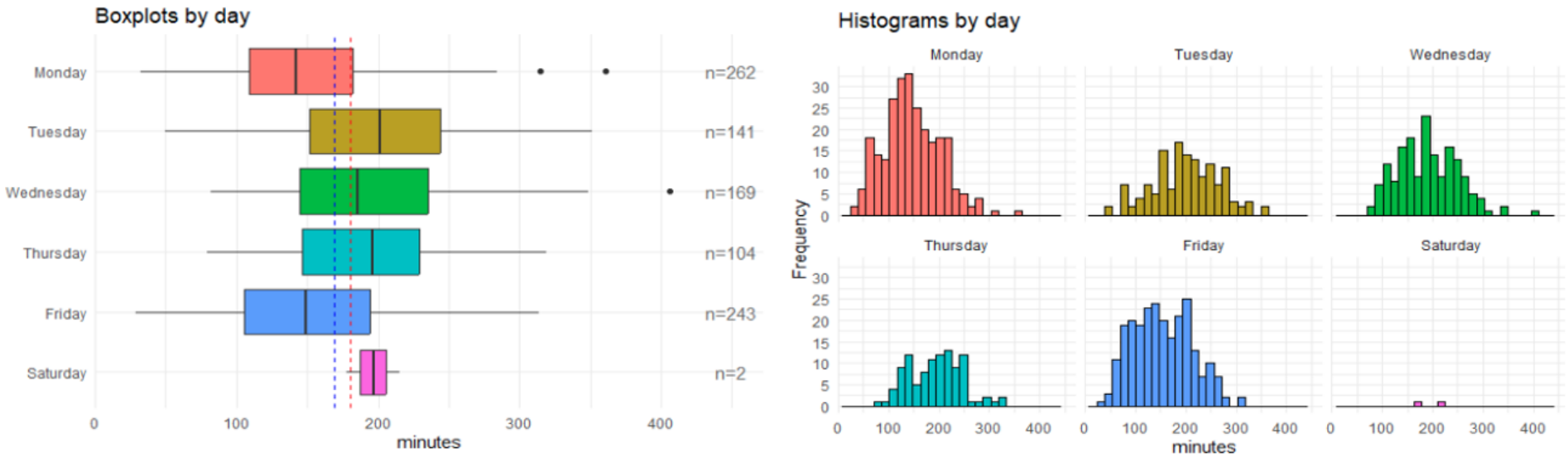

***Figure 18**. OM2 distribution boxplot egg collection day, GSTT-ACU 2022 data*

The data set (n=921) is shown as a boxplot distribution (left) depending on the day of the week where EC is carried out. This allows a visual understanding of values per day of procedure. The blue line shows the mean value of OM2 from the 2022 dataset, the red line showing the target line of 180 minutes. The n number on the right of the figure indicates the number of values in the set

The data set (n=921) is also shown as a histogram distribution for each day (right)

OM2 outcome was measured primarily by Key Performance Indicator (KPI) fertilisation rate (FR) assessed one day following ICSI (FR= number of 2PN observed on day1/ number eggs inseminated x 100). The Vienna Consensus (Embryology, 2017) sets the FR competency value for ICSI at 65% and the benchmark value at 80%. FR data was plotted as an outcome to the different OM2 time durations (in hours), the data has shown an increase of fertilisation rate with the increase of OM2 with a p-value <0.05 (**Table 4**, **Figure 19**). The FR outcome is closer to The Vienna consensus recommendation from OM2 >3h.

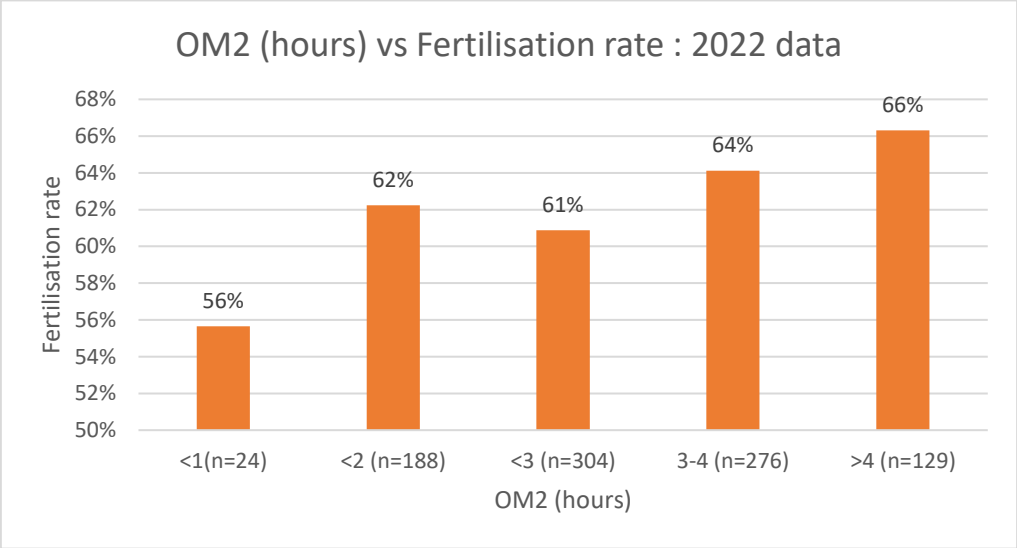

Figure 19. *OM2 versus fertilisation rate - 2022 data*

OM2 was stratified by time duration sets <1h, 1-2h (<2h), 2-3h (<3h), 3-4h (<4h) and >4h on the x axis. The corresponding FR were plotted on the y axis for each category showing a steady increase of FR as OM2 increases. The sample number in each category is shown by the number n

Table 4. *FR per OM2 duration - GSTT-ACU 2022 data*

The Chi-square statistic is 18.7514, p-value= 0.000879

OM2 (hours)	Count	Mean OM2 (minutes)	Inseminated eggs	2PN	FR
<1	24	49	230	128	56%
<2	188	95	1814	1129	62%
<3	304	148	3036	1848	61%
3-4	276	206	2717	1742	64%
>4	129	271	1253	831	66%
Total	**921**	**169**	**9050**	**5678**	**63%**

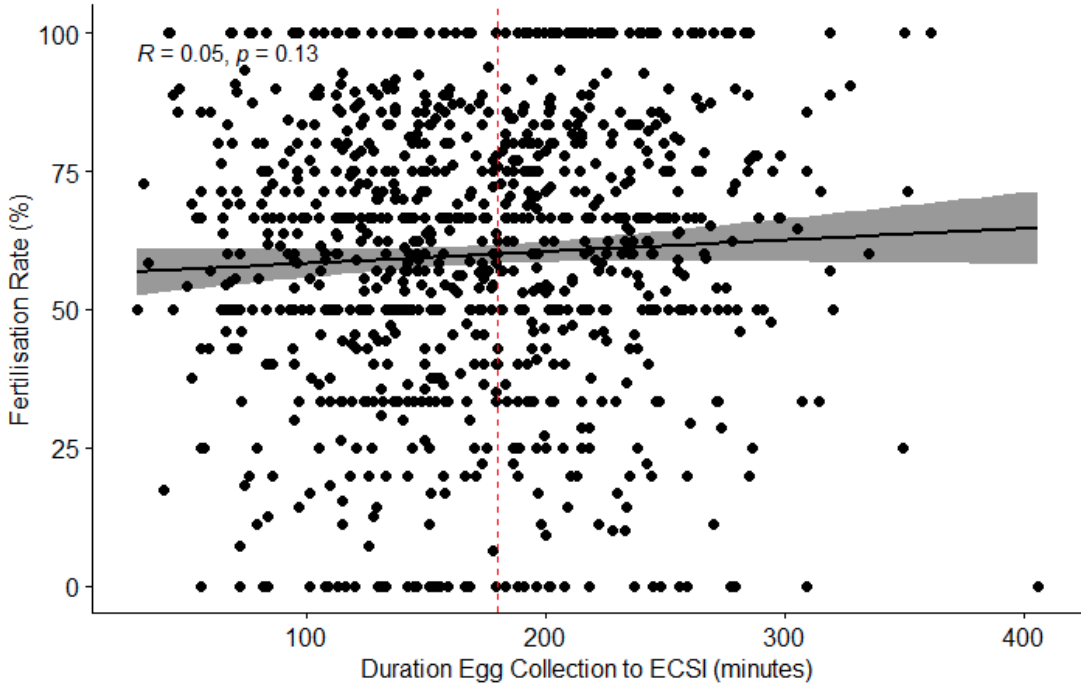

Figure 20. *Linear regression analysis between OM2 and FR- GSTT-ACU 2022*

OM 2(x axis) and FR (y axis). The equation is FR = 0.02 Duration + 56.19. The coefficient value 0.02 is not significant, p=0.126, >0.05

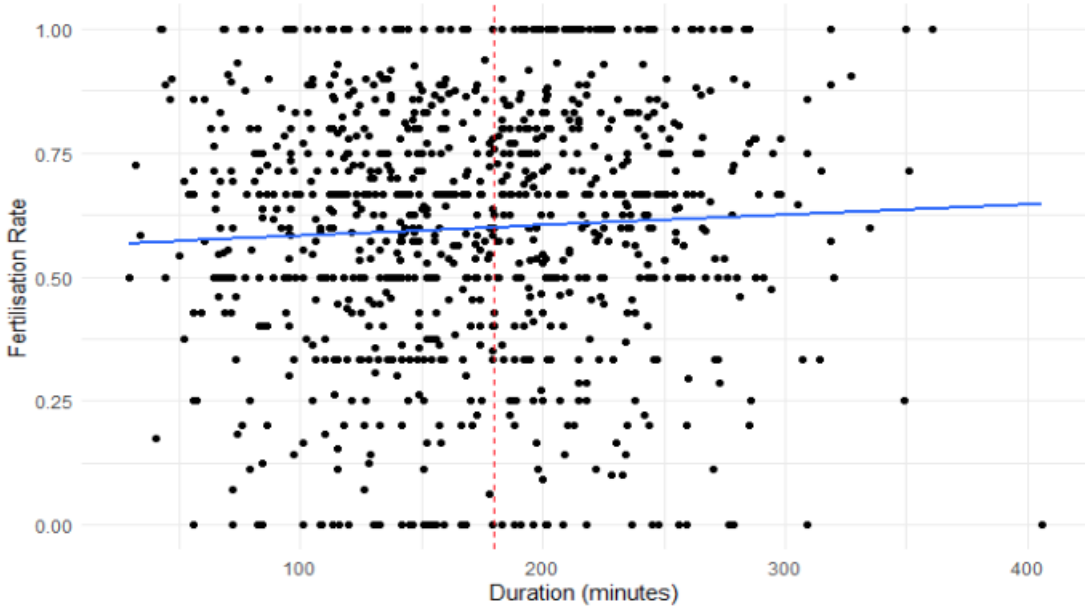

Figure 21. *Logistic regression analysis between OM2 and FR- GSTT-ACU 2022*

The logistic regression on the data set (n=9050 eggs) explores the link between OM2 in minutes (x axis) and FR as a probability of success 1= fertilised, 0= non fertilised. The coefficient of duration is significant (p=0.0013) suggesting FR becomes 0.12% more likely with each minute of duration.

A linear regression between OM2 and FR (**Figure 20**) assesses the correlation between both parameters and treats each point with the same weight, though some may be e.g. 75% from 15 out of 20 eggs vs others that are 3 out of 4. The equation is FR = 0.02 Duration + 56.19. The coefficient value 0.02 is not significant, p=0.126, so >0.05. This means that there is no correlation between both parameters OM2 and FR using linear regression as a statistic method. A different way of assessing correlation between both parameters OM2 and FR is logistic regression. For *logistic regression* **Figure 21**, the technique considers all eggs individually (n=9050), with each being fertilised (1) or not (0) each and the equation is

$$p(x) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 x)}}$$

Where x is the duration OM2 and p(x) is the probability of fertilisation of an (one) egg at duration value x. The coefficient of duration (Beta1 in the above) is 0.0011 and is significant (p=0.0013). The logistic regression suggests FR becomes 0.12% more likely with each minute of duration, a very small effect and one hour increase in OM2 duration increases the odds of fertilisation by 7.2%. The relationship is monotonic: it assumes the

fertilisation rate / probability carries on increasing with duration OM2 until it reaches 100% at some large duration which is not the reality.

4.1.3 OM3 distribution and link to outcomes- 2022 data

When using IVF as fertilisation method after collecting oocytes, the following step is fertilisation check which according to GSTT-ACU SOP (**Appendix 22**) is recommended to be carried out 16-20h after insemination (OM3 between16 and 20 hours). The literature review has shown recommendations of OM3 being 16-20h but some articles have shown that some pronuclei (PN) start fading before 20h (Kobayashi *et al.*, 2021) risking the fertilisation being missed which pushes the latest deadline to 18h. Retrospective data collected from RIW system (n=369) has shown that the distribution of **OM3** for 2022 has a mean of **17.1 h** and if we consider 16h as a 1st target, 4% of values were within the value of 16h and 96% within 18h. By the recommended time of 20h, all fertilisation checks are done. The boxplot distribution, we can see a few outliers (early and late).

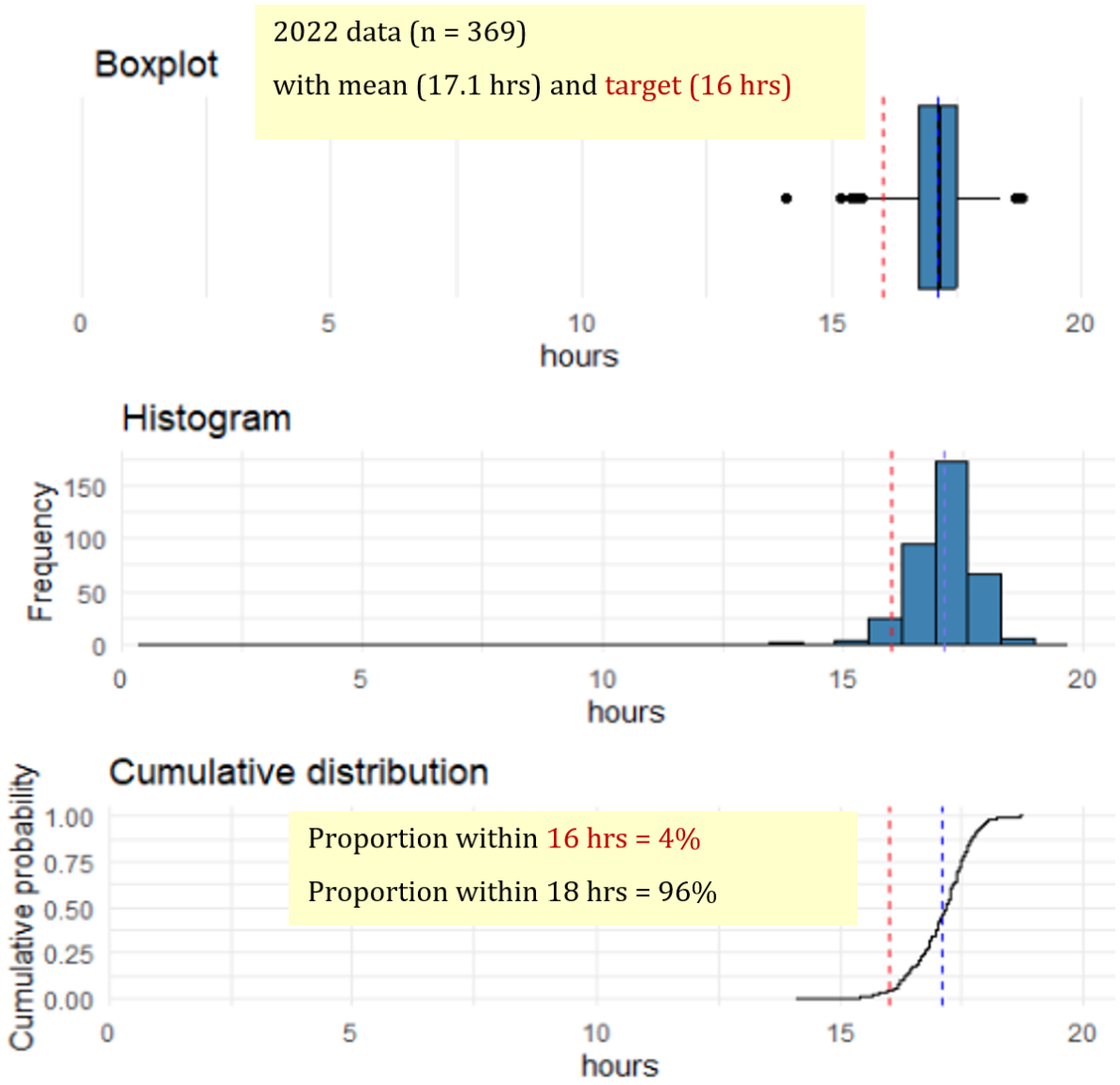

***Figure 22**. OM3 distribution GSTT-ACU 2022 data*

The dataset is represented by n=369 OM3 values. The distribution is presented in 3 different formats (a) boxplots (b) histograms and (c) cumulative distribution.

OM3 is a time duration covering two different days. The starting point (IVF insemination) happens on Day 0 (day of EC) and the fertilisation check happens the following day (day 1 post EC) which explains that the daily distribution covers the second time point (fertilisation check) that happens mostly between Tuesday (for Monday egg collection) and Saturday (for Friday egg collection) as most egg collections are mostly scheduled at GSTT_ACU between Monday and Friday. The mean value of OM3 is 17.1h (**Figure 22**) and

if we consider the targets as 16h and 18h, 4% of the values are within 16h and 96% of OM3 are within 18h. The daily distributions as shown on the boxplots and histograms (**Figure 23**) showed differences in distributions between working days. If the targets are considered as 16 and 18h (even though 20h is the actual limit), we have a few outliers where OM3 was <16h on Tuesday, Wednesday and Thursday. The median value is 16-18h for Tuesday, >18h for Wednesday to Friday. Most values along with median fall within 16-18h on Saturday.

To analyse the effect of OM3 on FR, a table was created (**Table 5**) showing the FR for each OM3 categorised in <16h, 16-18h, and >18h. The table shows that the majority of OM3 is distributed in the middle values of 16-18h and an increase in FR with the time increase of OM3 ($p<0.05$) which is also displayed in **Figure 24**. The Istanbul consensus recently published and a recent study confirmed that OM3 should be 17+/- 1h for optimum visible pronuclei which determine the FR. (Barrie *et al.*, 2021; Coticchio *et al.*, 2025)

Table 5. *FR per OM3-Day 1- GSTT-ACU, 2022 data*
Chi square statistic is 16.8, p-value is 0.000225

OM3 (hours)	OM3 mean (hours)	# eggs Inseminated	# 2PN	FR %
<16 (n=16)	15.6	181	94	52%
16-18 (n=338)	17.1	4078	2502	61%
>18 (n=15)	18.3	276	195	71%
Total (n=369)	17.1	4535	2791	61.5%

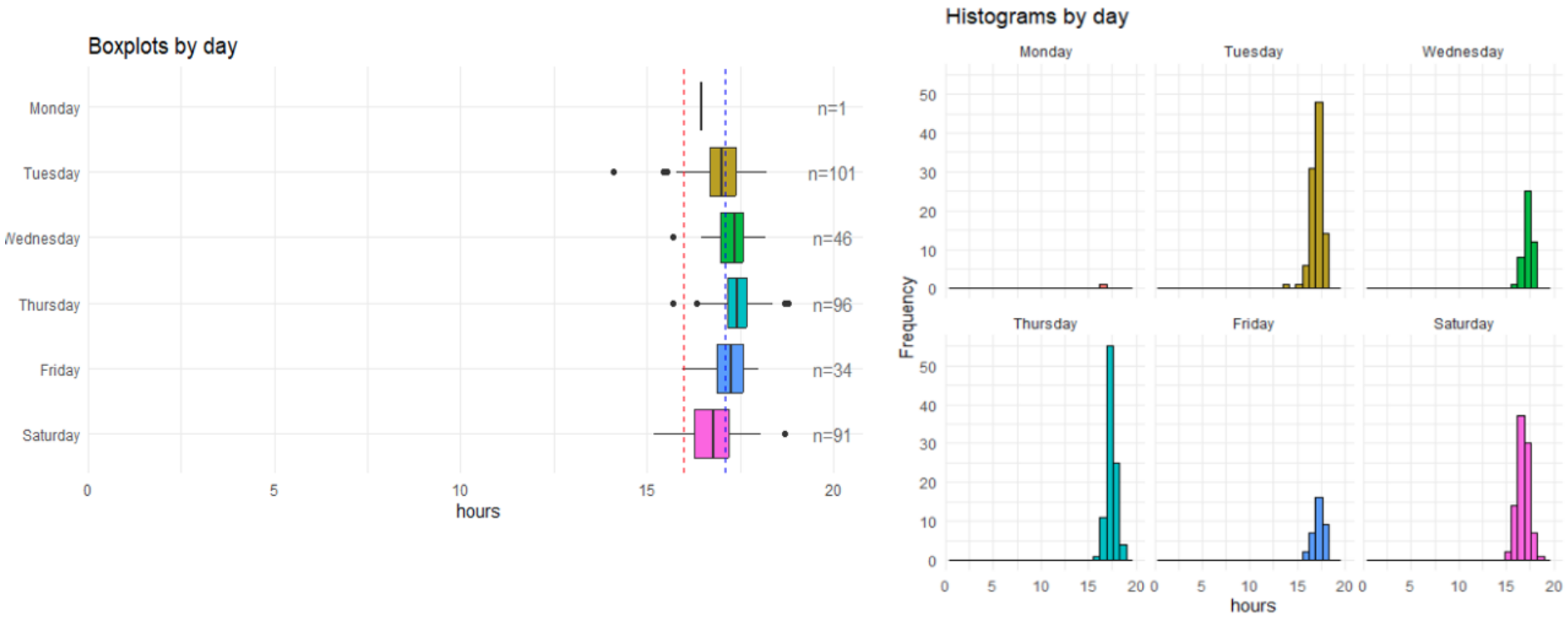

Figure 23. *OM3 distribution boxplot per fertilisation check day- GSTT-ACU 2022 data*

The data set (n=369) is shown as a boxplot distribution of OM3 (left) depending on the day of fertilisation check. This allows a visual understanding of values per second point of the procedure as OM3 goes over 2 days. The blue line shows the mean value of OM3 from the 2022 dataset; the red line shows the first target line of 16h minutes. The n number on the right of the figure indicates the number of values in the set. The same data set is shown in a histogram presentation (right) and allows a better visual check of the distribution each day

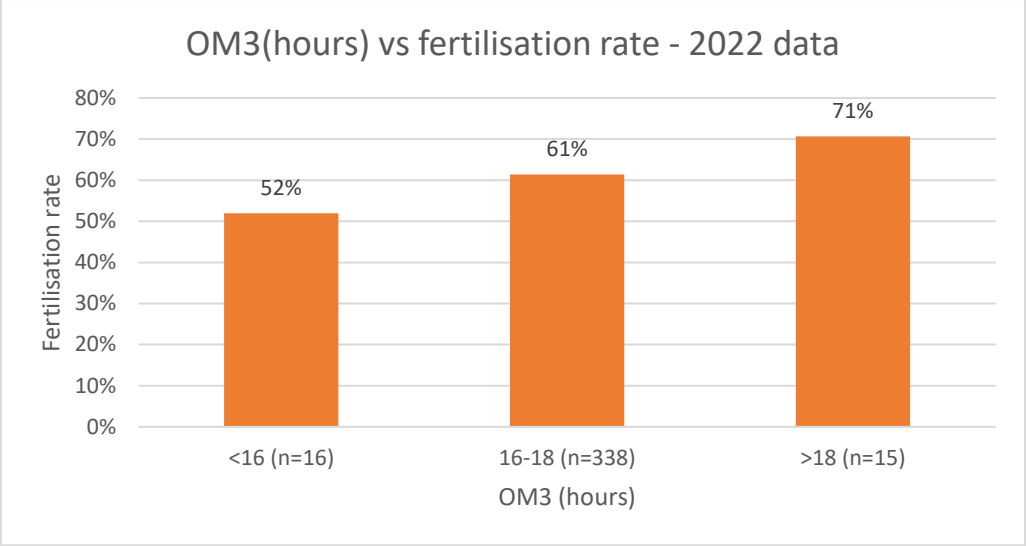

Figure 24. *OM3 vs FR, GSTT-ACU, 2022 data*

OM3 was stratified by time duration sets <16h, 16-18h, >18h on the x axis. The corresponding FR were plotted on the y axis for each category showing a steady increase of FR as OM3 increases. The sample number in each category is shown by the number n

Linear and logistic regression are statistical methods to establish if there is any correlation between both parameters OM3 and FR. The linear regression analysis of the link between FR and corresponding OM3 (**Figure 25**) sh**Error! Reference source not found.**owed a statistically significant relationship between both parameters but the effect was small. It suggested that each hour in OM3 adds 7% to the FR. The linear regression equation FR = 7.01 OM3 - 59.47.

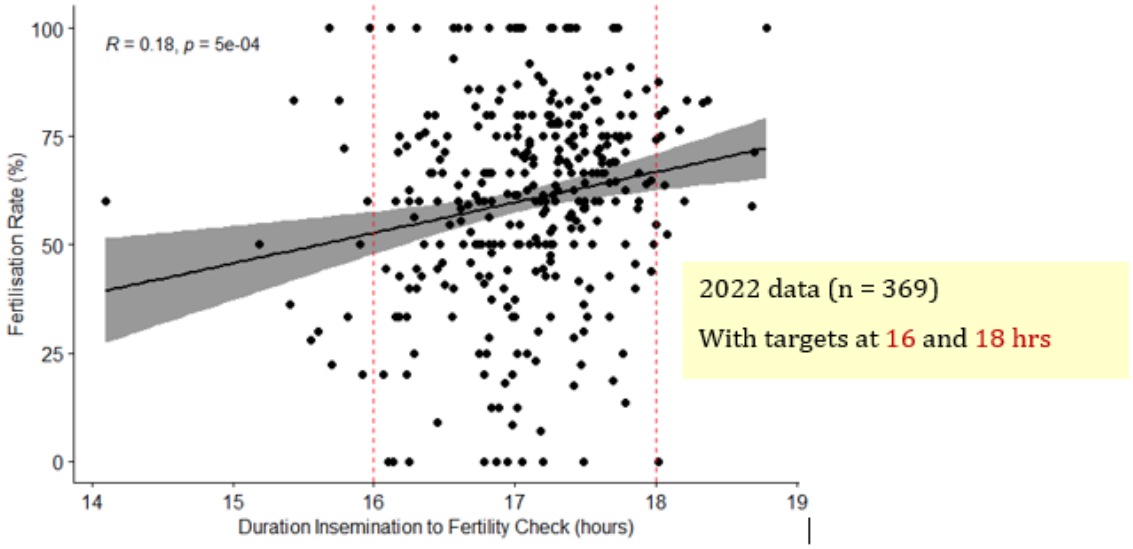

Figure 25*. Linear regression between OM3 and fertilisation rate - GSTT ACU 2022 data*

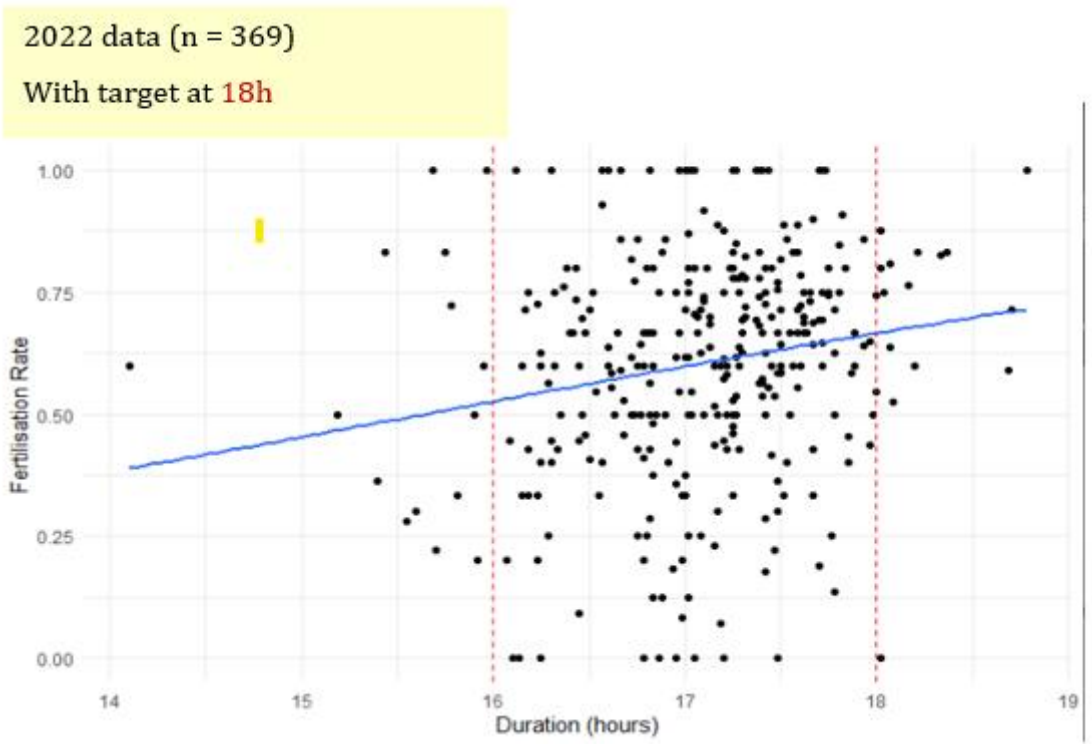

Figure 26. *Logistic regression between OM3 and FR, GSTT-ACU- 2022 data*

The logistic regression on the data set explores the link between OM3 hours (x axis) and FR as a probability of success 1= fertilised, 0= non fertilised. The coefficient of duration is significant (0.30083)

Logistic regression (**Figure 26**) between OM3 and FR showed a highly significant relationship with effect size : one hour increase in OM3 duration increases the odds of fertilisation by exp (0.30083) = 1.35098 or 35%.

The retrospective analysis of OM1, OM2 and OM3 distributions and effect on outcomes showed that OM1 distribution varied between days even though it was mostly close to the target assumed to be 2 hours. No outcome effect could be measured for OM1. OM2 distribution varies between days, Monday and Friday showing the largest gap between median OM3 and the assumed target of 3 hours. A linear regression showed a positive correlation between OM2 and FR outcome to reach international benchmark values, in favour of a value >3h. OM3 distribution varies between days but seems within the target 16-18h but a linear regression shows a strong link between OM3 and FR outcome in favour of OM3 being closer to the higher limit.

4.2 Study design

This project was conducted based on retrospective data, utilizing a one-year dataset gathered from GSTT-ACU from January to December 2022. It is important to note that the dataset used for building the simulation included a period of disruption due to an IT outage at GSTT between July and August 2022. During this time, time-stamped procedures could not be recorded because the electronic witnessing system (RIW) was inaccessible, but data was entered retrospectively on the PMS when the server came back to full working condition. Consequently, all processes were documented manually between July and August 2022 (Hosea, 2022).

4.3 Creating a conceptual model

The information required to construct the conceptual model included details about the activities involved in lab processes, the rate of arrivals into the system, the duration of each activity, and the availability of resources needed for each task (such as equipment, space, and staff).

4.3.1 Pathways

To achieve the proposed objectives, an accurate conceptual model was developed for the GSTT ACU IVF lab procedures (**Figure 27)**. This model is based on all clinical lab pathways included in the simulation, as outlined in **Appendix 26**, and the RIW diagram (**Figure 31**). The final conceptual model is presented in **Figure 27,** along with a simplified version in **Figure 28**. It is important to note that this model is specific to the GSTT-ACU IVF lab, as each lab has distinct SOP and pathways, even though the main tasks are generally carried out in the same sequence across different IVF labs. For instance, not all IVF labs perform embryo biopsies (PGT- trophectoderm biopsies), but when they do, most typically conduct them on Day 5 or Day 6 post-egg collection, with very few doing so on Day 7.

The IVF laboratory at ACU-GSTT operates from 8.30 am to 4.30 pm, Monday to Friday, to accommodate patient arrival schedules. The number of arrivals each day is variable, but they are assigned predetermined time slots:

- Patients arriving for EC are scheduled in 30-minute slots.
- Patients arriving for same-day FET are also scheduled in 30-minute slots.
- Sperm production for semen analysis, sperm freezing and for IVF/ICSI are scheduled in 30-minute slots.
- The IVF laboratory at ACU-GSTT is divided into four distinct subsections that are physically adjacent to one another, as shown on the floor plan (**Appendix 25**) These sections are also visible on the conceptual model created on **Figure 28Figure 27** with a colour code for each section: EC Theatre, where eggs are collected (green section) . The andrology lab, where all semen analysis, semen processing for IVF and semen freezing tasks are conducted (blue section in **Figure 27**). The main lab is the primary area for most lab tasks. The embryo Transfer (ET) Room is where fresh and frozen ET are performed (green section in **Figure 27**). The last section is the cryostorage room that is dedicated all long term cryo-storage in liquid nitrogen for gametes and embryos (Dewars light blue section on **Figure 27**).

The conceptual model (**Figure 27**) shows also where the time duration OM1, OM2, and OM3 (in red) are in relation to all processes

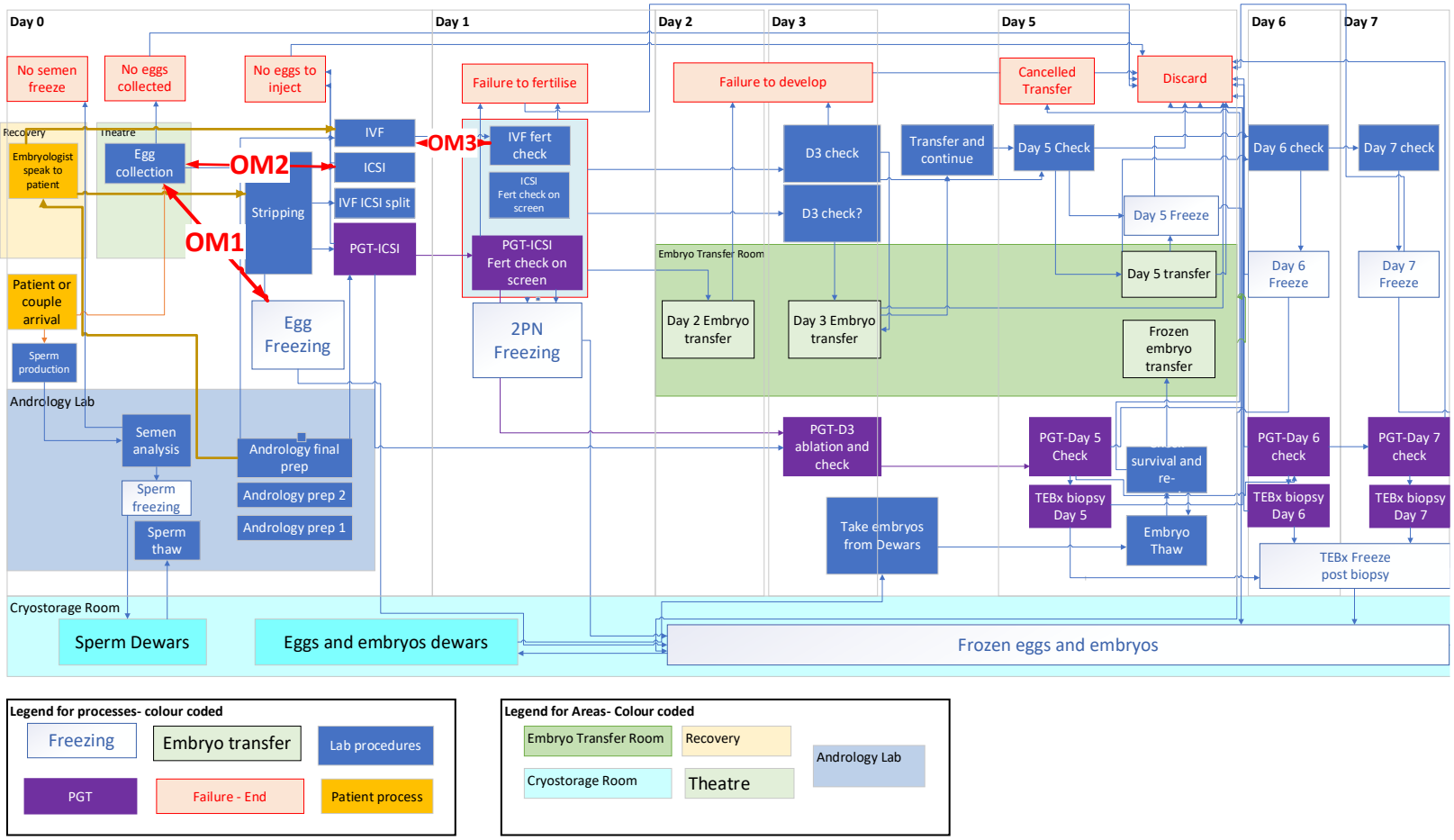

Figure 27*. Conceptual model of GSTT-ACU lab processes*

The conceptual model included daily lab processes generated from daily arrivals (EC, FET, Semen analysis and freezing) but also movement of gametes and embryos. Boxes and pathways are colour coded as per legend in the bottom. .Areas in the labs are colour coded to demonstrate their physical separation. The top part of the figure shows the processes timeline in the process

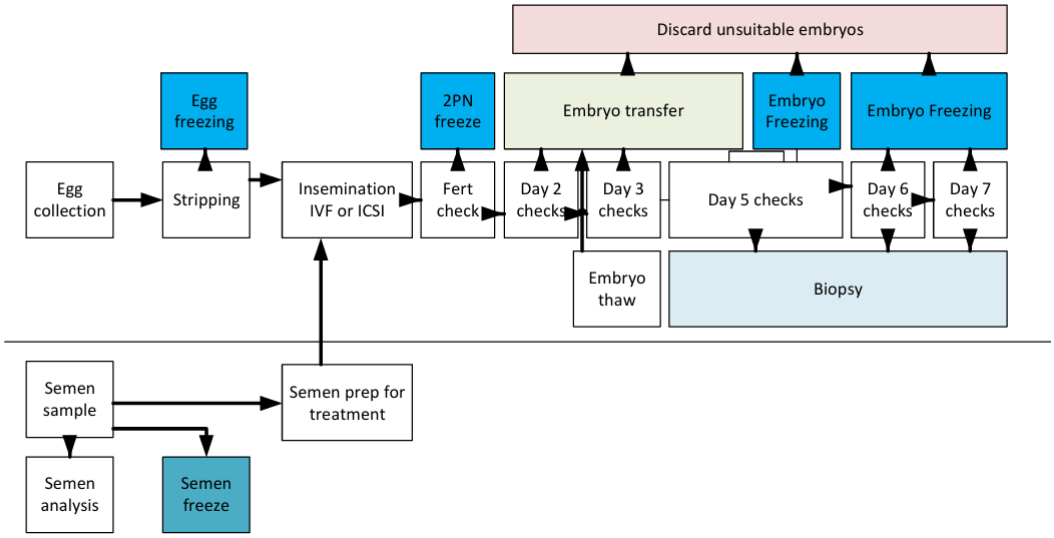

***Figure 28**. Simplified model of pathways and IVF lab processes at GSTT-ACU IVF lab. The diagram displays the sequence of main activities in GSTT-ACU lab colour coded and following the time sequence. This was used to explain the pathway to the Simul8 consultant. The top part occurs in the Egg collection room and main lab, the blue boxes represent all freezing processes. the bottom part representing the andrology lab where all semen analysis/freeze and preparation of for IVF is carried out*

The clinical lab tasks involving gametes and embryos handling that were included in the conceptual model were derived from the patient arrivals as detailed above. These tasks represent most of the clinical workload within the IVF laboratory, as shown in the RIW diagram (**Figure 32**). In addition to these tasks, the conceptual model also accounts for "discarding of gametes and embryos" at end of expiry consent or on patient's request. While these tasks are independent of patient arrivals, they are generated by the expiry of gamete and embryo consent after the statutory 10 years of storage or by specific requests from patients to discard their samples. Including these tasks in the model was essential, as they affect the number of available storage spaces in cryopreservation. A comprehensive overview of tasks included in and excluded from the simulation model, is described in **Table 6** below and length of each pathway are listed in **Table 7**.

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Table 6. *Inclusion and exclusion criteria of IVF lab tasks included in the simulation model*

IVF lab tasks carried out by embryologists and practitioners	
Included in the model	Excluded from the model
-Egg collection -Talk to patients after egg collection -Stripping -Egg freezing	- Ordering and stocking media and consumables for use
-Removing embryos from dewars for thaw -Embryo thaw, check for survival and re-expansion	-Egg thaw
- ICSI and IVF insemination - Fertilisation checks (IVF, ICSI on screen) - Embryo checks (grading) - Embryo freezing - Embryo trophectoderm biopsy - Embryo freezing post biopsy - Embryo and egg discards	-Support tasks: -Lab dishes preparation for same day and next day procedures, - Tagging dishes and labelling straws - Biweekly liquid nitrogen top up - QC and traceability checks - All gamete and embryo transport in and out (admin and lab related.)
-Double witnessing when required for all procedures included -Dishes discards when double witness is needed	- Lab meetings, Audits - KPI generation and analysis
-Admin tasks linked to lab tasks -Calling patients after fertilisation checks, data entry, -Preparing dishes and labels for some procedures egg freezing	Admin tasks: paper set up and patient consent checks prior to procedures Responding to emails and phone call queries (Duty scientist role) Communicating PGT results and follow ups
-Semen analysis -Sperm preparation for IVF ICSI -Semen freezing	-Intra uterine inseminations
-Sperm samples discards	-Donor sperm management,

Table 7. *Pathway lengths at GSTT-ACU IVF lab*

Female and male gamete pathways are interconnected (joining for fertilisation

Length of pathway	**Arrival**	**End**
Same day as arrival	Egg collection	Egg freezing
		No eggs collected
		No eggs to inject
	Sperm production	Semen analysis
		Sperm freezing
		No sperm freezing
		Final sperm prep (joins egg process at insemination)
	Embryo thaw	Frozen embryo transfer
One day post arrival	Egg collection	Day 1 - 2PN freeze
		failure to fertilise
Two days post arrival	Egg collection	Day 2 fresh transfer
Three days post arrival	Egg collection	Day 3 fresh transfer
Five days post arrival	Egg collection	Day 5 fresh transfer and discard
		Day 5 biopsy check, biopsy and discard
		Day 5 biopsy check, no biopsy and discard
		Day 5 freeze check, freeze and discard
		Day 5 freeze check, no freeze and discard
Six days post arrival	Egg collection	Day 6 biopsy check, biopsy and discard
		Day 6 biopsy check, no biopsy and discard
		Day 6 freeze check, freeze and discard
		Day 6 freeze, no freeze and discard
Seven days post arrival	Egg collection	Day 7 biopsy check, biopsy and discard
		Day 7 biopsy check, no biopsy and discard
		Day 7 freeze check, freeze and discard
		Day 7 freeze check, no freeze and discard

4.3.2 Resources

The resources incorporated into the model are outlined in **Table 8**. The workforce (staff resources) included in the model at GSTT-ACU comprises embryologists and reproductive science practitioners (referred to as practitioners). IVF lab administrative staff were excluded from the model, as their tasks do not pertain to laboratory work. The equipment and spaces included in the simulation primarily consist of stable resources essential for all mapped lab procedures, such as Laminar Flow Hoods, ICSI stations, and freezing stations. Smaller and disposable equipment, such as dishes and pipettes, were not included in the model.

Upon arrival for egg collection, female patients are directed to recovery, while male partners (if not involved in egg freezing) are directed to the sperm production rooms. The unit has six beds available for patient recovery and two sperm collection rooms.

Most lab procedures are conducted under Laminar Flow Hoods (LFH) , and specific procedures, such as ICSI, require access to one of the four available ICSI stations. All embryos are cultured in time-lapse incubators equipped with cameras, and the grading and observation of embryos necessitate access to a screen connected to the time-lapse incubator, known as the Embryoviewer.

Table 8. *Resources included in GSTT-ACU IVF conceptual model (staff, equipment and space)*

Type	Resource	Availability/number
Staff	Embryologist	8:30am-4:30pm According to staff availability on the annual leave spreadsheet
	Practitioner	8:30am-4:30pm According to staff availability on the annual leave spreadsheet
Equipment and Rooms	Sperm production room	2
	Laminar Flow Hood (LFH)	5
	Embryoviewer	2
	Bed space	6
	ICSI station	4 ICSI stations
	Freeze station	3
Cryostorage	Dewars for sperm storage	15000 spaces (to allow unlimited capacity not the real number)
	Dewars for egg and embryos storage	15000 spaces (to allow unlimited capacity not the real number)

4.3.3 Arrivals and schedule

The IVF laboratory pathways operate on a seven-day-a-week basis, with arrivals primarily following a five-day pattern and limited arrival activity on weekends. The pathways associated with each arrival can vary in duration, taking anywhere from the same day (0 days) up to 7 days to exit the model. All staff members are modelled to adhere to the standard operating hours of 8:30 AM to 4:30 PM, whether on a full time or part time basis (reduced number of days) although some staff may have different working patterns, including early starts or longer shifts with overtime. Each arrival generates a unique pathway, determining its exit from the model, whether on the same day or up to seven days later. All pathways are interconnected and are influenced by the outcomes of the tasks performed.

The pathways described in

Table 7 are interconnected, as illustrated in **Figure 27**. One specific pathway, related to the discarding of gametes and embryos, operates independently of patient arrivals. This pathway is triggered by either consent expiry or patient requests. Although this discard pathway was included in the model due to its impact on the number of available spaces in the dewars (Cryo Room), the time allocated for this task and the resources involved were not specifically planned within the simulation. This consideration ensures that the model accurately reflects the dynamics of resource availability while recognizing that the discard process does not directly align with patient arrivals.

4.4 Simulation design and visual representation

4.4.1 Computer model building

A computer model using the simulation software Simul8© was built by the team described in **Table 9** using the process map designed in the conceptual model phase (**Figure 27**) with help from S8C. Most "What if" scenarios could be generated as per agreement (**Appendix 13**).

Before the model could be used for analysis, it had to be continuously verified by the team and validated by comparing the output results from the simulation to the output results from the real data for same period. Validation makes sure that the model represents the behaviour of the actual real-life system as accurately as possible. The simulation design first step was to translate the conceptual model into its computer model copy on Simul8© Software. The simulation project team was composed of two members: the Author (principal investigator AK) and Simul8© Simulation consultant (S8C) with support from the Lab manager at GSTT-ACU (WKS). The project roles were shared as described in **Table 9**.

***Table 9**. Roles in the GSTT-ACU lab simulation project*
This table the table inspired from roles in simulation (Robinson, 2014a)

Doers	**Interveners**	**Project manager AK** **Modeller AK** **Model user (later stages) AK**
Done for	Clients Model user (early stages)	Problem owner AK Recipient of the model AK
Done with	Project team	Data provider AK, WKS Modelling supporter S8C
Done to	Those interviewed	Group from who info is obtained AK, AKS
Done without	Not involved but affected by the project	Staff, management team , patients at GSTT-ACU

AK: Aida Kaffel **WKS:** Aida Kaffel's workplace supervisor **S8C** : Simul8 consultant

The process of developing the computer simulation model unfolded in several methodical steps as outlined in **Table 10**. First, the team focused on translating the conceptual model into Simul8© software . This involved mapping out the pathway sequences previously described. Key components of pathways included activities, queues, and end points. Activities represent when work is performed on items. **Activities** were integral to the model and required various resources. A total of 60 activities were added to the model detailed in Appendix 28. **Queues**, serve as holding areas for work awaiting resources or activities, were also part of the pathways, 81 queues in total, listed in Appendix 27. Finally, 12 end points were created to sign where completed work exits the simulation, as specified in **Appendix 29**. The second step involved integrating resources into each process. This included staff, equipment, and the logical order of operations, all derived from the conceptual model resources shown in **Table 8**, and presented visually in **Figure 27**. The third step included adding probability to each process pathway. For instance, in the egg collection activity detailed in **Table 11.** Example of a process from conceptual model to Simul8 model

This is the IVF process of egg collection translated from a conceptual model pathway to a computer simulation Simul8 pathway, by following a step by step described in **Table 10.Table 11**, two potential outcomes were defined: a 1% chance of no eggs being

collected, leading to the end of the pathway, and a 99% chance of eggs being collected, allowing progress to the next step. The fourth step was the incorporation of time distributions for each activity. Using the egg collection example again, the duration of the process was established through a distribution format, leveraging StatFit for Simul8©. This tool, included with Simul8© Professional perpetual licenses, analyses raw data to identify a suitable statistical distribution that fits the observed data.

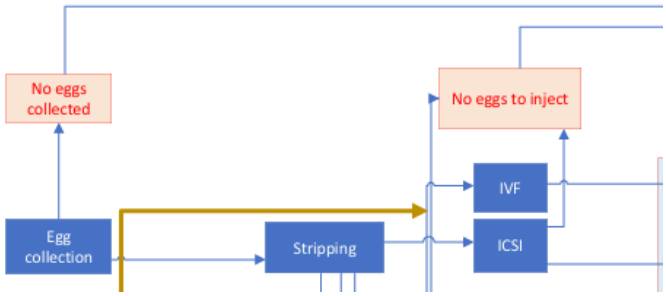
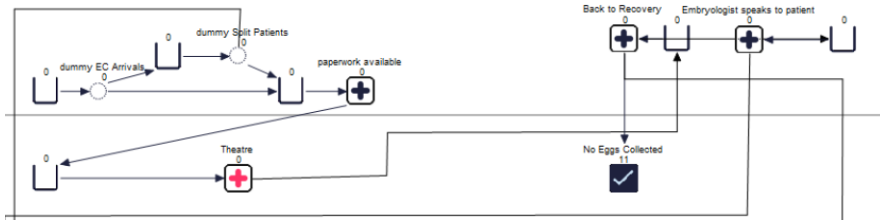
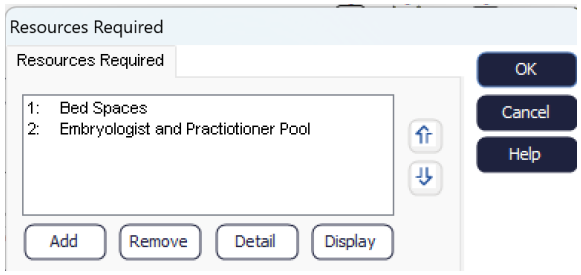
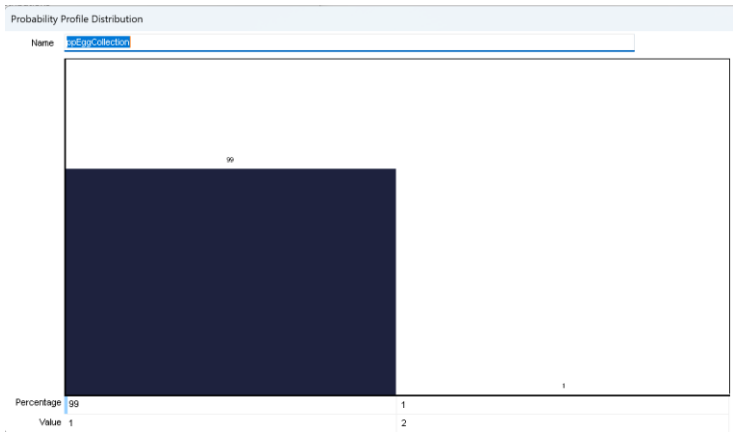
Table 10. *Steps followed to create a Simul8 computer model*

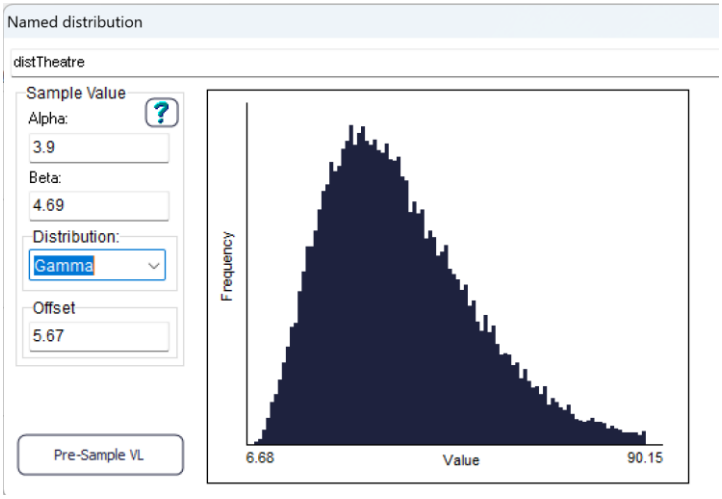
#	**Steps included in Simul8 simulation modelling**
1	Translate the conceptual model into a computer simulation model with activities, queues and end points
2	Add resources in each process: Staff, equipment, spaces
3	Add probability of each process pathway
4	Add time distribution for each activity

The entire model creation process was collaborative, involving the team mentioned above. The team meticulously advanced through each step, adding the necessary elements to ensure the model accurately reflected the conceptual framework.

Table 11. *Example of a process from conceptual model to Simul8 model*

This is the IVF process of egg collection translated from a conceptual model pathway to a computer simulation Simul8 pathway, by following a step by step described in ***Table 10****.*

Simul8 Step		**Egg collection from conceptual to Simul8 model**
1	Conceptual model	
2	Simulation model Activities Queues End points	
3	Add resources involved in the process	
4	Add probability of pathway	

5	Add time spent carrying out the activity in a distribution format from the data collected	

4.4.2 Visual representation of GSTT-ACU IVF lab

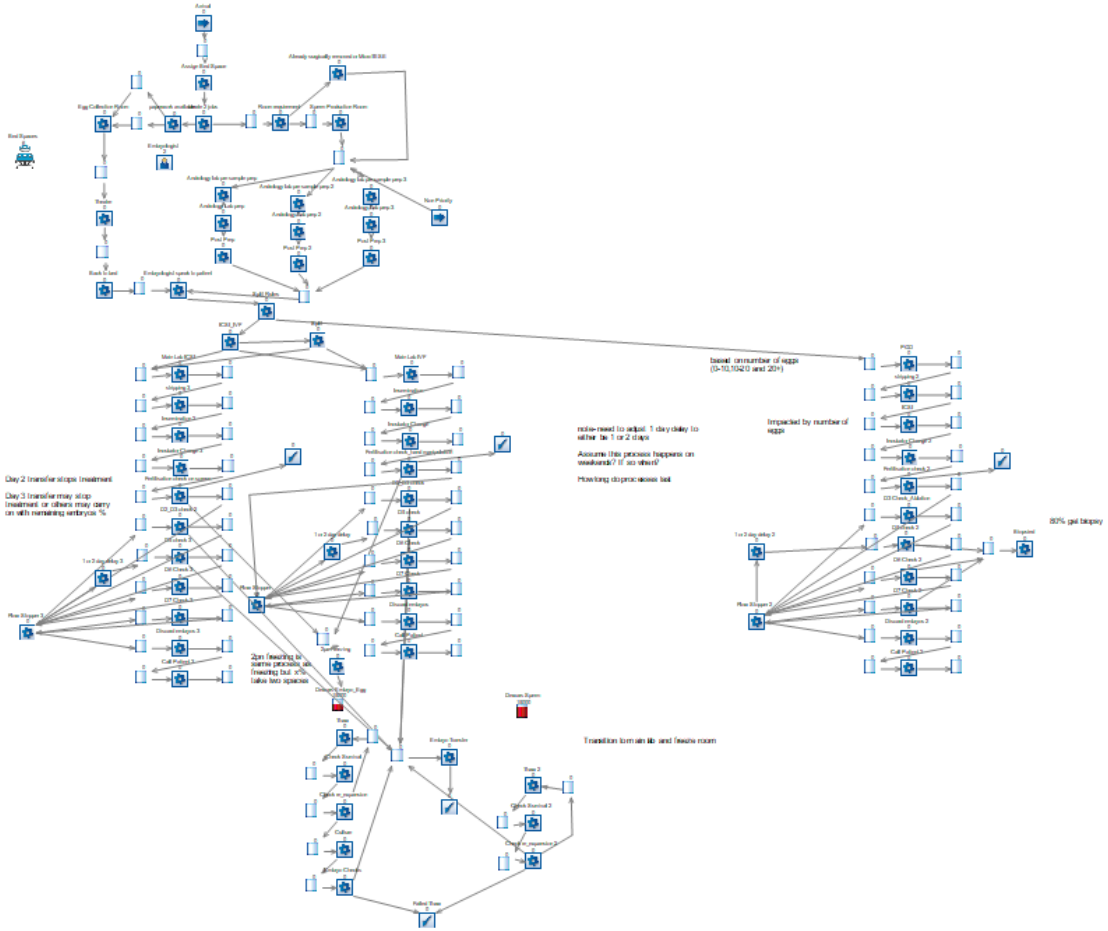
After over a year of dedicated effort, including weekly meetings and extensive offline work, the team advanced through more than 70 simulation versions. Ultimately, they arrived at a final version capable of running a full year of scheduled arrivals, spanning 52 weeks, ready for testing and scenario analysis. As we can see in **Table 13**, the visual display of GSTT-IVF ACU model changed over time to improve the display from one version to another. The model started as a built of all involved processes in a sequence to mimic the conceptual model as seen in version 5 and 15. In version 20, the team tried to incorporate the floorplan into the simulation to improve the visual understanding. It was improved further in version 35 which is closer to the final version used. Elements of pathways : Activities, queues and end points were represented as displayed in **Table 12**.

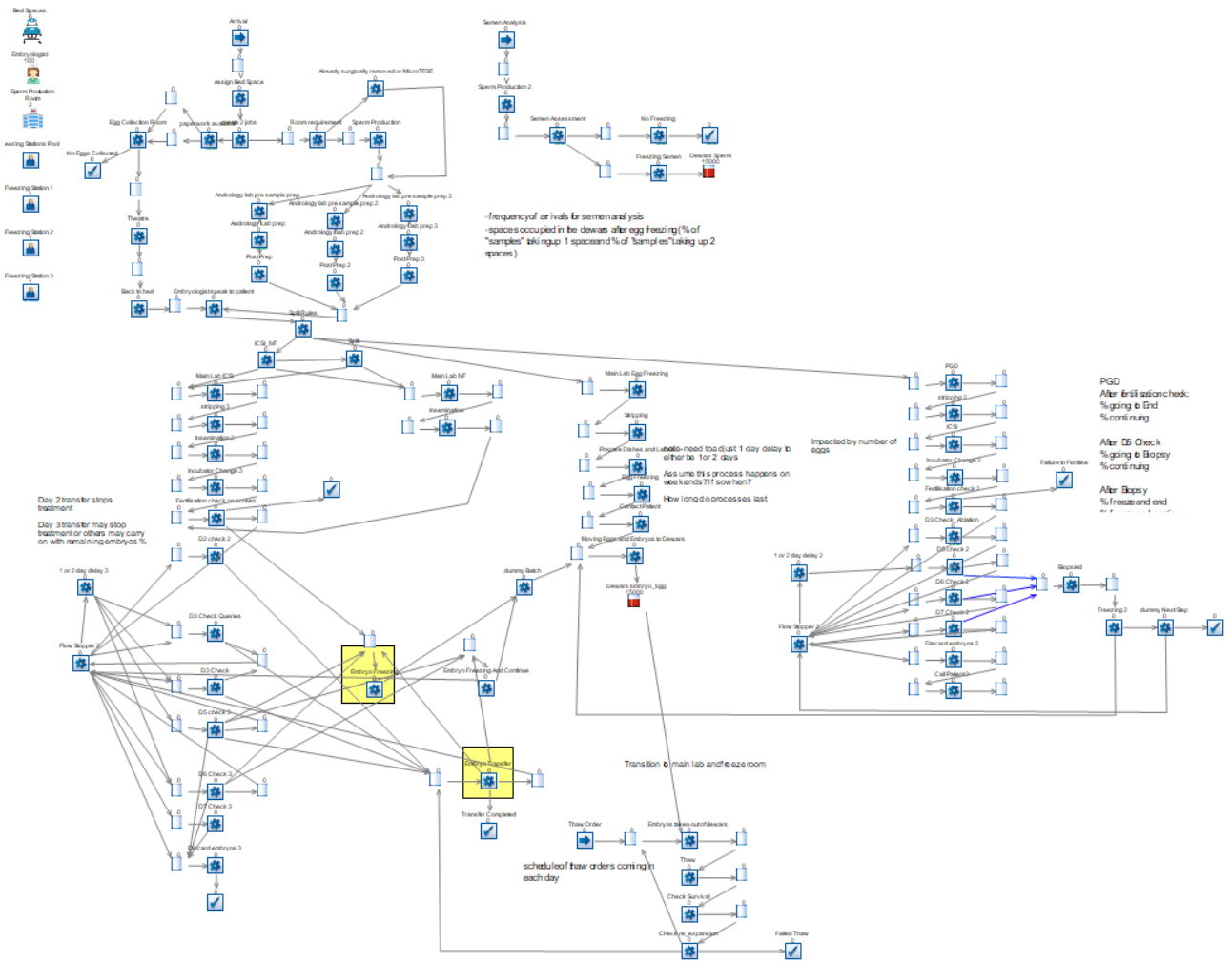
***Table 12**. Icons used for each step in Simul8.*
Activities, queues and end points are key components of DES computer models

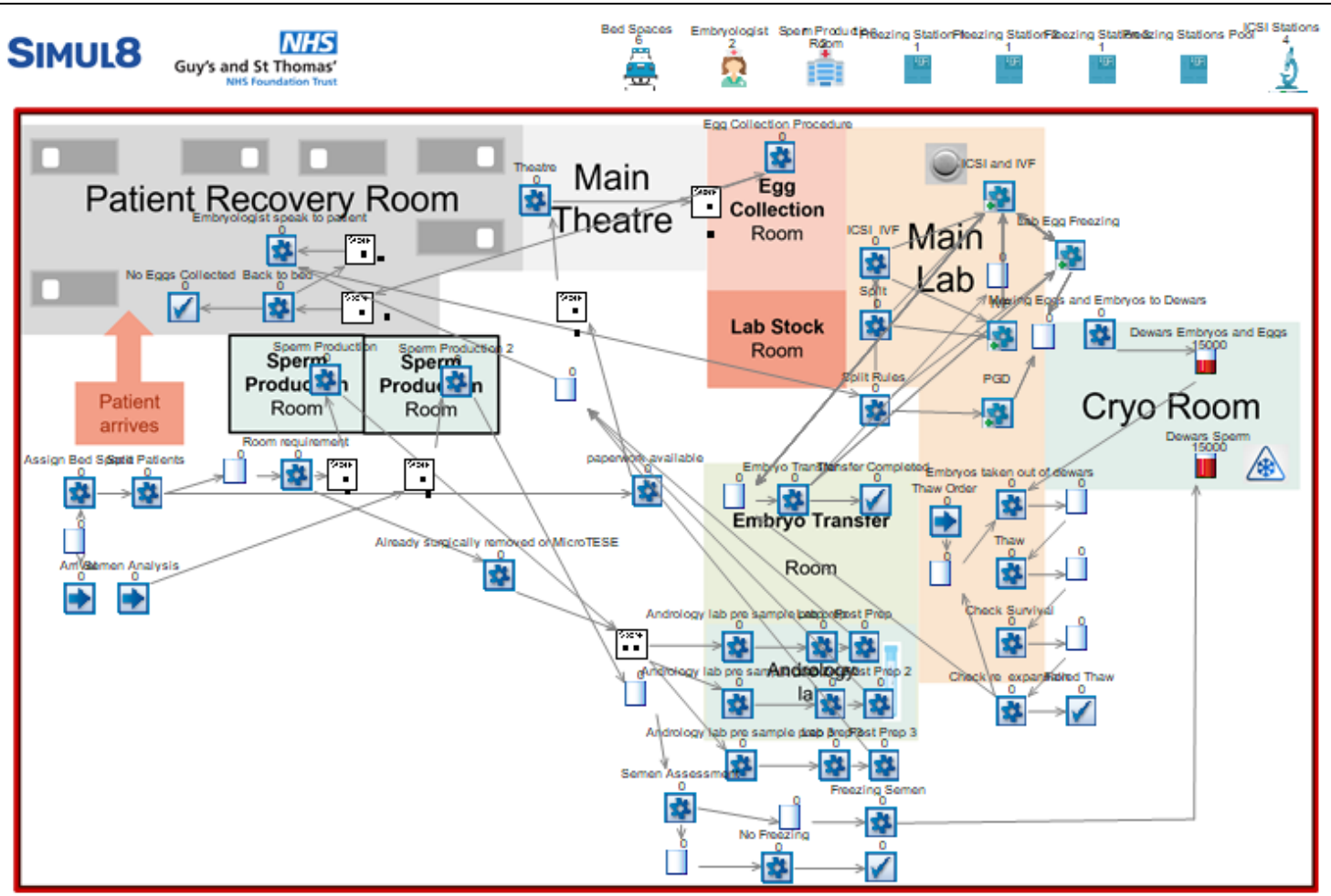
Icon used in Simul8	
	Activity
	Queue
	End point

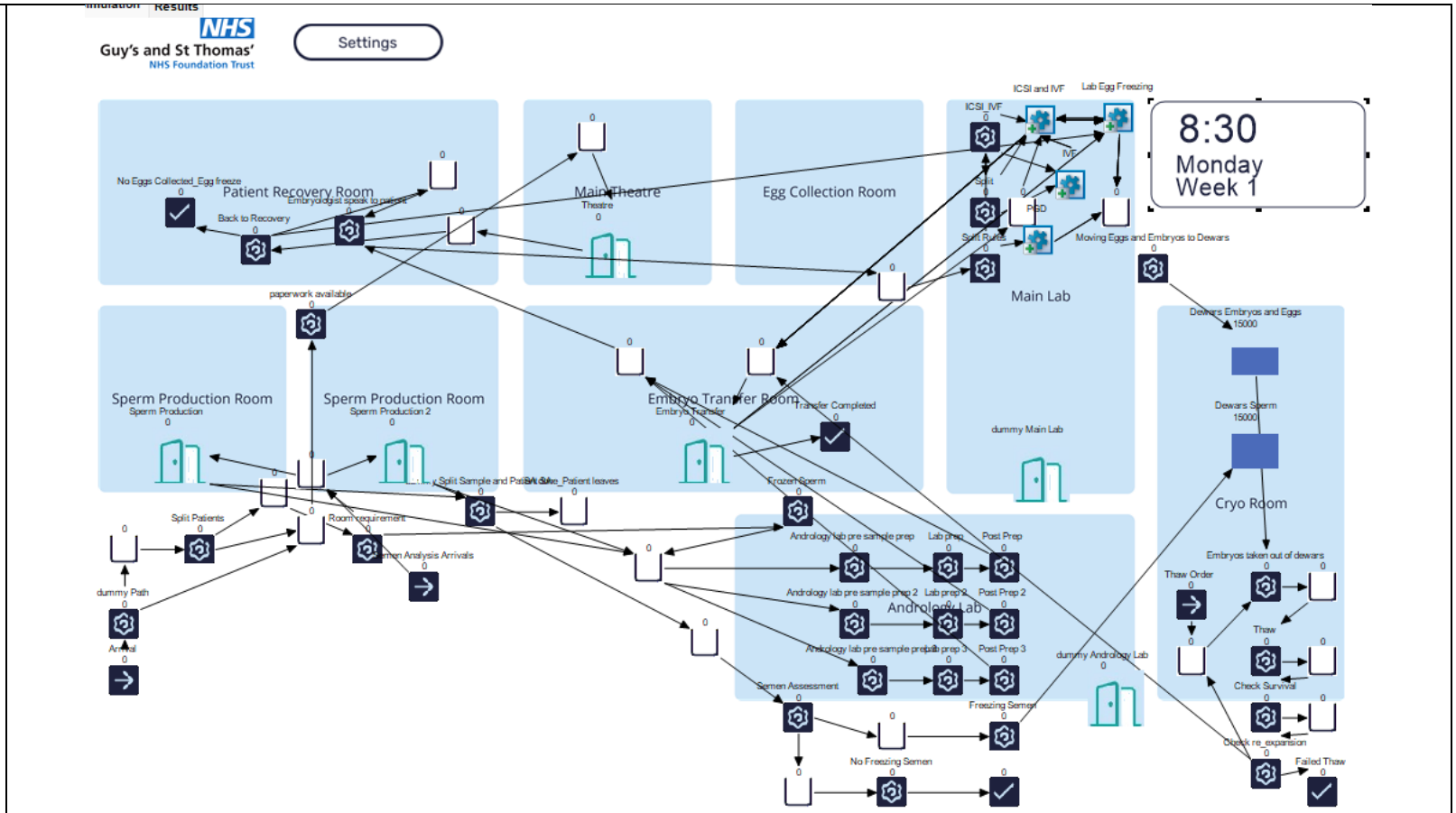
As shown on **Table 13**, the simul8© model versions were initially numbered (v1 to v35) and then they were referred to by dates of updates as the model evolved. Adding details to the model and making every detail visible is complex to visualise. **Table 13** shows the complexity of model and the complexity of the display. Making the visuals easy to read with including all the processes steps can be a challenge .

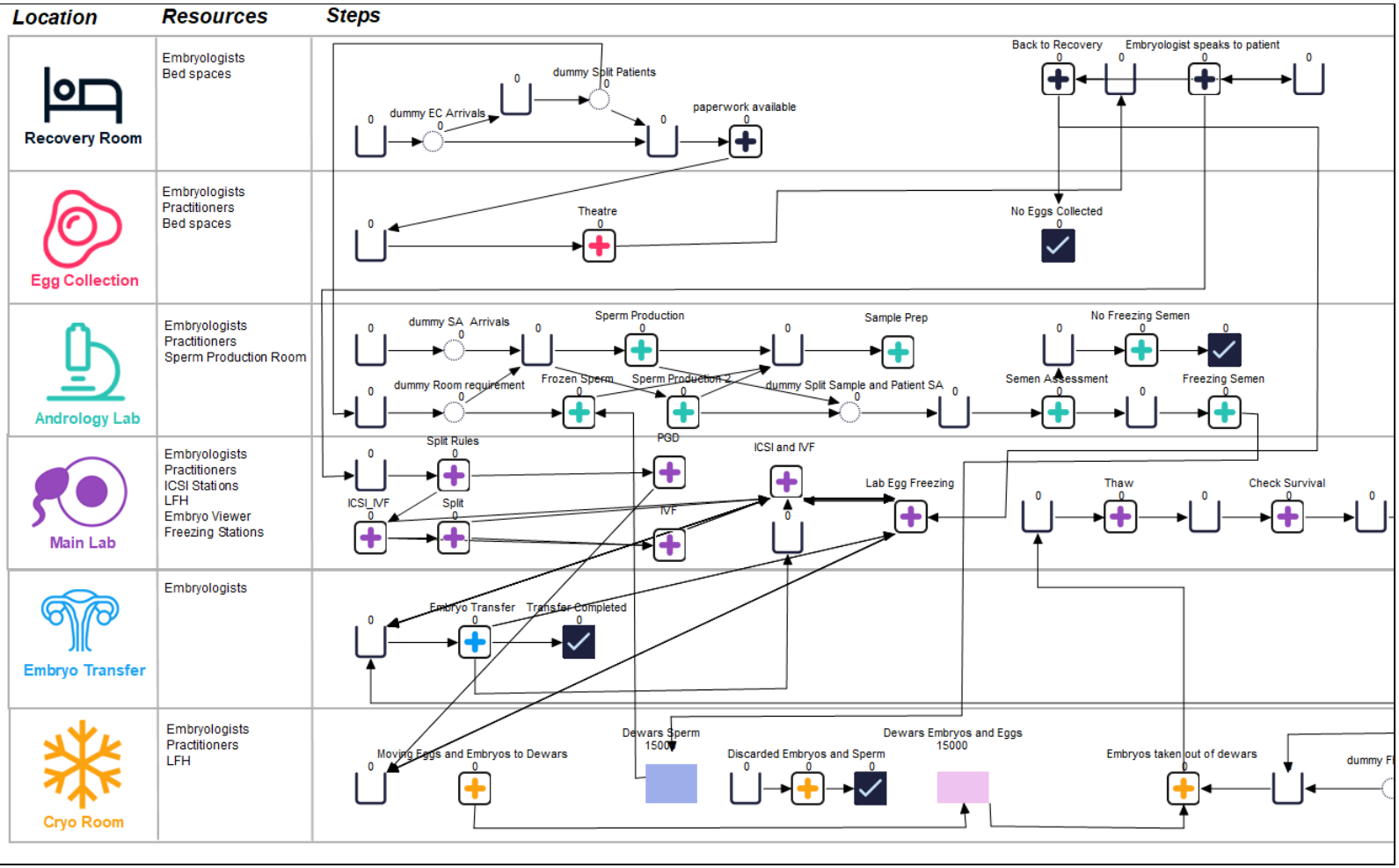
Table 13. *Visual versions of Simul8© models created throughout the project*

Version	***Visual display in Simul8 Software***
V5	

V15	 -frequency of arrivals for semen analysis -spaces occupied in the dewars after egg freezing (% of "samples" taking up 1 space and % of "samples" taking up 2 spaces) Day 2 transfer stops treatment Day 3 transfer may stop treatment or others may carry on with remaining embryos % Impacted by number of eggs Assume this process happens on weekends? If so when? How long do processes last PGD After fertilisation check: % going to End % continuing After D5 Check % going to Biopsy % continuing After Biopsy % freeze and end Transition to main lab and freeze room schedule of thaw orders coming in each day

V20	 SIMUL8 NHS Guy's and St Thomas' NHS Foundation Trust Bed Spaces Embryologist Freezing Stations Pool ICSI Stations Patient Recovery Room Main Theatre Egg Collection Procedure Egg Collection Room Lab Stock Room Main Lab ICSI and IVF Cryo Room Sperm Production Room Sperm Production 2 Room Patient arrives Embryologist speak to patient No Eggs Collected Back to bed Assign Bed Split Patients Arrive Semen Analysis Room requirement paperwork available Already surgically removed or MicroTESE Embryo Transfer Transfer Completed Embryo Transfer Room Thaw Order Embryos taken out of dewars Thaw Check Survival Check re-expansion Failed Thaw Split Split Rules PGD Dewars Embryos and Eggs Dewars Sperm Andrology lab pre sample Post Prep Post Prep 2 Post Prep 3 Andrology lab Semen Assessment Freezing Semen No Freezing

V35	 Results NHS Guy's and St Thomas' NHS Foundation Trust Settings 8:30 Monday Week 1 Patient Recovery Room Main Theatre Theatre Egg Collection Room ICSI and IVF Lab Egg Freezing Main Lab Sperm Production Room Sperm Production Sperm Production Room Sperm Production 2 Embryo Transfer Room Embryo Transfer Andrology Lab dummy Main Lab dummy Andrology Lab Cryo Room Dewars Embryos and Eggs 15000 Dewars Sperm 15000 No Eggs Collected_Egg freeze Back to Recovery Embryologist speak to person paperwork available Split Patients dummy Path Arrival Room requirement Transfer Completed Frozen Sperm Andrology lab pre sample prep Lab prep Post Prep Andrology lab pre sample prep 2 Lab prep 2 Post Prep 2 Andrology lab pre sample prep 3 Lab prep 3 Post Prep 3 Semen Assessment Freezing Semen No Freezing Semen Moving Eggs and Embryos to Dewars Embryos taken out of dewars Thaw Order Thaw Check Survival Check re_expansion Failed Thaw

May 2024	

Location
Resources
Steps
Recovery Room
Embryologists
Bed spaces
dummy Split Patients
dummy EC Arrivals
paperwork available
Back to Recovery
Embryologist speaks to patient
Egg Collection
Embryologists
Practitioners
Bed spaces
Theatre
No Eggs Collected
Andrology Lab
Embryologists
Practitioners
Sperm Production Room
dummy SA Arrivals
Sperm Production
Sample Prep
No Freezing Semen
dummy Room requirement
Frozen Sperm
Sperm Production 2
dummy Split Sample and Patient SA
Semen Assessment
Freezing Semen
Main Lab
Embryologists
Practitioners
ICSI Stations
LFH
Embryo Viewer
Freezing Stations
Split Rules
PGD
ICSI and IVF
ICSI_IVF
Split
IVF
Lab Egg Freezing
Thaw
Check Survival
Embryo Transfer
Embryologists
Embryo Transfer
Transfer Completed
Cryo Room
Embryologists
Practitioners
LFH
Moving Eggs and Embryos to Dewars
Dewars Sperm
15000
Discarded Embryos and Sperm
Dewars Embryos and Eggs
15000
Embryos taken out of dewars

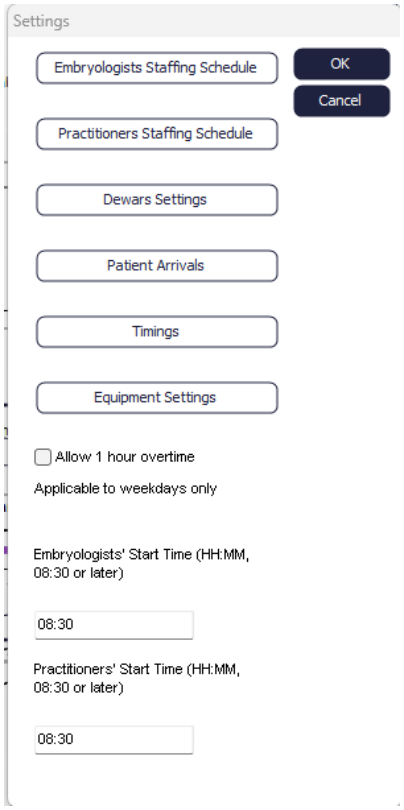
4.4.3 Model Assumptions

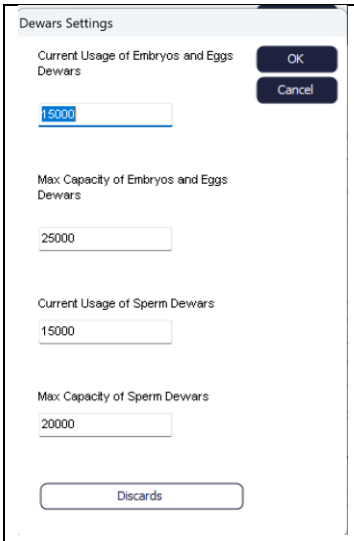
It is accepted that simulation models must be simplified to a certain extent by making assumptions and excluding certain details **(Table 6).** The following assumptions were made for the purpose of making the model possible to set up: Firstly, travel times between activities were considered as zero, meaning as soon as one task is completed it cannot be sent to the next activity instantly which leads to the fact that for a single work item/patient, activities will begin straight after one another if there is no queue and resources are available. There were no time or capacity limits in queues apart from the dewars that have limited capacity (that can be changed through Settings buttons, **Table 14**). The next assumption was that all resources have been considered as having the same efficiency (no staff are considered more efficient than others). In addition to that, staff were not tied to a certain work item, there were no individuality rules in place even if some tasks such as biopsy are only carried out by a qualified embryologists who are signed off for the procedure.

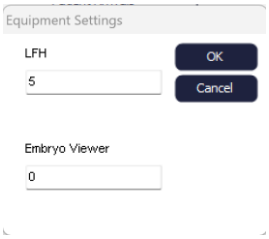
From the staff perspective, once a shift finished, staff members stopped working. tasks will continue without including the staff member so it does not account towards the staff utilisation rate as it is not part of its shift. Overtime work is only added when testing a scenario. When work is carried out on weekends, it is only done with available staff and (which can be controlled through the embryologists and practitioner schedules sheets). Finally, lunch breaks are included in shift timings 30 min per day assigned by the simulation randomly between 12-2pm even though in reality some staff have earlier lunches to accommodate workload or skip lunch and or leave early sometimes. All leave was included (annual leave, study leave) was included in the model based on the 2022 annual leave spreadsheet (**Appendix 32**).

Table 14. *Settings available in the Simul8© model.*

Settings is a function that the modellers decided to set up in the simul8 interface to make changes possible in arrivals, resources (staff and equipment and dewars), time distributions of procedures, dewars storage capacity and monthly discards schedule of embryos and gametes

Settings	The settings function in the model created allows access to the following items to change them Arrivals resources availability processes time distribution
	Embryologists Staffing Schedule Embryologist schedule links to a year spreadsheet with embryologists available for work Practitioners Staffing Schedule Practitioner schedule links to a year spreadsheet with practitioners available for work Dewars Settings Links to the number of spaces available. One space for one patient (see below) Patient Arrivals Links to arrivals (see below)) Timings Links to timings of activities and their distributions Appendix 30 Equipment Settings Links to number of equipment items that can be variable (see below)
Patient Arrivals	
Timings	Appendix 30

<table>
<tr>
<td> 
</td>
<td>Dewars are separated into
- Dewars for eggs and embryos
- Dewars for sperm

The number of spaces available (1 space per patient) can be modified in setting</td>
</tr>
<tr>
<td> 
</td>
<td> 
</td>
</tr>
</table>

4.4.4 Data collection and processing for creating the model

Qualitative data required to formulate the model was used from the conceptual model created and described above in addition of AK knowledge of the different pathways. Quantitative data required to complete the Simul8© computer model were mainly: Arrivals in the system : EC, SA, FET, activity time durations (in distributions), pathway probability, Resource availability (equipment and staffing) and embryo and sperm discard rate. Quantitative data required for the model is listed in **Table 15**. To build the model, the data was based on retrospective results from the year 2022. This data was added as spreadsheets (editable in settings, **Table 14**) linked to the model. Arrivals in the system were added into the model from the scheduled arrivals found in the PMS Babysentry©. The format used in the model is a spreadsheet that maps arrivals for the whole 2022 year (**Appendix 31).** Most activity time durations were retrieved from RIW database 2022 retrospective data (Coopersurgical, 2024). RIW is an electronic witnessing system used in the IVF laboratory where all dishes and tubes used in the lab for holding gametes and embryos are RIW tagged **Figure 31** . Most laboratory procedures were carried out on surfaces where there is a reader that captures date/time/operator carrying out the procedures using a Radio Frequency Identification RFID tag attached to

all dishes where gametes and embryos are kept. RIW records time and date of procedures and time spent from one step to another for each patient. RIW does not calculate the activity duration. To be able to calculate the durations, data extracted from RIW for procedures was exported into excel spreadsheets. The author calculated the length of processes by calculating the time difference between two steps as followed by RIW diagram **Figure 32**.

Table 15. *Data source for GSTT-ACU Simul8© model building.*
The table below shows all the data required to build the simul8 model for GSTT-ACU-IVF lab and where this data was sources from (GSTT databases by AK)

Data required	**Data source**
Arrivals in the system	PMS Babysentry scheduler
Activities involved in the process	Process maps from conceptual model **Figure 27**
Pathway probability	KPI from Babysentry 2022 data
Activity time duration	Mainly RIW (distributions) Some tasks timed by team members
Resource quantities	Process maps from AUT
Resources availability	Yearly annual leave embryology lab spreadsheet

If we take as an example the process egg collection (EC) to calculate the time spent carrying out the EC. According to RIW pathway **Figure 29**, the steps are first, assigning the ID card = start of egg collection, second, assigning the egg collection dish = end of the egg collection. This means that the duration of process = Time Egg collection dish assigned – time Patient ID.

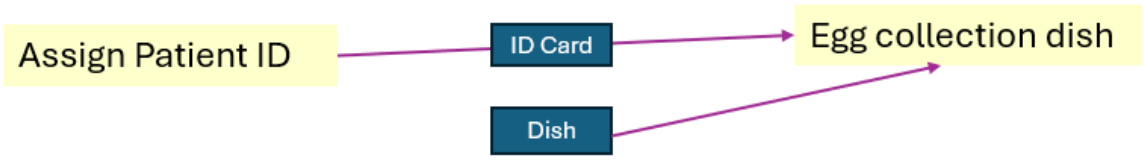


Figure 29. *RIW pathway – EC*
This diagram shows the steps included for EC RIW pathway: first assigning the ID card at patient ID check and then assigning the EC dish by adding ID card and a dish at the end of the procedure

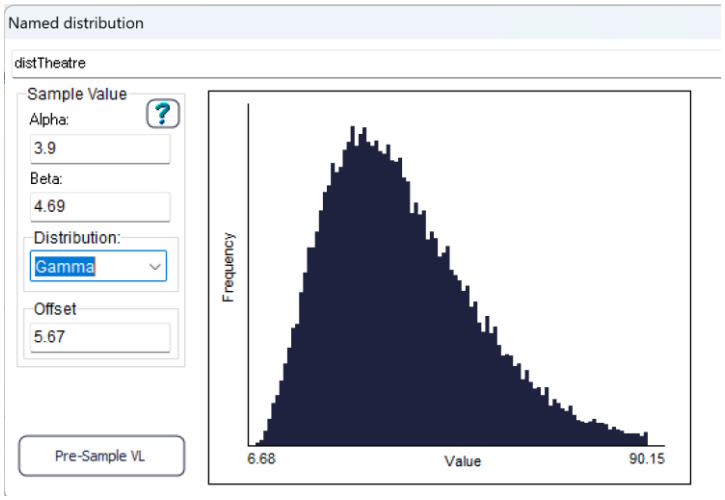
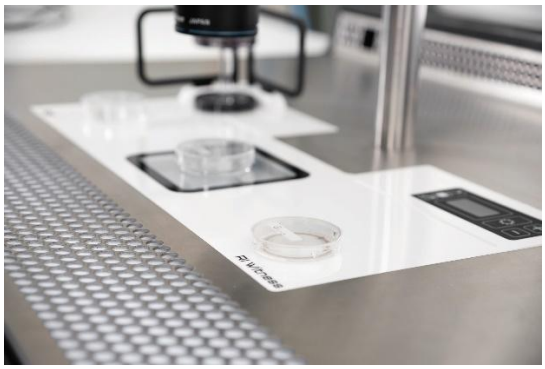


***Figure 30**. RIW Stat Fit distribution for EC.*

The data of time spent doing the EC was extracted from RIW procedures and integrated into StatFit for Simul8 © that recognised the distribution model for the time duration as a gamma distribution. This was then added the Simul8© model.

As all movement of gametes and embryos must be registered by the RIW system or manually to comply with HFEA code of practice.(HFEA, 2023), this is a very valuable concept for building an accurate simulation model especially in relation with timings. Time durations of each procedure were calculated based on data from 2022 (in exception of a month where there was a server issue (Hosea, 2022). Distributions were created for each process based on all year data 2022 and based on how the witness process map was built for each process. Each data set for each process obtained was introduced into StatFit for Simul8© to determine the type of distribution (as shown in **Table 16** and **Figure 30**) if there is any and this was integrated into the model **Appendix 30**. Some procedures in the conceptual model did not involve movement of embryos so could not be captured by RIW to have a time stamp and calculate durations: checks on embryoviewer screen (fertilisation check, D3 check, D5/6/7 checks etc..), taking embryos to dewars and out of dewars. These procedures were manually timed by staff over a week to give mean values.

a



b

Figure 31. *RIW electronic witnessing system used at GSTT-ACU IVF lab*

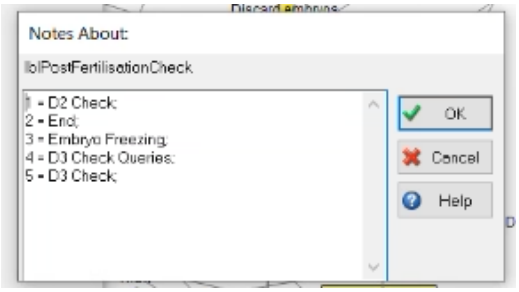
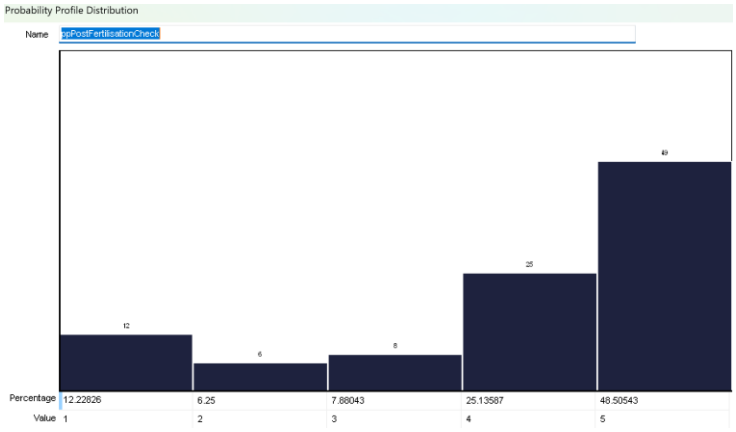
All dishes and tubes used in the lab for holding gametes and embryos are RIW tagged ***(a)****. Most laboratory procedures are carried out on surfaces where there is a reader* ***(b)*** *that captures date/time/operator carrying out the procedures using a Radio Frequency Identification RFI tag attached to all dishes where gametes and embryos are kept.*

Pathway probability

The pathway probabilities linked into each pathway in the Simul8© model were created from GSTT-ACU lab KPI data 2022- extracted from PMS Babysentry ©. **Table 16** shows the 5 different pathways possible at the point of fertilisation check (D2 transfer, end which is failure to fertilise, embryo freezing at 2PN, D3 check, D3 check query for possible transfer on Day3 or 5 depending on result). All pathway possibilities were linked to the process of fertilisation check on Simul8© model (b) and each possibility of pathway was assigned a probability (c) according to the KPI percentages extracted from PMS.

Table 16. *Example of pathway probability data addition into Simul8© model*

This is an example for the fertilisation check step. There are 5 possible outcome pathways following fertilisation check, each having a probability (a) and that was extracted from the lab KPI for 2022. (b) shows how these options are entered into Simul8 pathway and (c) shows how the percentages are set in Simul8©

<table>
<tr><td>Babysentry© data (PMS)
Pathways at fertilisation check: KPI 2022</td><td>Simul8©
Pathways at fertilisation check</td></tr>
<tr><td>
<table>
<tr><th></th><th>ICSI</th></tr>
<tr><td>D2 check</td><td>90/736 12%</td></tr>
<tr><td>End (failure)</td><td>46/736 6%</td></tr>
<tr><td>Embryo freezing (2PN)</td><td>58/736 8%</td></tr>
<tr><td>D3 queries</td><td>185/736 25%</td></tr>
<tr><td>D3 check</td><td>357/736 48%</td></tr>
</table>
</td><td> 
</td></tr>
<tr><td colspan="2">(c) Simul8 Probability profile distribution
 
</td></tr>
</table>

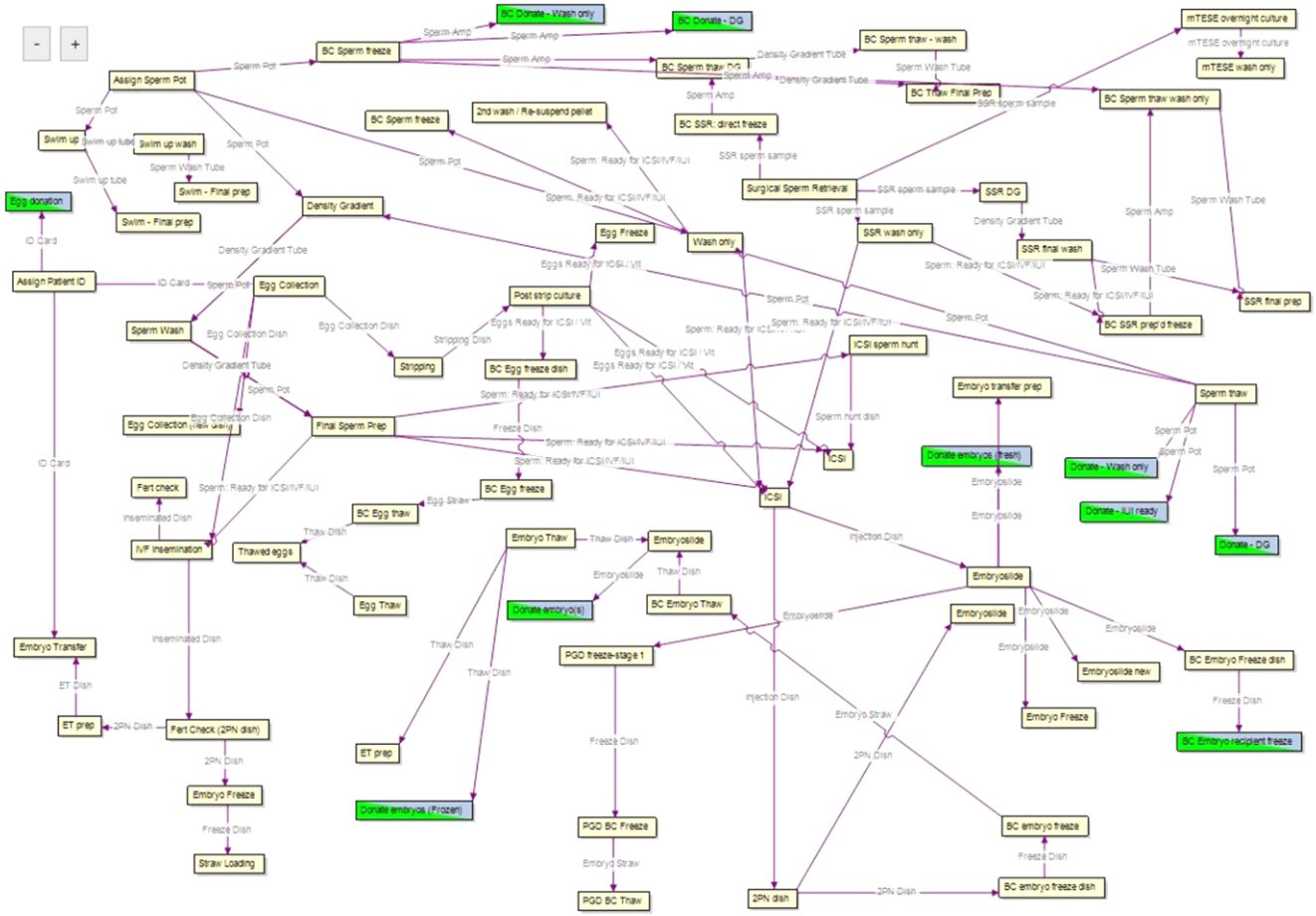


Figure 32. *RIW pathway diagram for GSTT-ACU IVF lab workflows*

This diagram was extracted from RIW software settings. This diagram sets out how procedures are recorded using RIW software, it is specific to GSTT-ACU lab following its SOP: to determine: how many staff members are involved, processes sequence and names are dishes given in the sequence.

Resources availability :

All annual leave, time off in Lieu, sickness leave or study leave absences for embryologists and practitioners are recorded into a spreadsheet team mapping every day of the year **Appendix 32**. The spreadsheet was on GSTT server and managed by the lab manager and senior embryologists to match staffing with workload demand. Data was extracted and pooled from the annual leave spreadsheet to create a spreadsheet for Simul8© model including all embryologists and practitioners that are present as opposed to contracted **Appendix 33**. The spreadsheets (embryologists and practitioners present every day) linked to the Simul8 model were editable to allow scenario testing.

4.5 The output analysis

4.5.1 Model Base Run / Base Case

Simulations require a lot of data entry (data hungry) but also generate a lot of data. In our case, the model has been created to run for a year (52 weeks) and start from the first week of January 2022 where the system is empty. In fact, GSTT-ACU closes for the Christmas period (last week of December and first week of January) and the only items present in the system (initial condition) are the dewars that have stored gametes and embryos. In simulation model, the dewars are set to have several spaces occupied (can be modified in settings, **Table 14**). As a result, the system does not have a warmup period and the only initial condition is the dewar occupancy. The model created on the base of 2022 data settings was called Base Case (BC) or Base Run as well as all results generated by this model and will be the initial model used to validate against real life data. The results from the BC were analysed and then compared to different scenarios to tested.

4.5.2 Types of output results from Simul8©

There are multiple ways to get results from any simulation and this can be determined by the objective of the model created. The types of results that can be available in Simul8© software are (1) Objects' Results : number of work items entered and number resulted. (2) Start point results : number of work items entered at one point , lost and remained (3) Queue results : number of work items in queue (Currently, minimum, mean, maximum, total Entered), (4) Queueing time (minimum, mean, maximum, standard

deviation, number of non-zero queueing times, percentage within x time limit), (5) Activity results : number of work items in addition to percentage (awaiting work, working, blocked), (6) end point results : work completed, (7) resource and resources pool results : Utilisation , travelling time, productivity.(8) Time interval results : Useful when the process is not stable over time (e.g., certain times/days are busier than others), (9) transaction logs : this is the time spent between two activities. Three types of transaction logs can be determined : First by area: to monitor the time between entry or exit of work items between specified pairs of objects. Second by object to monitor the entry and exit of work items from all (or some) the objects in the simulation. Third transaction log is by resource: to monitor the work carried out by the resource(s) in the simulation. (10) The last type of results is a summary called high level analytics panel**:** it gives an instant snapshot of the simulation. It can be used to identify bottlenecks and areas for improvement, track KPIs over the simulation run and check utilisation statistics on activities and resources and compare how KPIs have performed across previous runs.

4.5.3 Types of output results chosen

The choice was made to create our own result panel. The choice of the data the model was mainly focused on answering the research questions: Can the results show that the IVF lab can be modelled into a DES Simul8© model by showing that entering arrivals (egg collections, FET and , do we get outputs such as transfers, freezes, biopsy and sperm freezing and the dewars are filling. These results will be showing that all pathways are working. The second set of results had to answer whether the number of outputs were coherent with real life data for the validation research question. Transaction logs representing parameters OM1, OM2, OM3 described above were part of the results chosen to validate the model. We also needed metrics that could be useful for giving an insight on how the system works and whether there are ideas of improvements and what root causes of problems may be. The last set of results is to compare “what if scenarios” to BC model and answer the question : Do the scenarios tried give the answer of what are the optimum working conditions.

Simul8© main results screen was set up in this project to deliver results in 4 formats where all the result outputs mentioned above will be collected. This will be a result of

Input and output of items: Input were the number of egg collections planned, number of frozen embryo transfers planned. The output were the number of embryo transfers (fresh and frozen), number of embryo /egg freezing, number of biopsies and number of semen analysis, number of semen freezes. OM1, OM2 and OM3 were used as output metrics to validate the model. The insights of how the system works came essentially from staff utilisation time over specific days of the week but also as yearly means, but also from queue results, unfinished tasks and transaction logs. These metrics summarised in **Table 17** were used to answer the research questions.

Table 17. *Results delivered by GSTT-ACU-IVF Simul8© model*

Results	
Process Metrics (PM)	**Queuing results (Q)**
Input metrics: Planned egg collections , Frozen embryo transfers and semen analysis planned (all determined by arrivals) Output metrics: number of egg freezing, embryo transfers (fresh and frozen), embryo biopsy, embryo freezing, sperm freezing	All queues identified in the simulation were included in the results but only process time sensitive queues were focused on (ICSI, fertilisation check, egg freezing) Queues were expressed in mean and maximum (minutes)
Time Interval results (TI)	**Unfinished activities /tasks (UT)**
We have chosen embryologist utilisation EU and practitioner utilisation PU as two parameters to observe on a daily basis during the simulation run	List of all activities included in the simulation and number unfinished each day during the whole time of the simulation (52 weeks)
Transaction logs per area	**Transaction log per resources**
Time duration between OM1 Egg collection-egg freezing OM2: Egg collection-ICSI OM3 : IVF insemination-IVF fertilisation check	List of activities carried out per resources chosen (embryologists and practitioners here)

4.6 Model verification and validation methods

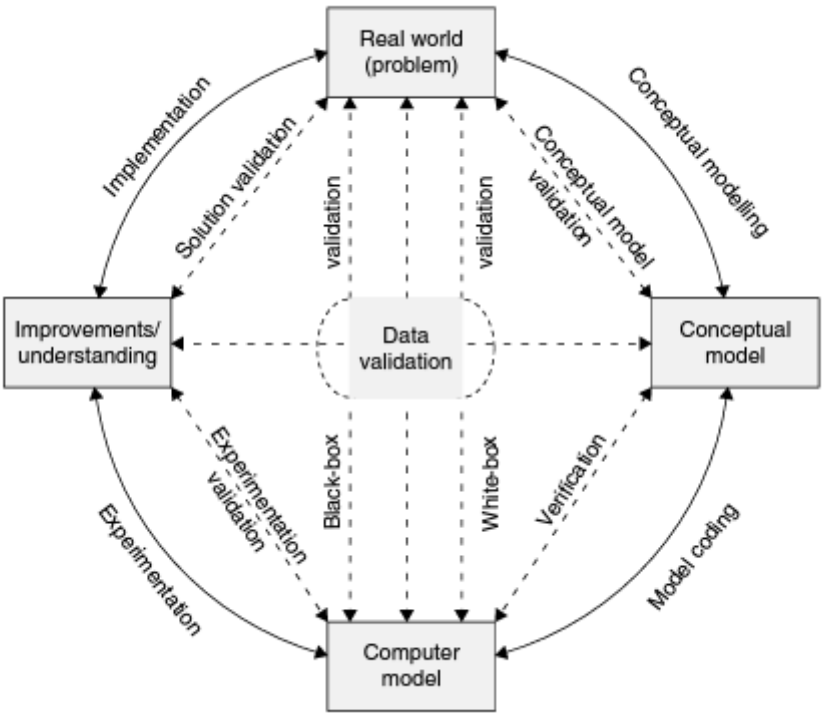


***Figure 33**. Simulation model verification and validation in a simulation study*
The diagram(Robinson, 2014a) showcases the importance of validation in the life cycle of simulation modelling Data validation as shown confirms the validity of the conceptual model and the computer model and enhances the effectiveness of its use

Verification and validation are continuous processes throughout the life cycle of a simulation (**Figure 33**, **Figure 34**). It is impossible to prove that a model is valid so verification and validation are processes to increase confidence in the model to the point that it will be used for decision making. Verification is done throughout the model built by checking that each process step is behaving as expected. As an example, at egg collection arrival, a couple arrives, the male partner goes to sperm production room and the female partner goes to egg collection. One verification done was by adding 10 arrivals and observing the dynamic. At the start, the model was blocked at the sperm production room where the queue was building up while egg collections were going through. This was a verification that highlighted a glitch in the model built and was hence rectified. This verification process was part of every step addition of a new process when the model was built.

To validate a model, we must compare simulation model output data from the simulation system with output data collected from the real-life data for the same period which is called results validation. According to Law (Law and Winter Simulation), the simulation analysts and Subject Matter Experts (SME) should review the simulation results for reasonableness. If the results are consistent with how they perceive the system should operate, then the simulation model is said to have face validity. The same concepts are called by Robinson (Robinson, 2014a) White box and black box validations

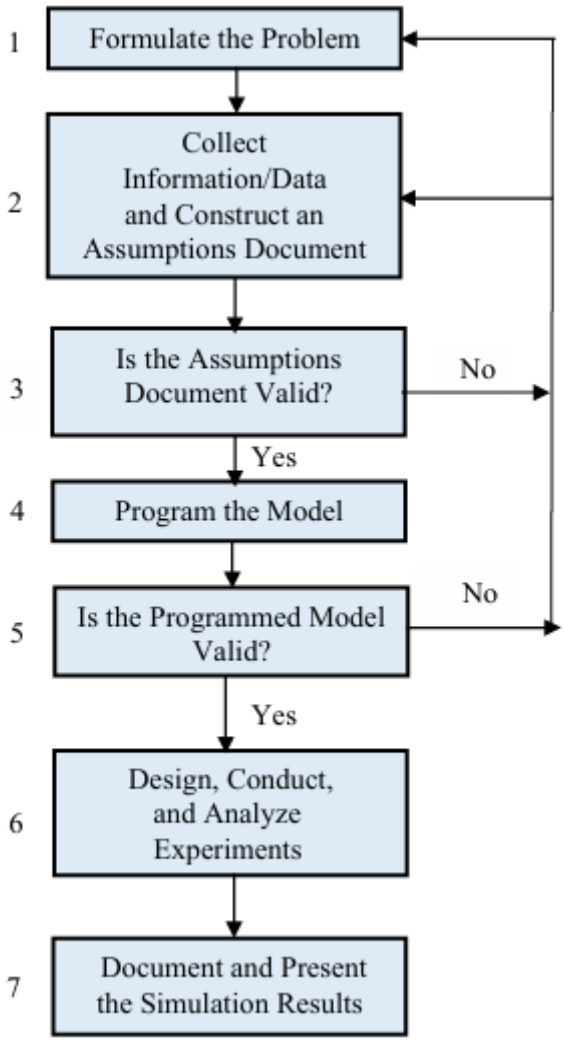


Figure 34. *Seven step approach for conducting a successful simulation study*

Law gives a 7-step approach (Law and Winter Simulation, 2022) to conduct a successful simulation study which includes a result validation step (5) where results delivered by the simulation are compared to real life output results with the same input.

4.6.1 White box validation

Ensuring the constructed model reflects the IVF lab procedures accurately, its structure and model results were tested thoroughly. The model's structure validity was tested using white-box validation method which dissects the overall model into different steps and examines whether each of them is behaving according to the design. The white-box validation was done in a one-year simulation and paused time by time so the model can be evaluated for each timestamp before collecting several runs for the real simulation. The white box validation was also done twice spending a whole day going through each step individually, checking pathway, percentages and distributions or missing data. The last white box validation one was done on 29/07/2024.

4.6.2 Black box validation

In our case, to obtain sufficient accurate data for the results outputs chosen, Simul8 suggested to run 106 trial runs. The simulation model results are compared to historical 2022 data through 110 trial run**s** (the maximum of number of runs suggested by Simul8 to have been 107. A Trial run (or experiment) is a series of runs of the simulation, performed with the same settings for all parameters. The only thing changing are the "random numbers" that Simul8© uses for sampling values from distributions. As the simulation is intended to resemble real life scenarios (i.e. with variability), it is important to run a simulation more than once. A Trial gives a more rounded results and improves accuracy in terms of proposed performance measures (results).

The purpose of a trial is to check the reliability of results. At the end of just one run we have simulated one year in your organization. A Trial is a run of several years and the trial results summarize the results of these several years under the same settings. If the two sets of data compare "closely," then the model of the existing system is considered "valid." (The accuracy required from the model will depend on its intended use and the utility function of the decision-maker.) Several statistical tests (t, Mann-Whitney, etc.) have been suggested in the validation literature for comparing the output data from a simulation model with those from the corresponding real-world system However, classical statistical tests based on independent, identically distributed (IID) observations are not directly applicable. Since the model is only an approximation to the actual system,

a null hypothesis that the system and model are the "same" is clearly false. We believe that it is more useful to ask whether or not the differences between the model and the system are significant enough to affect any conclusions derived from the model. (Law and Winter Simulation)

4.7 "what if scenarios"

The step following model validation is to apply "what if scenarios" (**Figure 35**) to investigate answering the questions and suggestions the team had to resolve the issues of staffing-workload to be able to carry out the tasks on time. The assumption is that the staffing level expressed by Utilisation rate of embryologists and practitioners is a limiting factor and bottleneck. To reduce the pressure on staff and be able to carry out the tasks involved in the simulation, different strategies have been applied to the model and resulting results were analysed. The scenarios tested were applied to areas identified as bottlenecks or assumed as bottlenecks by the embryology team. The simulation model created by the team allowed a lot of flexibility to be able to change input and try scenarios.

The first experiment was by changing Arrival schedules for all 3 entry points (Andrology, egg collection and frozen embryo transfers). The second experiment was directed to resources by applying it to staff : allowing overtime and observing staff utilisation change/queues/unfinished tasks, then changing staff numbers. Some of the resources that we could try changing through the model are dewar capacity and embryoviewers capacity. The way the model was set did not allow other experiments on number of beds, sperm production rooms or ICSI stations. The third scenario to test was in processes by changing proportions of pathways: proportions of egg freezing and IVF or apply entire weeks of PGD cycles. Some scenarios could in theory be tested but weren't because of lack in timing or impossibility to include in the model the way it was set: change procedures' timings, different staff shifts.

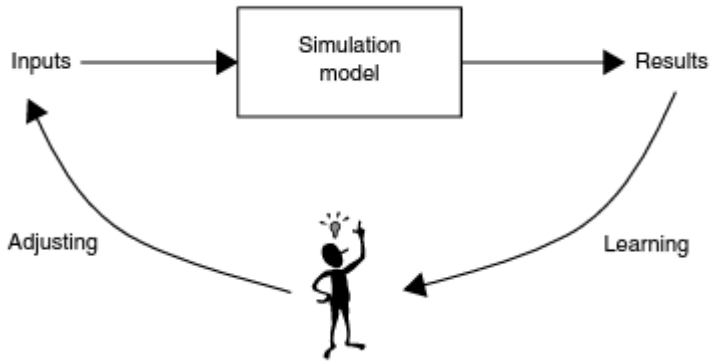


Figure 35. *What if scenarios.*

This is the goal of simulation modelling : trialling different ideas and strategies and analysing their effects. Yet again it is a circle where, the input is adjusted to try a strategy, the results change and a learning is obtained which might change the next strategy

4.8 Staff and patient involvement (questionnaires)

The project was initially presented in an overview format in December 2022 to GSTT ACU during the weekly educational meeting. Simul8© team joined in the meeting to show applications of simulation in healthcare. At that point, the project was still an idea to be developed. There was a plan to use simul8© but the possible outcomes were not clear. The objective was mainly as to have a visual model that raises awareness with stakeholders and capture the team attention about the IVF lab complexities. There was also a plan to investigate bottlenecks and check whether it matches with the internal/common interpretations. The team had confidence in the project but was very apprehensive about the possibility to map the complexity of the IVF lab.

The team main beliefs were that

- The main bottleneck came from the unpredictable workload distributed unevenly during the week (Monday and Friday being the busiest days)
- Workload was higher than the capacity of the lab (staffing not matching workload)
- Delays in the entry point (egg collection) mean that many time-sensitive procedures in the lab were delayed (ICSI, Egg freezing).
- The staffing situation meant that procedures were done based on staff availability within their shift rather than physiological recommendations.

Nearly two years following that, the project final simulation and results were presented to the embryology team at GSTT ACU on 17th September 2024. Some staff members knew about the project from the presentation 2 years before (41.7%).

4.9 Innovation

The model was created by a collaboration between an embryologist who has been part of the team and a good understanding of all pathways and a software company specialist. The innovation comes from using a novel approach to explore the IVF lab but also a interest that is from what (Law and Winter Simulation) considers as a SME Subject Matter Expert someone internal to the clinical embryology team rather than senior management or an academic. The involvement of a SME gives better chances for the simulation to lead into implementation and to have buy-in from stakeholders.

4.10 Limitations

Simulation has the potential allow experimentation to try many scenarios without taking any risks in real-life. The main disadvantage and limitation are that simulation modelling is data hungry and needs collection of enough data to create a reliable model. In a project team composed with 2 members and with a time limit and a budget constraint, the simulation model had to be simplified using some assumptions. Simulation could be time consuming and in a project that covers a whole activity, some assumptions and simplifications had to be made. The main assumptions made are the travel time between tasks weren't included but prioritisation of tasks was not included.

5 RESULTS

5.1 Can the IVF lab be modelled into a "DES digital twin"

This question can be answered by visualising the model interface and verifying its closeness to real life processes, doing face value validation and black box validation by comparing the data delivered by the model versus real life data.

5.1.1 Visualisation of GSTTACU IVF lab model

The first result of the simulation modelling is a dynamic visualisation of the IVF lab workflows. The model created using Simul8© Software has a dynamic interface The simulation can run over a determined period for up to 52 weeks. The simulation base case **BC** is based on the year 2022 timetable (Egg collections, Frozen embryo transfers, semen analysis and semen freezes) and Resources available on site for 2022 (staff present and equipment available) in addition to pathway proportions in addition to the time duration distributions. The BC the model is based on all working conditions of Year 2022 but all parameters can be changed in the settings section (**Table 14**) to try "What if scenarios". The simulation was set to be able to run for up to 52 weeks. The starting point has been set as the 1st Monday of January 3rd January 2022. The first week of the simulation is part of what is scheduled as Christmas shutdown. The model basic case can be run multiple times with new randomness to check consistency and increase confidence in results delivered. A video of the model interface created with Simul8 is available to view online (Kaffel, 2024a). After running a simulation (**Figure 36**), results can be displayed by selecting the RESULTS display result button (**Figure 37**, **Figure 38**)

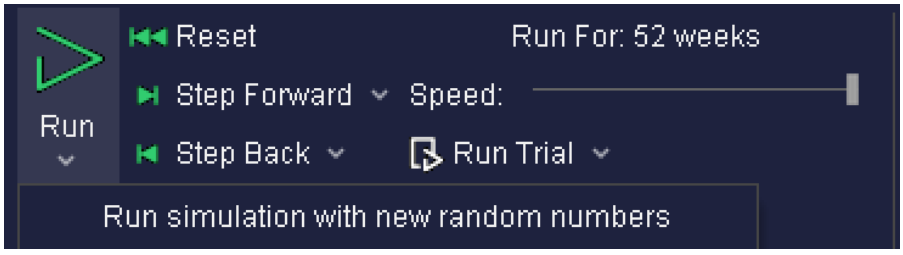


Figure 36. *Simulation run button*

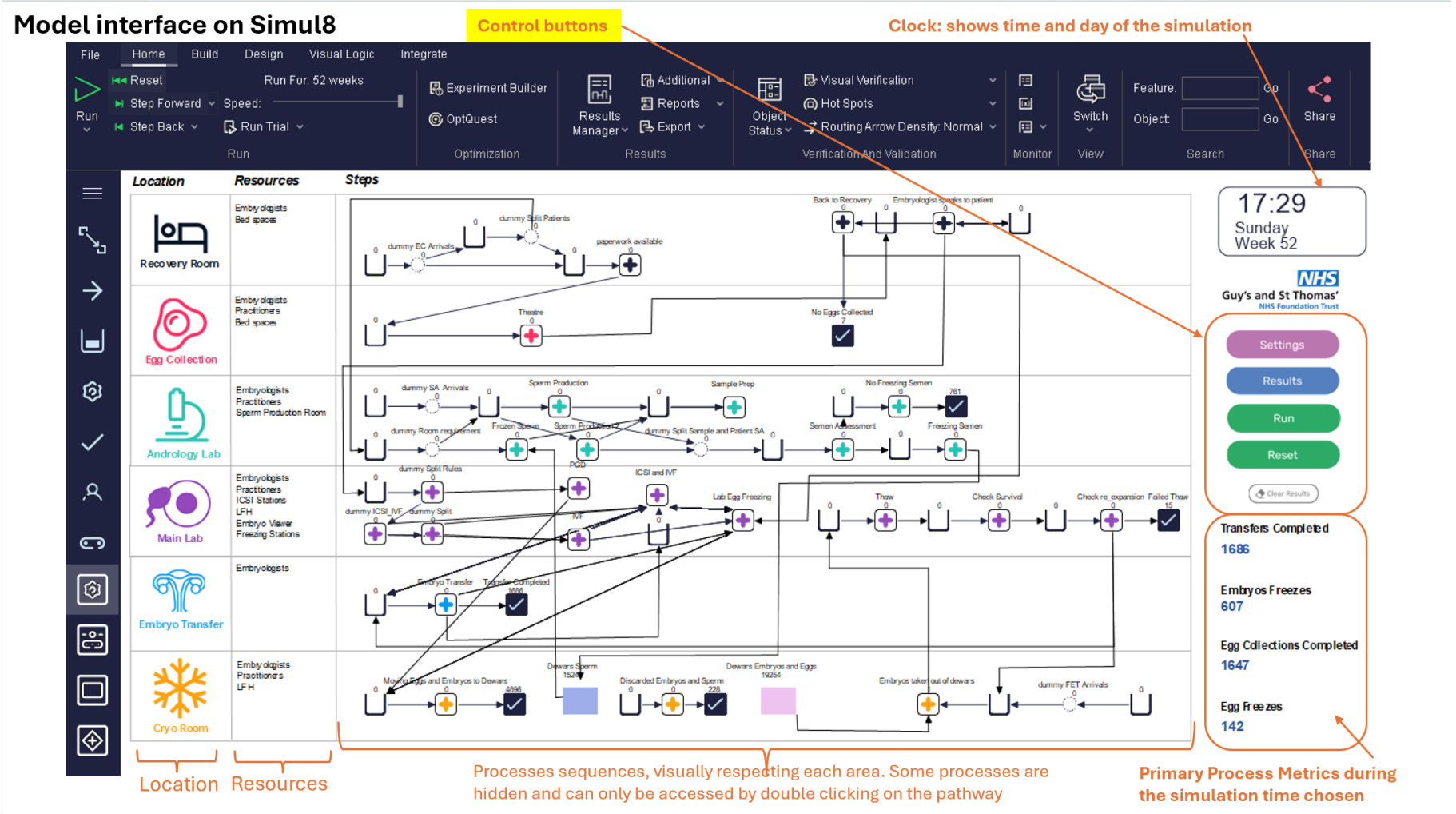
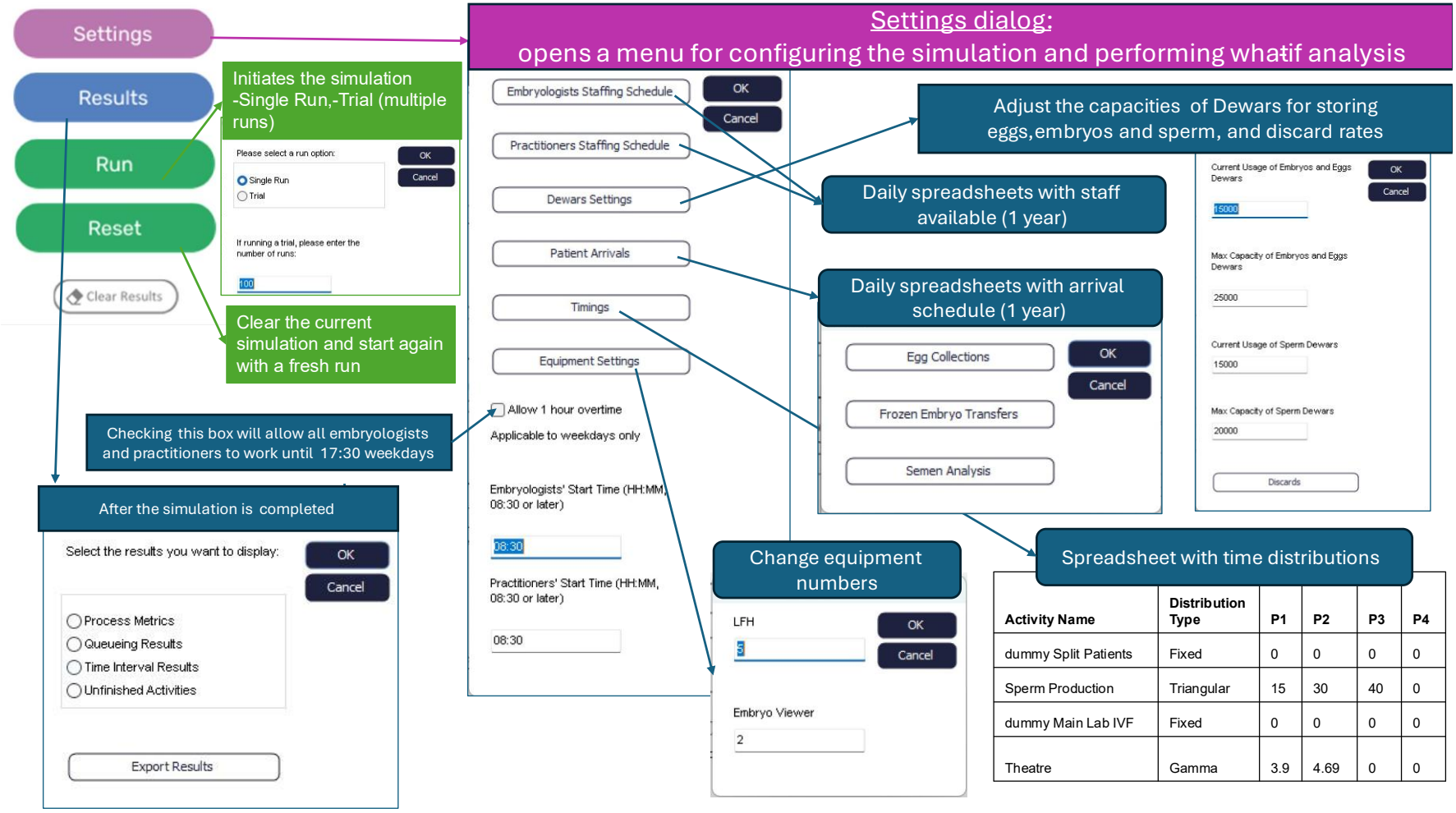


Figure 37. *Visual display of GSTT-ACU IVF lab simulation (model interface).*

The display shows all 5 areas (Recovery area , egg collection theatre, andrology lab, main lab embryo transfer room and cryo room)



Activity Name	Distribution Type	P1	P2	P3	P4
dummy Split Patients	Fixed	0	0	0	0
Sperm Production	Triangular	15	30	40	0
dummy Main Lab IVF	Fixed	0	0	0	0
Theatre	Gamma	3.9	4.69	0	0

Figure 38. *Control button functions in the simulation interface.*

The diagram shows the different options each control button gives and the diagram explains what each section allows the user to operate and change to adjust the model

5.1.2 Verification and validation of the simulation

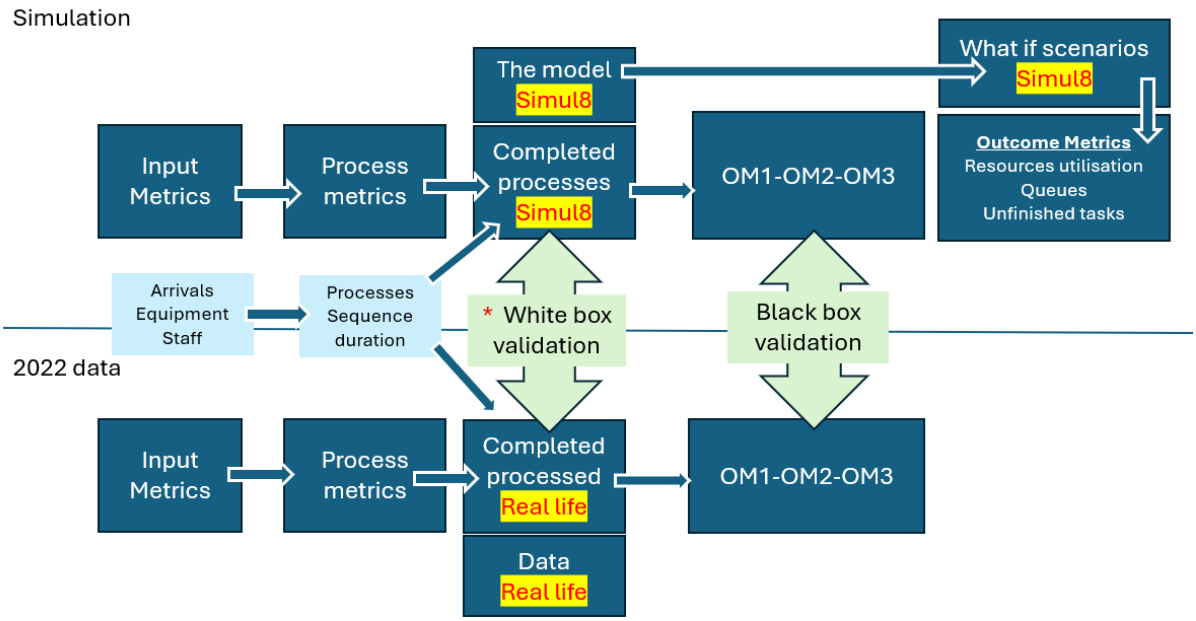


Figure 39. *Simulation results validation and scenario testing*

** In Simul8, the trial calculator recommends several runs to use for trial, we have chosen to run 110 trials for white box validation and 5 runs for black box validation. Only one run was compared to the BC scenario for scenario testing*

5.1.2.1 Verification of the model

Verification of the model was a continuous process all through the built of the simulation (**Figure 39**) and trialling it to make sure every step drawn in the conceptual model is mapped in the Simul8© model (**Figure 33**). As an example of a continuous verification. When the model was built with all the lab steps, the first trial was to introduce a random number of egg collections as an input, after running the model, we noticed that all patients stayed in the queue for the beds as they were not discharged. A step was missing and was then introduced. This verification step was done every time a pathway is introduced and numbers were checked after running the model.

5.1.2.2 White box validation

White box validation was done by observing how the model behaves in general and was based on the embryologist (considered as SME here) experience, this is what is also called face value validation. White box validation was also done by comparing the process

metrics of the model to real life data. As an example, we put through the model som e input metrics such as arrivals for egg collections, semen analysis and frozen embryo transfers (all planned tasks), we run these through the model created and we observe what the model produces in terms of process metrics: number of tasks completed : egg collections, egg freezing, fresh transfers, embryo biopsy. Etc…

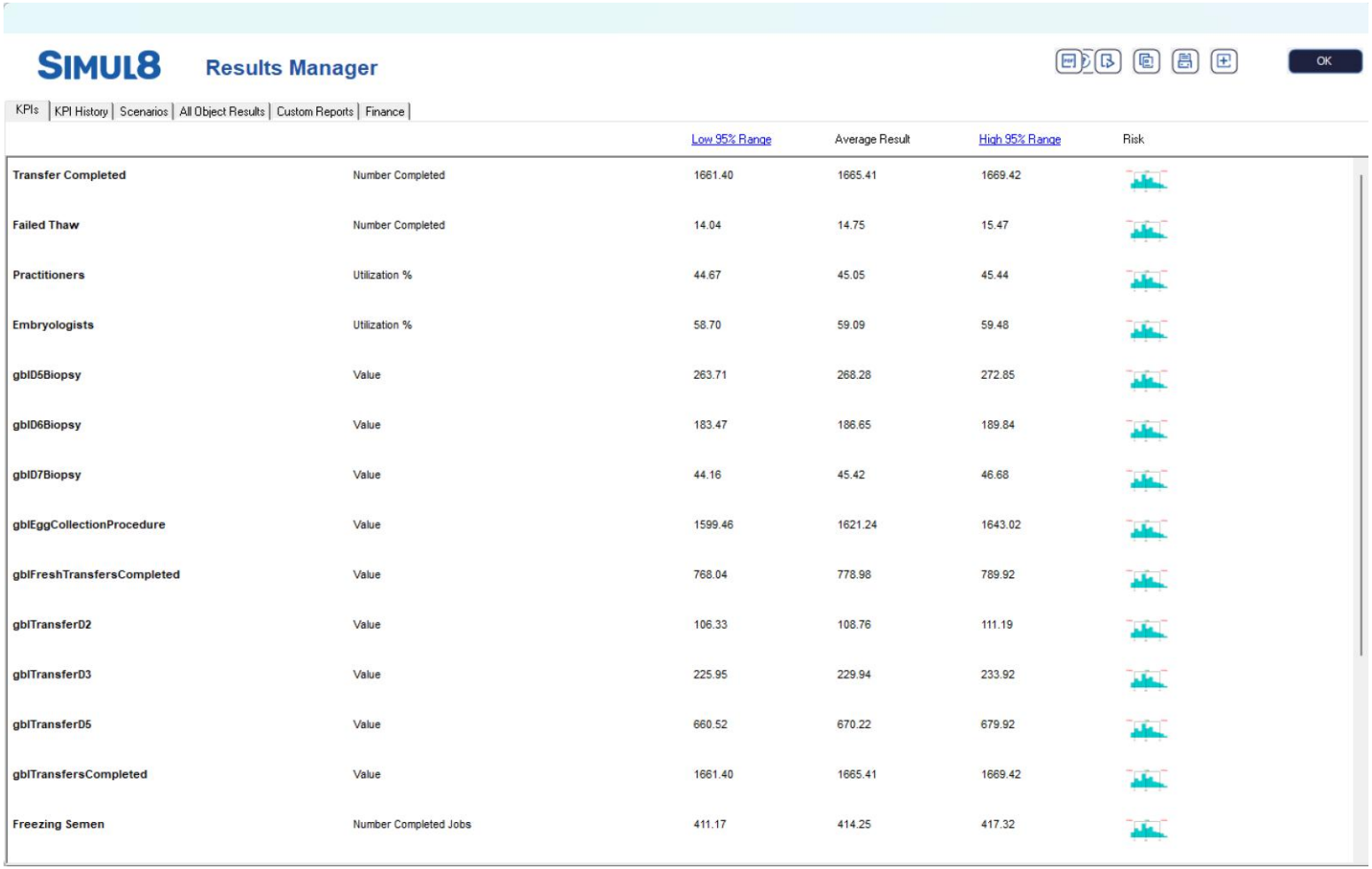
In Simul8©, a calculator recommends a specific number of trial runs to use for each parameter tested in results. The recommendation is based on the required precision of the confidence limits around the estimate. The required precision was set up as 5% of the mean. A Trial (or experiment) is a series of runs of the simulation, performed with the same settings for all parameters. The only thing changing are the "random numbers" that Simul8 uses for sampling values from distributions. As the simulation is intended to resemble real life scenarios (i.e. with variability), it is important to run a simulation more than once. A Trial gives more rounded results and improves accuracy in terms of proposed performance measures (results). The purpose of a Trial is to check the reliability of results. For the process metric results described above, the maximum number of trial runs for accuracy was 107 trials (**Table 18**). Consequently, the number of trial runs used for validation was 110 trial runs that we compared to real life data from year 2022. The data is shown in **Appendix 34**, **Table 19** and **Figure 40**. Following 110 trial runs, we uploaded the 110 results for each parameter and we created histograms to show the distribution from 110 runs for each parameter (**Figure 41**, **Figure 42**, **Figure 43**, **Figure 44**, **Figure 45**, **Figure 46**)The white box validation was done by plotting real-life data into the histograms to make sure that the data falls within the distribution to confirm that the model behaves as real-life.

***Table 18**. Recommended number of trial runs for each parameter*

Simul8 suggests a specific number of trial runs that we must run the model for to deliver reliable results. The recommendation is based on

	Recommended number of runs
Embryologists Utilization %	*21*
Practitioners Utilization %	*26*
Egg collections	
Egg Collections Completed	*42*
NO Eggs Collected	*116*
Embryo transfers	
Transfers Completed (FET)	*4*
Transfers Completed (Fresh)	*22*
Day 2 Transfers	*26*
Day 3 Transfers	*26*
Day 5 Transfers	*23*
Number of Biopsies	
Day 5 Biopsies	*44*
Day 6 Biopsies	*45*
Day 7 Biopsies	*62*
Egg Freezing	*42*
Andrology	
SA Completed	*4*
Semen Freezing completed	*6*
Failed procedures	
Failed Fertilisations ICSI	*57*
Failed Fertilisations IVF	*64*
failed thaw	*107*

When we run trials in Simul8©, the summary results are displayed as confidence intervals rather than just single numbers (**Figure 40**, **Table 19**). The confidence intervals help establish how much trust we can put in a single mean value.



		Low 95% Range	Average Result	High 95% Range	Risk
Transfer Completed	Number Completed	1661.40	1665.41	1669.42	
Failed Thaw	Number Completed	14.04	14.75	15.47	
Practitioners	Utilization %	44.67	45.05	45.44	
Embryologists	Utilization %	58.70	59.09	59.48	
gblD5Biopsy	Value	263.71	268.28	272.85	
gblD6Biopsy	Value	183.47	186.65	189.84	
gblD7Biopsy	Value	44.16	45.42	46.68	
gblEggCollectionProcedure	Value	1599.46	1621.24	1643.02	
gblFreshTransfersCompleted	Value	768.04	778.98	789.92	
gblTransferD2	Value	106.33	108.76	111.19	
gblTransferD3	Value	225.95	229.94	233.92	
gblTransferD5	Value	660.52	670.22	679.92	
gblTransfersCompleted	Value	1661.40	1665.41	1669.42	
Freezing Semen	Number Completed Jobs	411.17	414.25	417.32	

***Figure 40**. Simul8© GSTT-ACU IVF results display after 110 BC trial runs*

The central column of figures gives the result mean across the 110 trial. This gives a guide as to what we expect the long-term mean to be. The left and right columns give an indication of how reliable the central (mean) figure is.

Table 19. *Data from GSTT-ACU IVF lab 110 Simul8 BC runs vs 2022 data*

The table shows the total number of procedures completed at the end of the year 2022 (1st column2022 data) by the IVF lab at GSTT that is compared to the same results generated by 110 Simul8 BC runs. Simul8© presents the results as a Confidence Intervals with the mean in the middle

Process	***2022 data***	***Low 95%***	***mean***	***High 95%***
Egg collections	*1792*	*1586.05*	*1615.86*	*1645.68*
No eggs collected	*14*	*14.31*	*15.09*	*15.88*
Egg freezing	*156*	*141.55*	*144.86*	*148.17*
Frozen embryo transfer	*1437*	*1436.53*	*1437.25*	*1437.98*
Failed thaws	*14*	*14.02*	*14.75*	*15.47*
Fresh embryo transfer	*826*	*761.29*	*776.24*	*791.18*
Day 2 transfer	*122*	*105.76*	*108.57*	*111.39*
Day 3 transfer	*251*	*224.39*	*229.36*	*234.34*
Day 5 transfer	*673*	*654.65*	*667.66*	*680.67*
Semen analysis	*747*	*728.68*	*731.75*	*734.83*
Semen freezing	*399*	*411.14*	*414.22*	*417.29*
Day 5 biopsy	*292*	*261.54*	*267.22*	*272.90*
Day 6 biopsy	*278*	*181.72*	*185.72*	*189.72*
Day 7 biopsy	*31*	*44.09*	*45.59*	*47.10*

Table 19 shows the data from 2022 in comparison to the results generated by 110 Simul8 runs in a confidence interval format. The model shows lower confidence intervals results in comparison to 2022 data (egg collections, egg freezing, fresh embryo transfers, semen analysis , day 5 and 6 biopsy) which can indicate areas of improvements that the model can benefit from. It also probably indicates the need to examine the distributions a bit closer.

Andrology

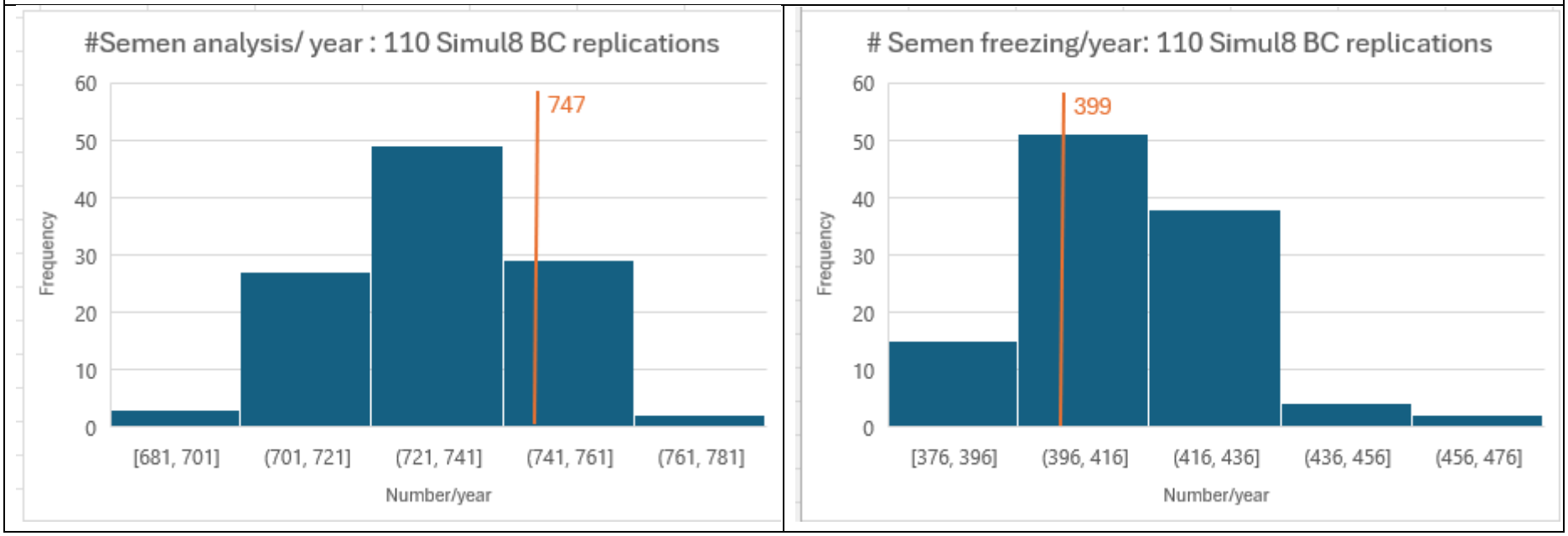


***Figure 41**. Distribution of andrology process metric results from 110 Simul8 base case runs*

The histograms show the results from 110 Simul8 BC runs and the orange bar shows in each histogram the 2022 data plotted into the distribution. This is a visual face value check that the model created on Simul8© is working as expected

Egg collection

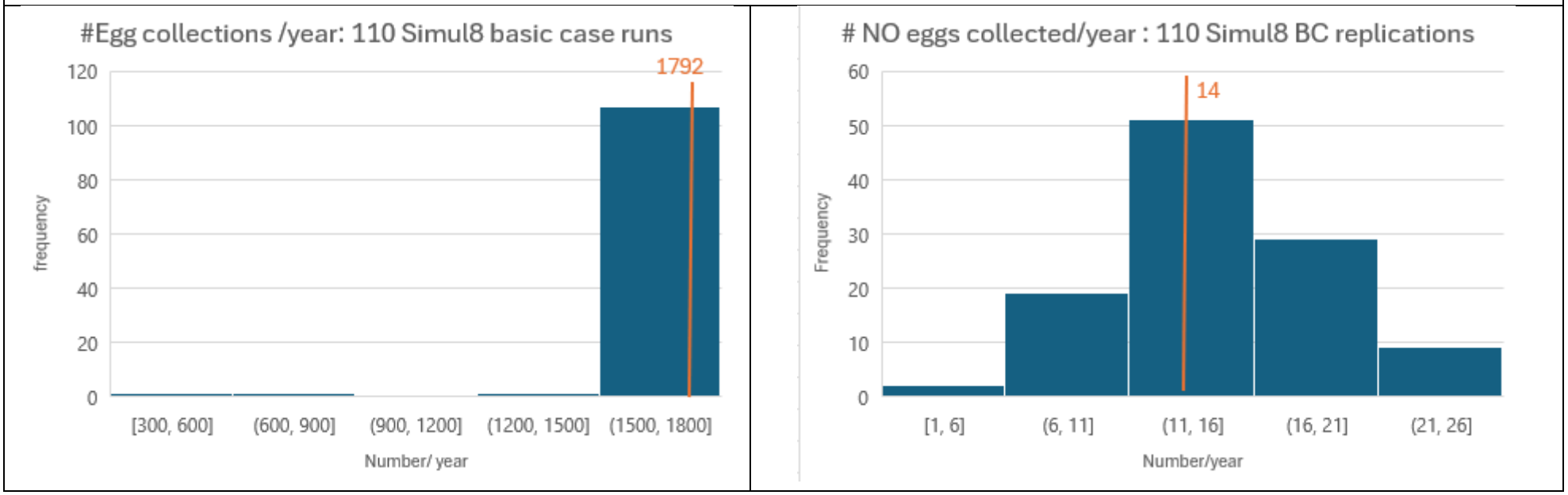


Figure 42. *Distribution of egg collection process metric results from 110 Simul8 base case runs*

The histograms show the results from 110 Simul8 BC runs and the orange bar shows in each histogram the 2022 data plotted into the distribution. This is a visual face value check that the model created on Simul8© is working as expected

Thaws

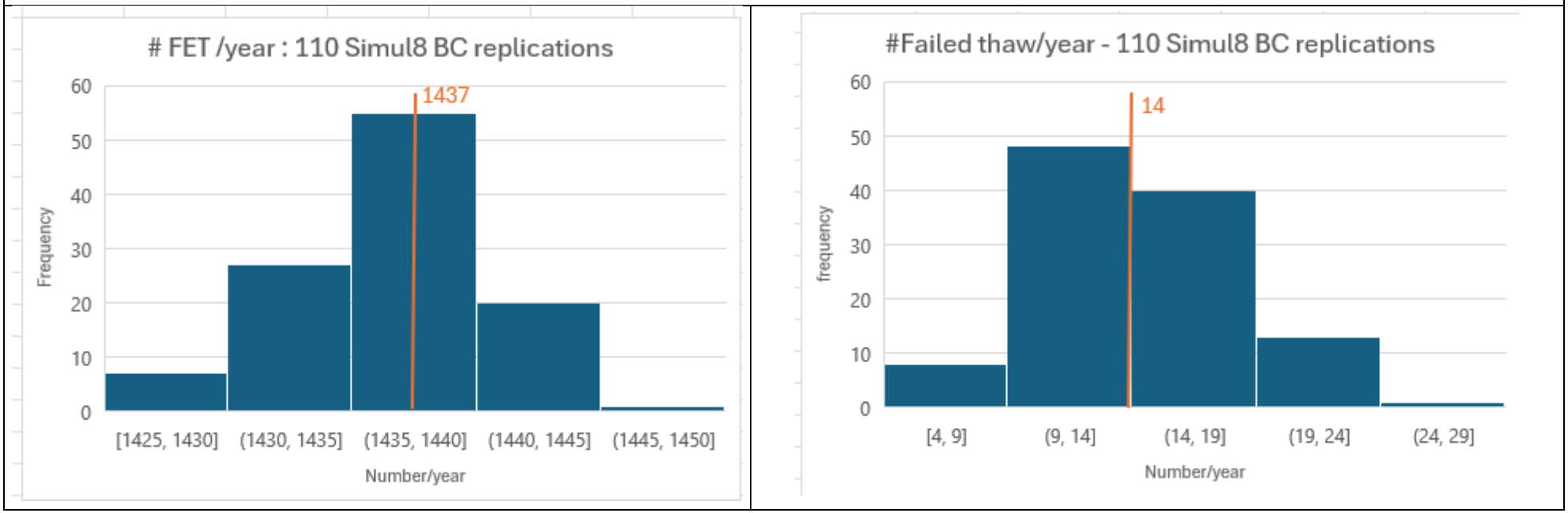


Figure 43*. Distribution of frozen embryo thaws for transfer process metric results from 110 Simul8 base case runs*

The histograms show the results from 110 Simul8 BC runs and the orange bar shows in each histogram the 2022 data plotted into the distribution. This is a visual face value check that the model created on Simul8© is working as expected

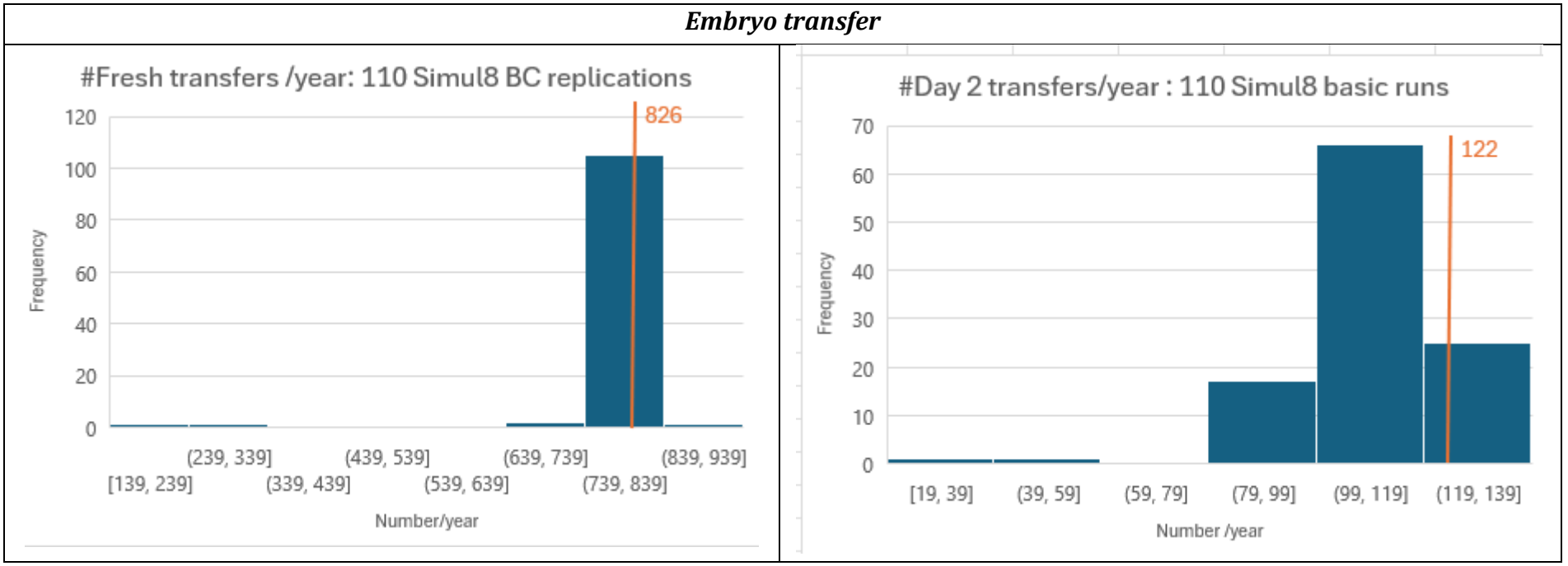


Figure 44. *Distribution of total fresh and day 2 embryo transfer process metric results from 110 Simul8 base case runs*

The histograms show the results from 110 Simul8 BC runs and the orange bar shows in each histogram the 2022 data plotted into the distribution. This is a visual face value check that the model created on Simul8© is working as expected

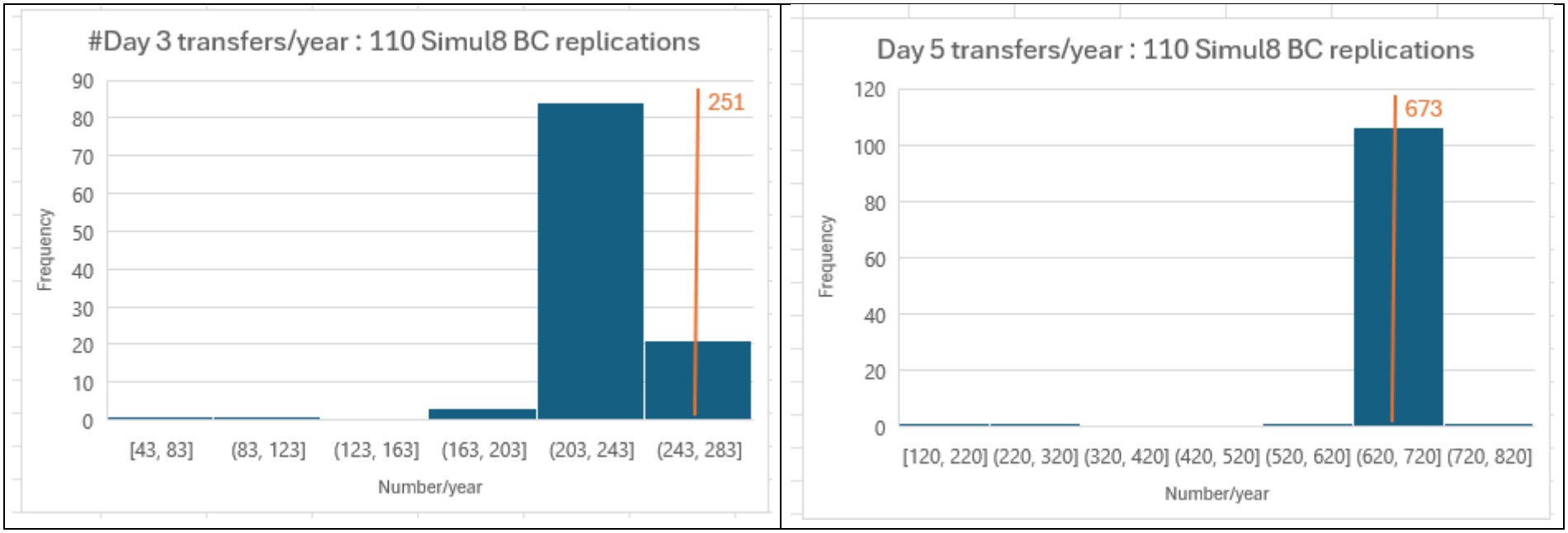


Figure 45. *Distribution of day 3 and day 5 embryo transfer process metric results from 110 Simul8 base case runs*

The histograms show the results from 110 Simul8 BC runs and the orange bar shows in each histogram the 2022 data plotted into the distribution. This is a visual face value check that the model created on Simul8© is working as expected

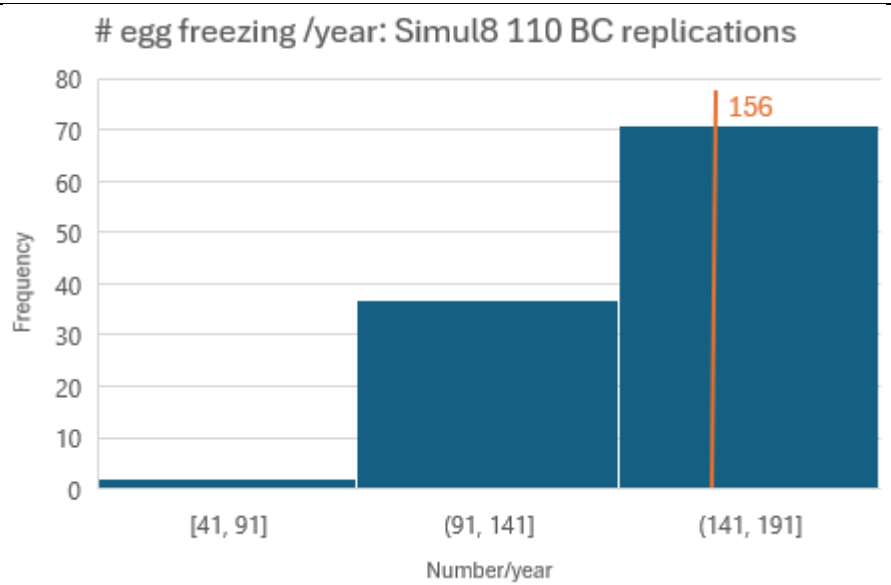
Egg freezing


Figure 46*. Distribution of egg freezing process metric results from 110 Simul8 base case runs*

The histograms show the results from 110 Simul8 BC runs and the orange bar shows in each histogram the 2022 data plotted into the distribution. This is a visual face value check that the model created on Simul8© is working as expected

5.1.2.3 Black box validation

Black box validation in GSTT-IVF Simul8© model has been carried out by comparing output metrics OM1, OM2 and OM3 results from the BC model results to real life data 2022. To make sure that the data from the model is representative, 5 randomly selected different BC runs results were compared to 2022 data for OM1, OM2 and OM3.

***Table 20**. OM1 Simul8© results (5 BC runs) vs 2022 data.*
P-value of t-test comparing each run to 2022 data

OM 1	RUN1	RUN2	RUN3	RUN4	RUN5	2022 Data
Size	148.0	164.0	141.0	142.0	126.0	144.0
Mean	97.7	84.1	91.4	134.3	112.9	92.1
Median	77.0	76.2	73.8	81.6	77.7	83.0
SD	67.8	37.7	74.6	176.1	178.8	45.3
Min	45.1	45.4	48.1	47.8	35.9	30.0
Max	466.6	362.7	727.0	1414.7	1637.2	394.0
P value	0.41	0.09	0.91	0.006	0.20	NA

Table 20 compares OM1 (time between egg collection and egg freezing) data from 5 randomly selected Simul8© base case runs versus 2022 data showing very similar mean and median for OM1 between what the model creates and what real life data is. Sample sizes are different between different Simul8© runs but comparing visually OM1 boxplot results (**Figure 47**) shows very similar distributions of OM1 around very similar median values. The most noticeable difference on the boxplot is that maximum values from 3 Simul8 base runs have outliers represent >500 minutes (>8 hours) while 2022 data maximum value is 400 minutes and the literature recommendation is 120 minutes. This showed that Simul8© model did not have a function applied to this activity to avoid going over the recommended 2 hours or a working day (7.5 hours). In the model, the task was dependent on resources availability while in real life data, resource availability is adapted

using workarounds to make OM1 meet the recommended time. This can be added to an improved version of a the same Simul8 model. Testing a model by comparing it to real life data is part of validating it to offer improvements.

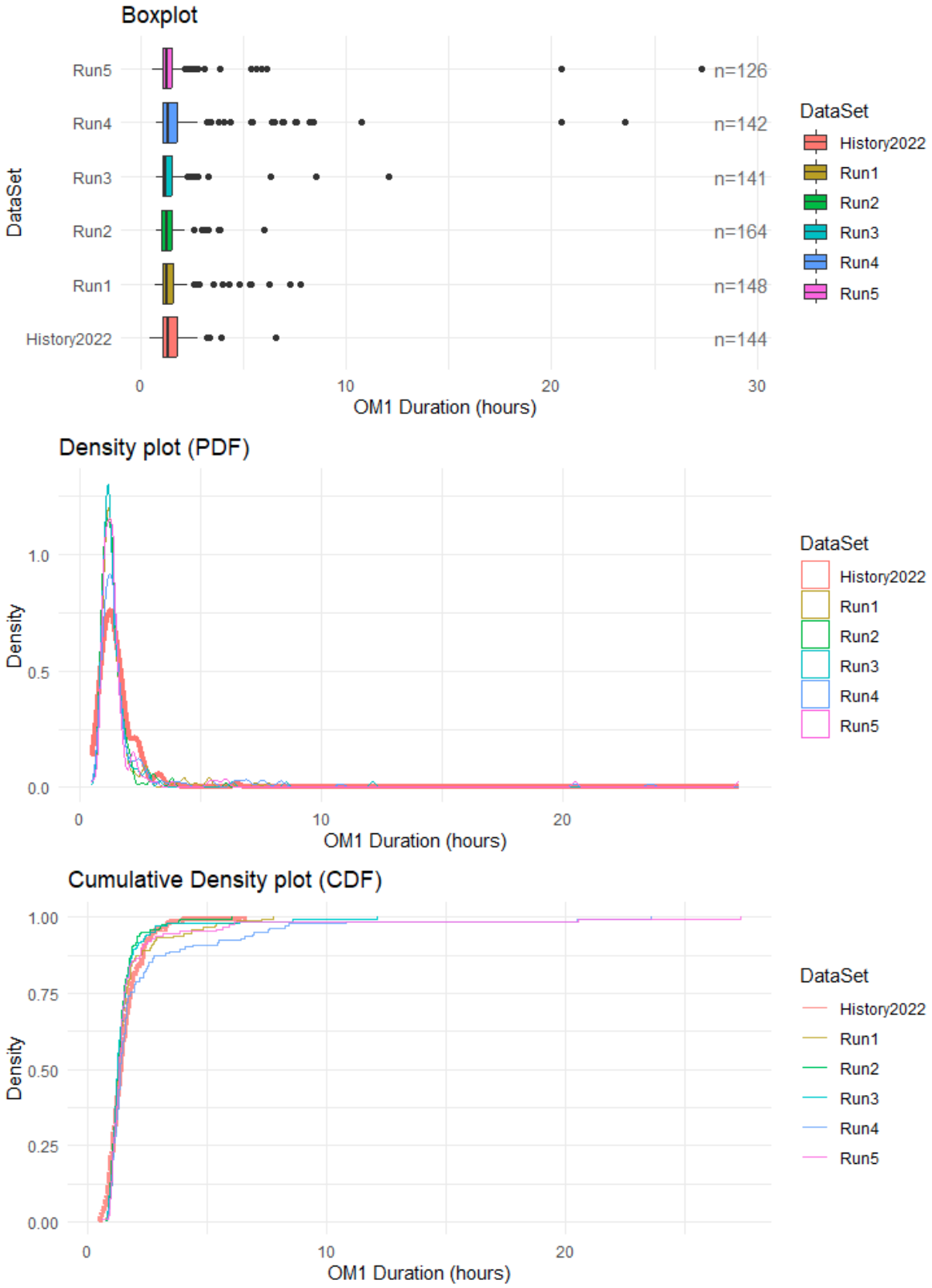


***Figure 47**. OM1- 5 Simul8 BC results vs 2022 data*

The results from 5 Simul8 BC runs for OM1 were plotted for comparison to 2022 data in a boxplot format, density plot format and cumulative density format.

***Table 21**. OM2 Simul8 results (5 base runs) vs 2022 data*
P-value of t-test comparing each run to 2022 data

OM2	RUN1	RUN2	RUN3	RUN4	RUN5	2022 Data
Size	1163	1102	1166	1147	1111	921
Mean	68.7	76.7	77.8	71.3	78.0	169.3
Median	54.0	55.1	54.7	54.5	53.5	167.0
SD	82.7	109.3	126.2	100.7	131.9	62.3
Min	82.7	25.4	22.8	25.1	23.1	29.0
Max	1257.0	1421.2	1395.3	1488.0	1552.8	406.0
p-value	<0.01	<0.01	<0.01	<0.01	<0.01	NA

Table 21 compares OM2 (time between egg collection and ICSI) data from 5 Simul8© base runs versus 2022 data showing that the model runs consistently faster than real life for OM2. OM2 boxplot results (**Figure 48**) show visually a tight distribution. Apart from the shift in OM2 in the model, the most noticeable difference on the boxplot is that maximum values from all 5 randomly selected Simul8© base runs have outliers >400 minutes (>8 hours) while 2022 data maximum value is 400 minutes and the literature recommendation is 3-4 hours (up to 240 minutes). This showed that Simul8© model behaves in a way that does not account for workarounds. There was not a function applied to this activity (ICSI) to have a minimum of 2-3 hours or not go over the recommended 4 hours or a working day (7.5 hours). In the model, the task was dependent on resources availability while in real life data, resource availability is adapted using workarounds to make OM2 meet the recommended time and not go over the working day by prioritising it. Adding a prioritisation is an improvement that can be added to the model created in a different version.

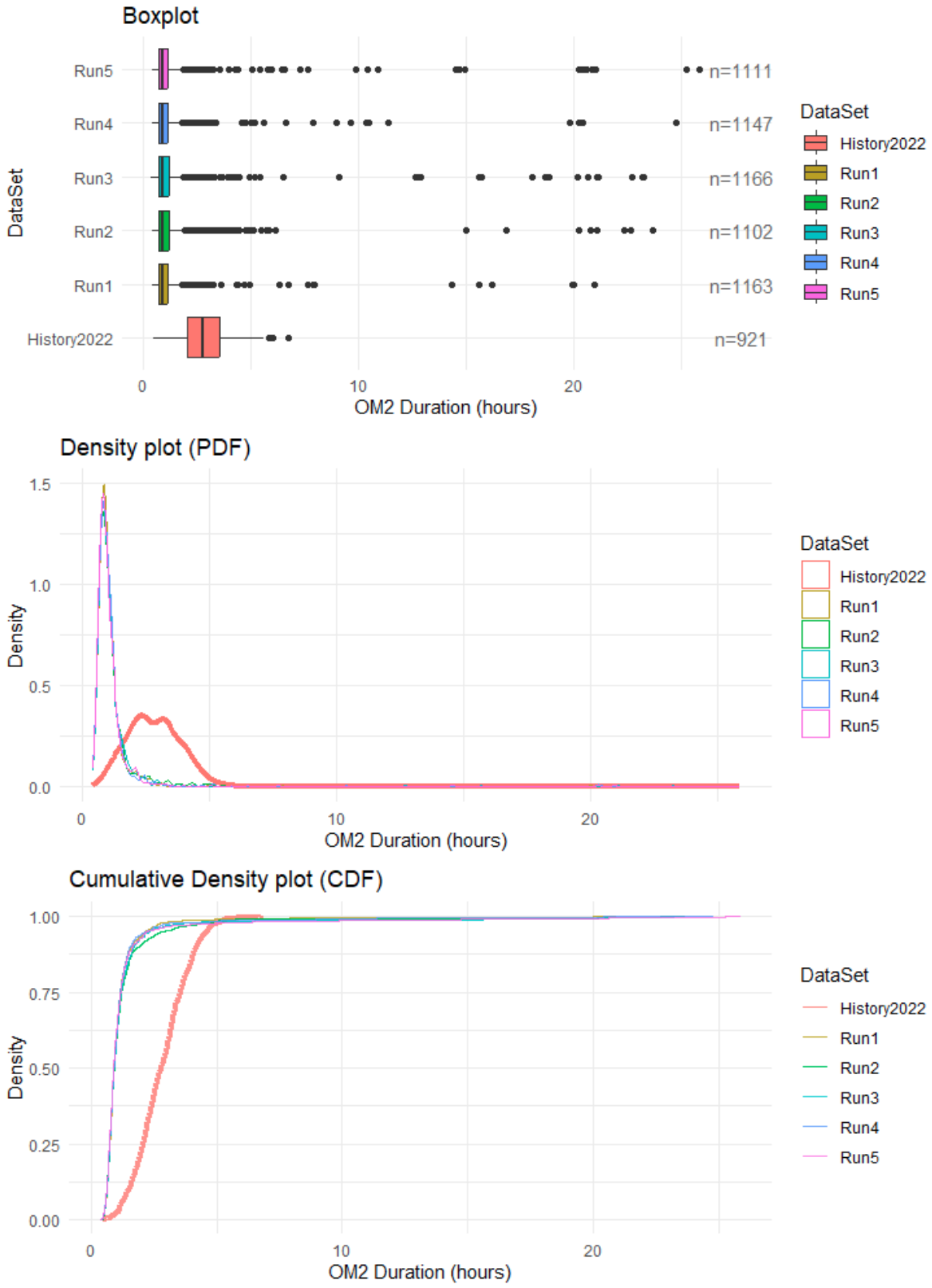


Figure 48. *OM2 - 5 BC Simul8 scenarios vs 2022 data*

The results from 5 Simul8© BC runs for OM2 were plotted for comparison to 2022 data in a boxplot format, density plot format and cumulative density format.

Table 22 compares OM3 (time between IVF insemination and next day fertilisation check) data (in hours) from 5 randomly selected Simul8© base runs versus 2022 data showing that the model runs consistently from 16h onwards while real life data shows occasional shorter OM3 (<16h) despite SOP recommendation being a minimum of 16h for OM3. The table also shows that OM3 is within very close range to recommendations (16h) but is shorter in the model comparing to real life. In summary, Simul8© model runs faster than reality for OM3.

***Table 22**. OM3 (hours) Simul8 results (5 base runs) vs 2022 data*
P-value of t-test comparing each run to 2022 data

	RUN1	**RUN2**	**RUN3**	**RUN4**	**RUN5**	**2022 Data**
Size	391.0	415.0	374.0	403.0	452.0	369.0
Mean	16.5	16.5	16.4	16.5	16.5	17.1
Median	16.2	16.2	16.2	16.2	16.2	17.2
SD	1.0	1.0	0.8	1.1	1.1	0.6
Min	16.0	16.0	16.0	16.0	16.0	14.1
Max	26.8	23.8	23.6	25.2	24.2	18.8
p-value	<0.01	<0.01	<0.01	<0.01	<0.01	ns

OM3 boxplot results (**Figure 49**) showed a tighter distribution in real life around the median. Simul8© model runs from 16h and faster but allows OM3 to go beyond recommendations (20h). This analysis revealed again that Simul8© model behaves without accounting for workarounds. The only function applied to the activity IVF fertilisation check was only to assign a minimum of 16h which explains the minimal value from Simul8 runs while in real life, embryologists can carry out the task earlier than 16h. There was not a function applied to fertilisation check (ICSI) to have a maximum of 20h so the model allows OM3 to go over 20h recommendation which does not happen in real life. In the model, the task was dependent on resources availability while in real life data, resource availability is adapted using workarounds to make OM3 meet the recommended time and not go over the 20h.

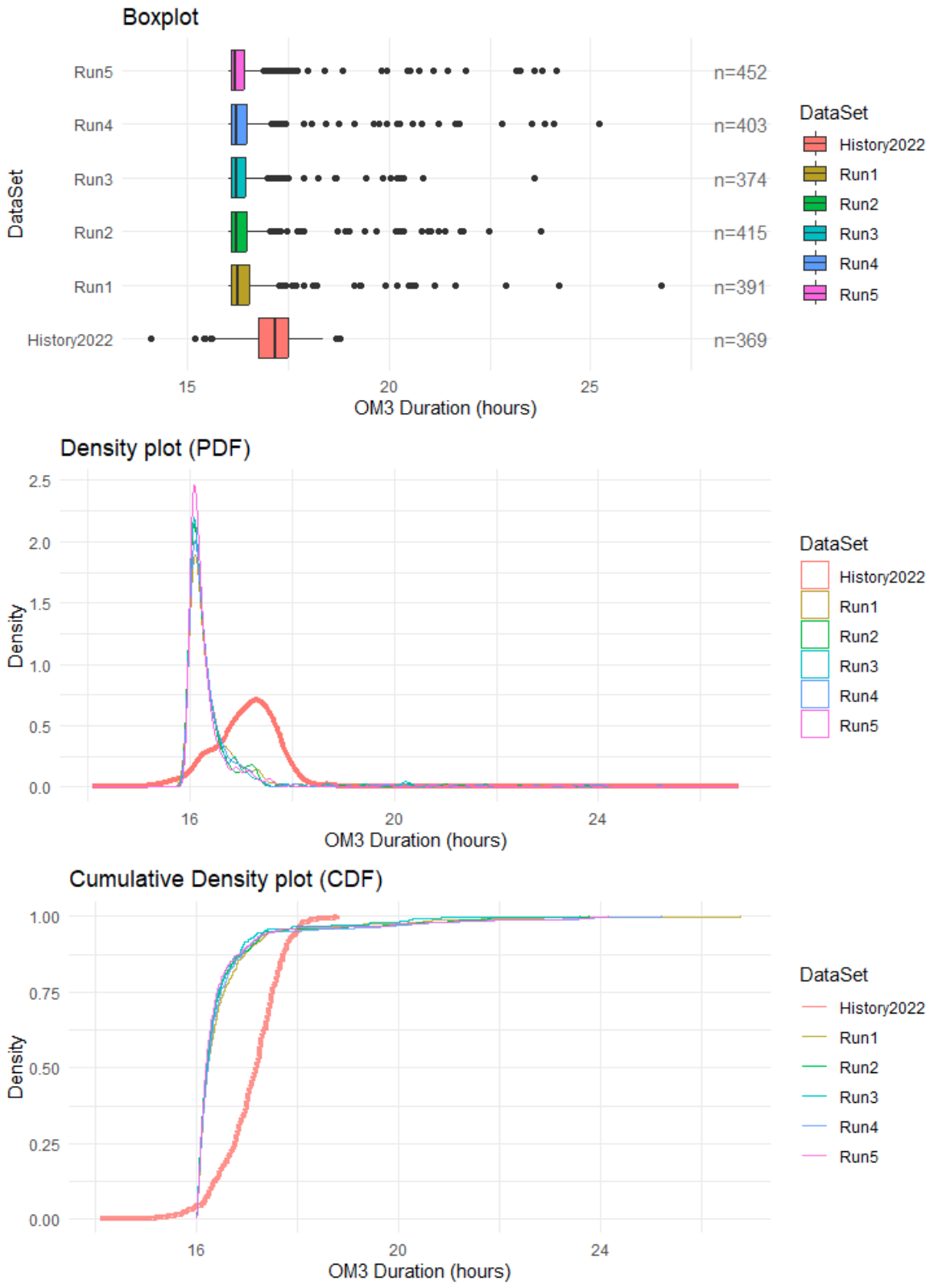


Figure 49. *OM3 - 5 BC Simul8© scenarios vs 2022 data*

The results from 5 Simul8 BC runs for OM3 were plotted for comparison to 2022 data in a boxplot format, density plot format and cumulative density format.

As a summary, the IVF lab from GSTT-ACU was successfully modelled into a DES Simul8© interface. The Simul8© model created for GSTT-ACU globally behaves similarly to real life with no major discrepancies as revealed by the face value, white validation. With the same input as 2022 data (arrivals, resources), the model results of Process Metrics were very similar. The Black box validation focused on Output Metrics that were identified previously as good metrics linked to success outcomes could be considered as proxy to success rates. Black box validation showed very similar distributions between real life data and Simul8© model data for OM1. The main difference in the simulation model for OM1 is that the model can run OM1 for longer while it is not recommended in real life

All three OM distribution have shown that the model runs faster than real life for the OM2 and OM3. The other limitation is that the model set up for the associated activities is mainly dependant on resources activities which makes all 3 OM run for longer while in real life, workarounds are applied to make OM1, OM2 and OM3 meet recommendations. The main variations in the Simul8© model of these parameters were dependant on workload and staff availability. Even though the model does not run on same timings as real life due to workarounds, it does still hold information about the primary drivers of the OM : workload and resources as per **Figure 11**.

5.2 Can the model created generate metrics useful for insight into how the real system works

In this part, the different results generated from GSTT-ACU IVF lab case base model were shown. This was carried out to investigate whether these results can be useful to analyse the real system in operation, identify trends, bottlenecks and : the IVF lab. As per the driver diagram **Figure 11**, the primary drivers of success that can be used as proxy for OM1, OM2 and OM3 (time duration contributing to success) are resources (staff and equipment) and workload.

Resources utilisation expressed in percentage (equipment and staff) can represent two parameters in one. Utilisation expresses the resource time utilised to carry out the workload. It is expressed as a proportion of the time the resource available. The higher

the utilisation rate is, the more time is occupied to carry out the workload. We examined staff utilisation (practitioners and embryologists) in addition to equipment utilisation.

Queues (Q) are places where work to be done can wait until appropriate resources or activities are available. Queues are expressed in minutes and are dependent on resources and workload. If an activity is ready to be done, it can't be done until the resources (staff, equipment) are available so a queue form waiting. The assumption is that the longer is the time in the queue is, the more it indicates overload or lack of staff and can measure the system performance the less staff there is for it. In the literature, queue performance is proportional to the variation in the queue x utilisation x service time. In this study, the queues were used as an identification for workload variability. Unfinished activities or tasks (UT) is a parameter that can show the nature and the number of tasks that were not completed at the end of the day shift. This parameter can be a measure for workload as well as queues for tasks. The analysis of the BC simulation can help to find change ideas (CI) that can lead to testing « *what if scenarios* ».

5.2.1 Embryologist utilisation EU

Embryologist utilisation (EU) distribution was analysed through 110 trial runs to observe if there is any variability between randomly selected simulation runs and it showed that most values were within 58.7-59.7 with an mean of 59.2% (**Figure 50**, **Appendix 34**).

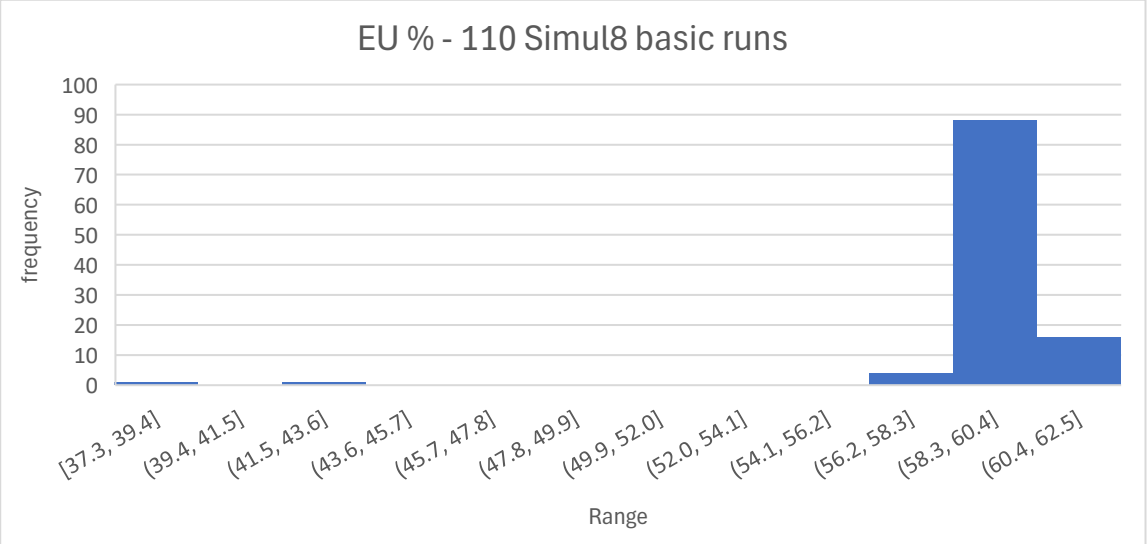


***Figure 50**. EU distribution from 110 Simul8© base runs*

Observing the daily EU over one year (**Figure 51**) showed a high variability of EU throughout the year. The EU starts at zero as the model starts empty with no lab workload the first week of January, and as time progresses, EU rises slowly showing the build of workload from same day arrivals in addition to previous days embryo culture reaching a peak on day 26 of the simulation where it reaches a 100%.

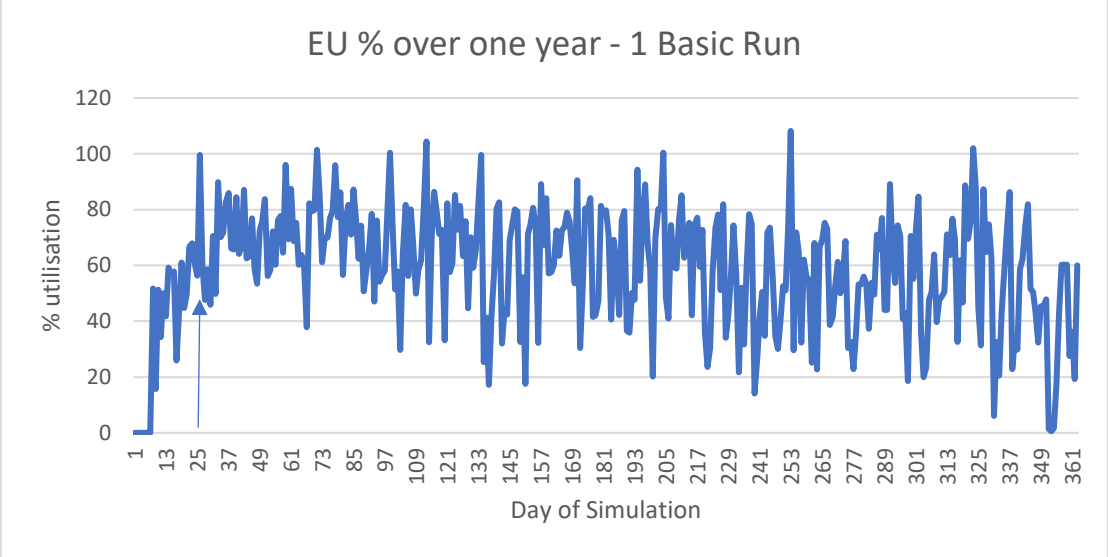


***Figure 51**. Display of EU over a year: one base case simulation run*

EU reaches 100% on some weekdays which were all identified as Mondays. The box plot of EU from 5 base case runs confirms visually that Mondays have consistently the highest EU, followed by Fridays during weekdays (

Figure 52). **Figure 53** confirms the same trend in terms of mean EU per weekday. Saturday and Sunday have also higher EU with less variability than weekdays. The cumulative frequencies of EU shown on **Figure 54** shows that >50% of EU is over 60%.

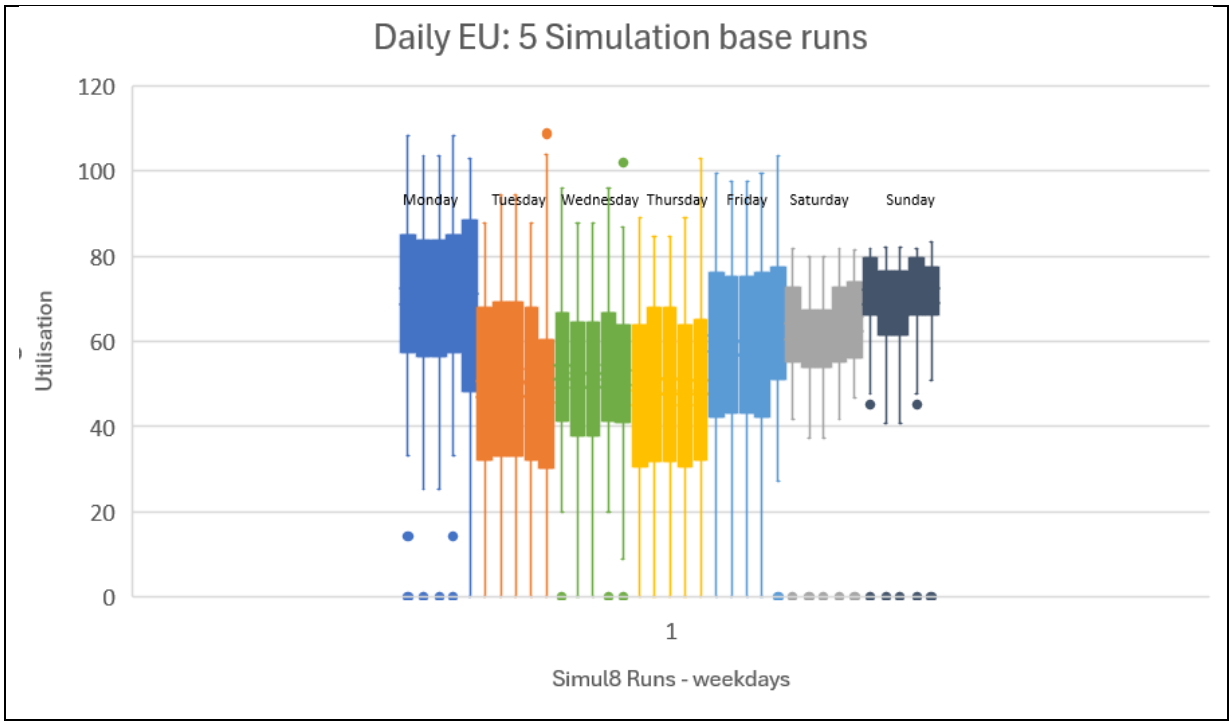


***Figure 52**. boxplot of Daily EU from 5 Simulation base runs*

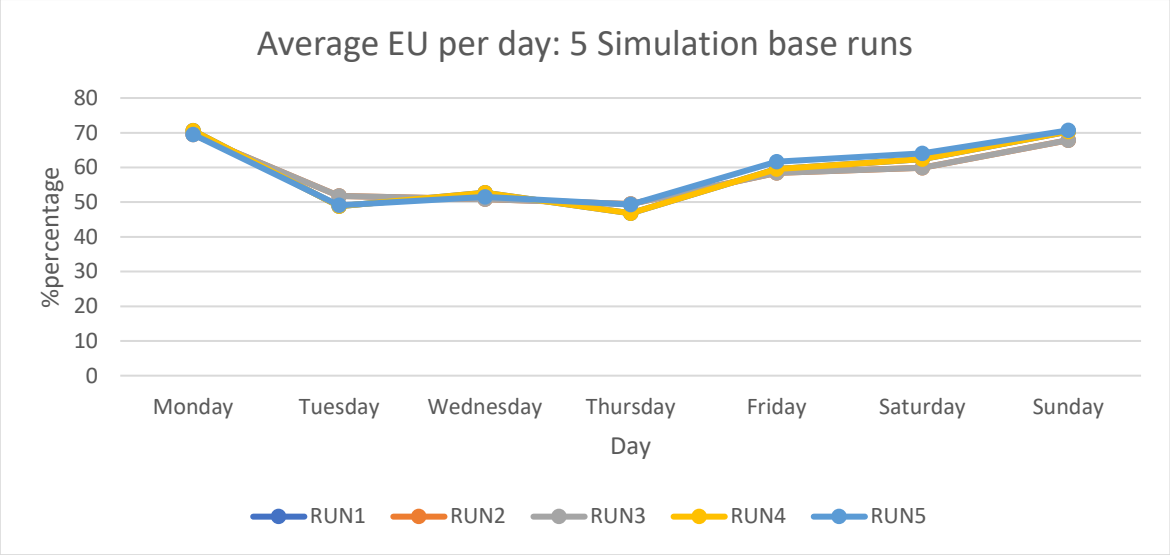


Figure 53. *Mean EU per day - 5 BC runs*

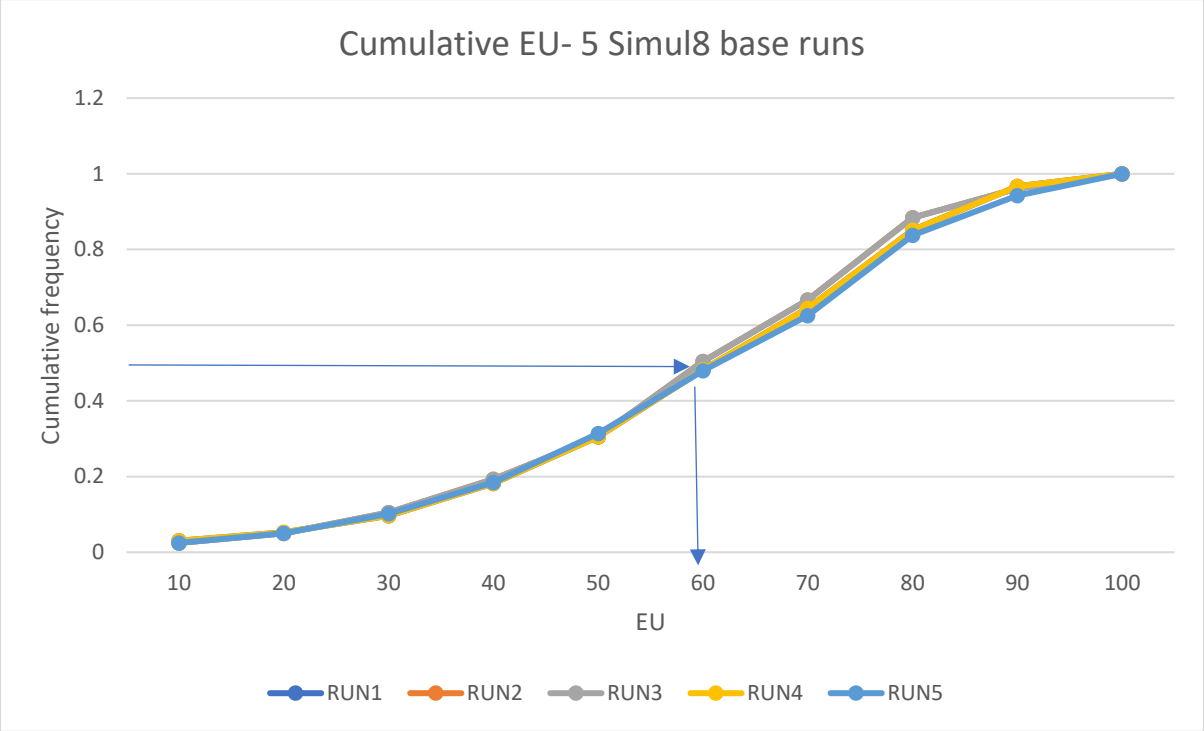


Figure 54. *Cumulative frequencies of EU - 5 BC simulation runs*

As part of analysing Embryologist utilisation, the model allows to track all the activities carried out by a resource as a number of tasks format. This gives an idea on workload distribution. For embryologists, the tasks were grouped by area (Main lab, Cryoroom, egg collection). In the main lab area, the tasks were divided into manual (need handling gametes and embryos) and screen based (Embryoviewer) as displayed in **Table 23**. Andrology lab has been divided in two parts that are independent : Diagnostic and prep

(for IVF treatments). Main lab manual procedures and andrology preparation procedures occupy the highest rank (

Table 23). The breakdown of tasks allowed a visual understanding of the workload distribution. As an example, the main lab embryoviewer tasks are all based on screen observations rather than manual tasks. These tasks can be done remotely if there is a possible remote access. Tasks that are linked to andrology diagnostic operate for a different service provided by GSTT-ACU. If the andrology diagnostic tasks were removed, the time saved can be quantified following the introduction of this change idea. Understanding the distribution of workload can be an analysis tool for change ideas.

Table 23. *Tasks carried out by embryologists*
Tasks carried out by embryologists in the Simulation model (1BC - 1year)

Task	Number per BC Run (1 year)	Proportion
Main lab – manual tasks	8322	27%
Andrology prep	8185	26%
Cryoroom	5044	16%
Main Lab - Embryoviewer	3919	13%
Andrology Diagnostic	2480	8%
Embryo Transfer	2195	7%
Egg collection	840	3%

5.2.2 Practitioner utilisation PU

Practitioner utilisation (PU) distribution was analysed through 110 trial runs to observe if there is any variability between simulation runs and it showed that most values were between 44-45% with an mean of 44.6 % (**Figure 55** and **Appendix 34**).

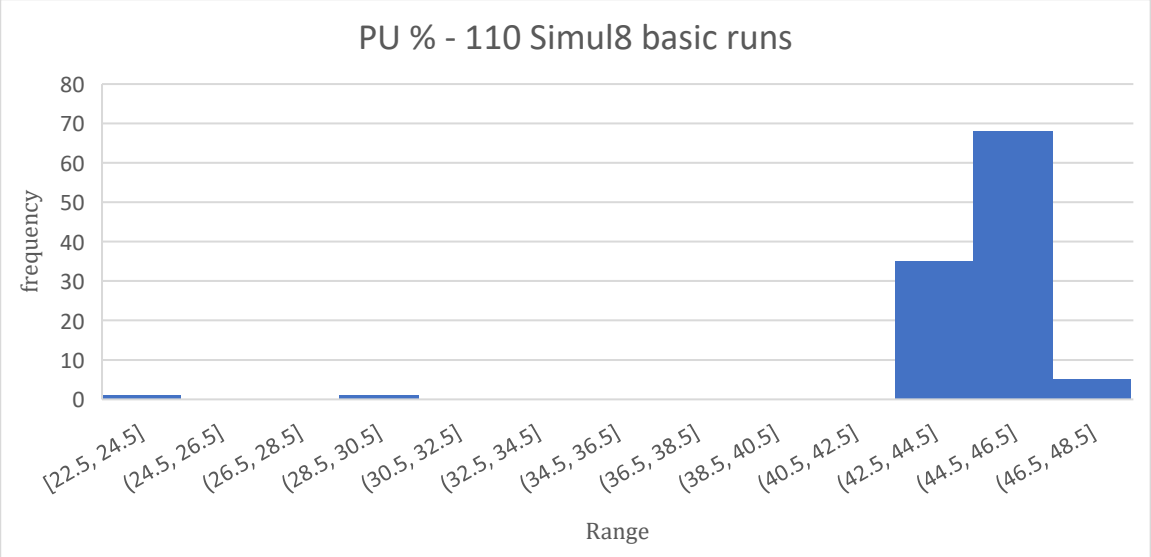


***Figure 55**. PU distribution - 110 Simul8 BC runs*

Observing the daily PU over one year showed high variability of PU through the year (**Figure 56**) It is to be noted that there is no data for Saturday and Sunday as practitioners do not work weekends hence the display goes to zero end of week. The PU starts at zero as the model starts empty with no lab workload the first week of January, and as time progresses, PU rises slowly showing the build of workload from same day arrivals in addition to previous days embryo culture reaching a peak on day 26 of the simulation where it reaches 86%.

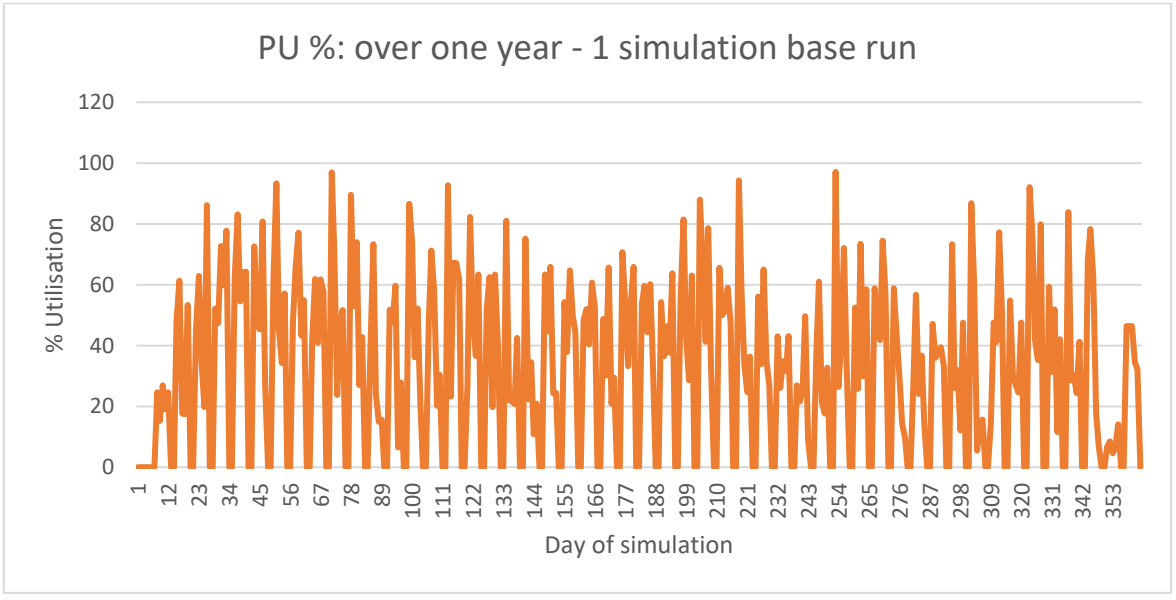


***Figure 56.** Display of PU over a year: one base case simulation run*

PU reaches 100% on some weekdays which were all identified as Mondays. The box plot of PU from 5 base case runs confirms visually that Mondays have consistently the highest PU, followed by Tuesday (**Figure 57**). **Figure 58** confirms the same trend in terms of mean PU per weekday. The cumulative frequencies of PU shown on **Figure 59** shows that >50% of EU is over 40%.

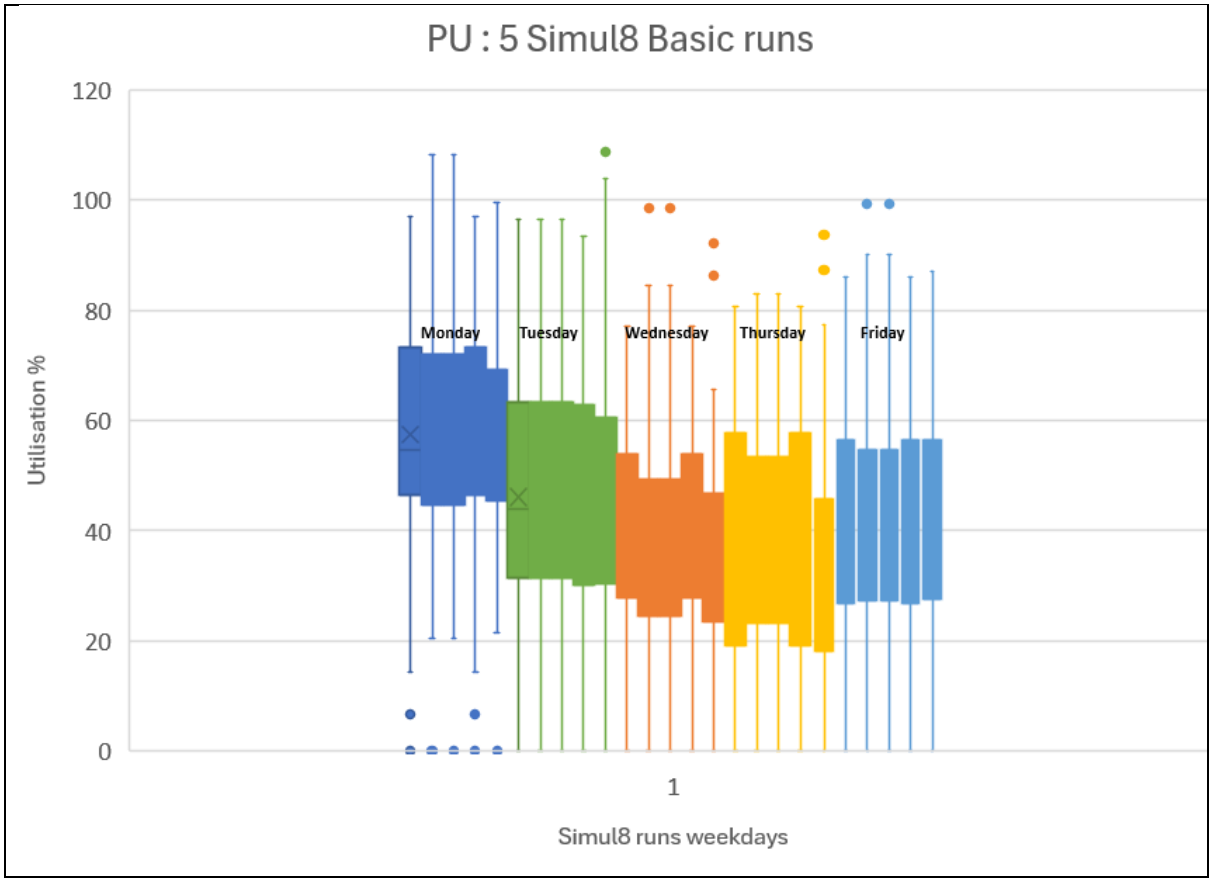


***Figure 57**. boxplot of Daily PU from 5 Simulation base runs*

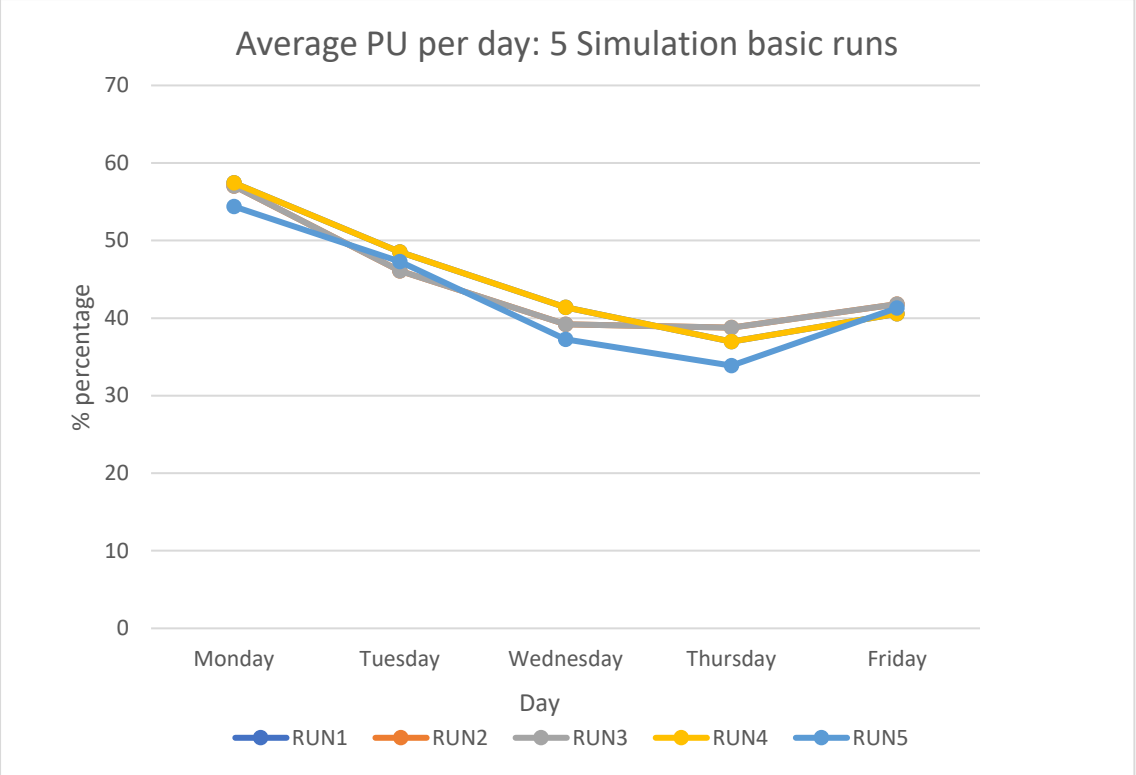


Figure 58. *Mean PU per day 5 Simul8 base runs*

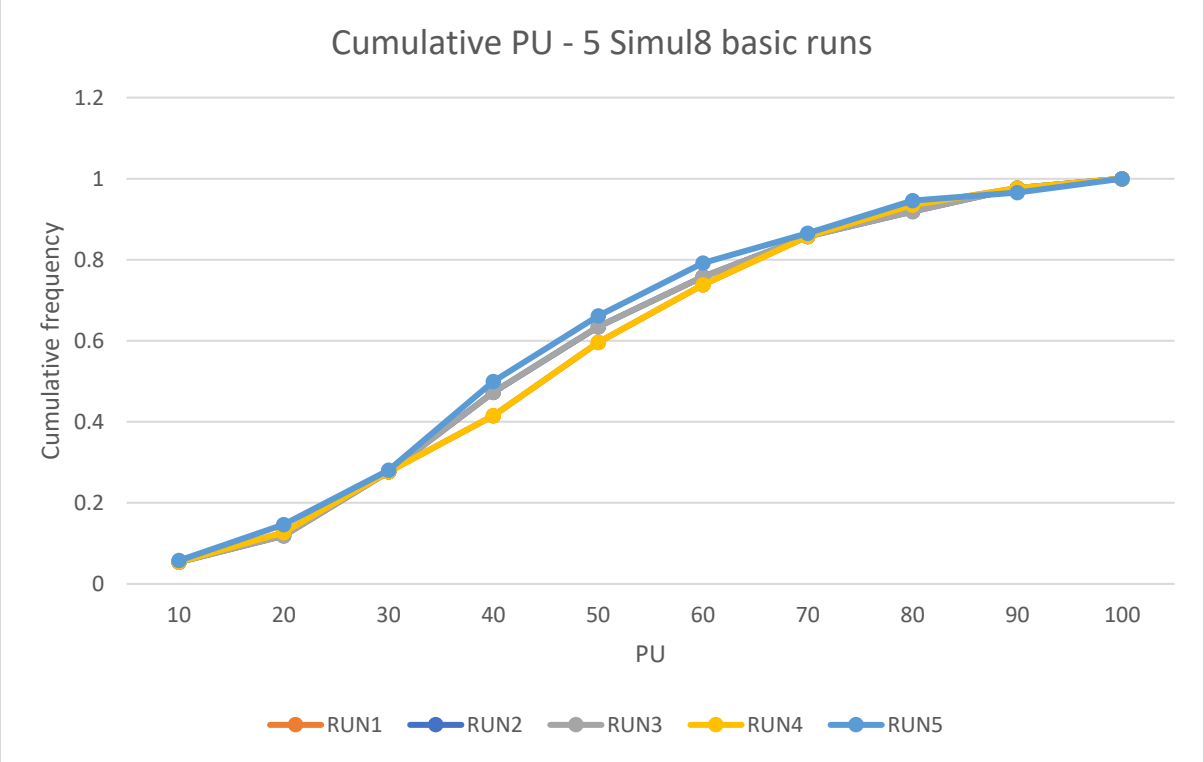


Figure 59. *Cumulative frequencies of PU from 5 base case simulation runs*

Table 24 summarises the findings from a base case analysis simulation showing that Mondays have consistently the highest EU and PU highlighting a high workload and a

lower staffing in comparison to the workload. Saturday and Sunday are non working days for practitioners hence the absence of data.

Table 24. *Mean Staff utilisation percentage % per day from 5 Simul8© base runs*

	EU	PU
Monday	69.9	56.7
Tuesday	50.1	47.3
Wednesday	51.7	39.7
Thursday	48.4	37.1
Friday	59.5	41.2
Saturday	61.7	
Sunday	69.4	

Table 25*. Comparison between FTE/WTE calculation - Simul8© BC (2022) The comparison includes the FTE per month, workload - and staff utilisation from the Simul8 BC model*

		Jan	*Feb*	*Mar*	*April*	*May*	*June*	*July*	*Aug*	*Sep*	*Oct*	*Nov*	*Dec*
WTE	*Embryologist*	*13*	*13*	*12*	*13.2*	*13.2*	*13.2*	*13.2*	*13.2*	*14.2*	*14.2*	*15.2*	*15.2*
	Practitioner	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Workload	*EC*	*133*	*157*	*144*	*153*	*162*	*149*	*127*	*134*	*124*	*161*	*154*	*56*
	FET	*117*	*127*	*125*	*92*	*125*	*118*	*115*	*127*	*121*	*162*	*136*	*87*
	Monthly ratio EU E/(EC+0.5xFET)	*0.07*	*0.06*	*0.06*	*0.07*	*0.06*	*0.07*	*0.07*	*0.08*	*0.06*	*0.07*	*0.07*	*0.15*
	SA	*56*	*64*	*62*	*57*	*79*	*73*	*35*	*100*	*52*	*79*	*55*	*21*
	Sperm freeze	*34*	*33*	*31*	*32*	*40*	*28*	*39*	*34*	*34*	*41*	*38*	*29*
Simul8	*EU (5 BC Runs)*	*40.1*	*71.2*	*79.2*	*65.1*	*56.6*	*57.3*	*65.9*	*53.8*	*52.1*	*52.7*	*57.6*	*41.2*
	PU (2 BC Runs)	*23.9*	*53.2*	*61*	*44.2*	*41.3*	*45.1*	*52.2*	*41.3*	*40.8*	*41.9*	*38.6*	*35.7*

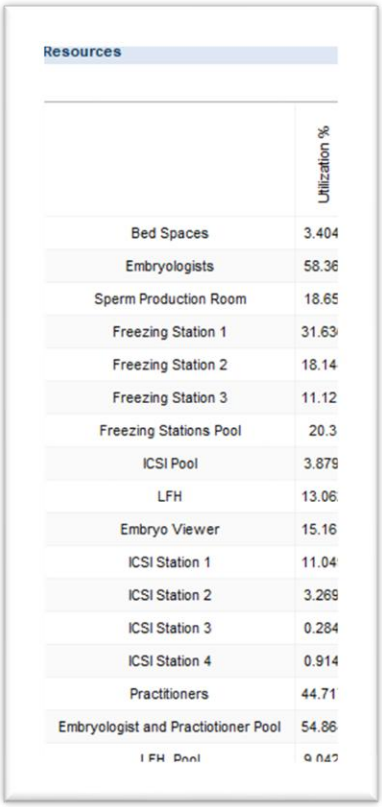
Table 25 shows the number of FTE contracted staff in the IVF lab month by month during the year 2022. The number of FTE embryologists ranged from 12 to 15 and the number of practitioners contracted was 5 each month. The same table shows the workload in the

lab expressed in number of egg collections and number of frozen embryo transfers (FET). Andrology semen analysis and semen freezes were not shown on the table even though they contribute to the daily workload. The number of FTE embryologists at GSTT-ACU varied from 12 to 15 in 2022. Using the recommendations for staffing from the published literature as shown in **Table 26**, it showed variability in the number of embryologists from 24 up to 42 which is much lower that the FTE embryologists contracted. To link staffing and workload, a ratio was calculated in **Table 25**, number of FTE embryologists divided by (EC+ 0.5x FET) on the assumption that the demand from FET is half of what the demand is from EC. The ratio did not vary much apart from the month of December where the demand is the lowest. On the other hand, the link between staff and workload in Simul8 © through expressed in staff utilisation varied from 40 to 79% for embryologists and 23 to 61% for practitioners.

Table 26. *GSTT-ACU embryologists numbers recommended according to published data*

	ASRM (US)	**ESHRE (EU)**	**Australia**	**ASEBIR (Spain)**	**ARCS (UK)**	**US (Private)**
Article	(Committee, 2022)	(De los Santos *et al.*, 2016)	(Lee *et al.*, 2023)	(Veiga *et al.*, 2022)	(Kasraie and Kennedy, 2024)	(Alikani *et al.*, 2014)
Recommendation	Number of cycles 1-150 : 2-3, 151-300 : 3-4, 301-600 : 4-5, >600 1 additional every 150 cycles	For 150 cycles – 2 embryologists	Online calculator using excel sheet	Online calculator https://asebir.com/cassandra-calculadora-de-rrhh/ Minimum of 2 qualified embryologists	1 state registered scientist every 80-100 cycle	One embryologist every 100 cycles
Limits	No andrology included	No clear guidance	Valid for lab with similar working patterns	Working patterns specific to Spain A = 30 days including Saturdays and Sundays	A cycle is not determined exactly	No andrology included
Number of embryologists if applied to GSTT-ACU	13 if retrievals only included 22 if retrievals and FET included	24 if retrievals only included 42 we include retrievals and FET	19.6 if same QC patterns as model	Unable to use the calculator	18 to 22.5 if retrievals only included 32 to 40 if retrievals and FET included	18 if retrievals only included 18+14 retrievals and FET included
Workload at GSTT for 2022: 1792 retrievals including 155 egg freezing, 1406 FET, 747 semen analyses, 399 sperm freezes.						

5.2.3 Resources utilisation



Resources

	Utilization %
Bed Spaces	3.404
Embryologists	58.36
Sperm Production Room	18.65
Freezing Station 1	31.63
Freezing Station 2	18.14
Freezing Station 3	11.12
Freezing Stations Pool	20.3
ICSI Pool	3.879
LFH	13.06
Embryo Viewer	15.16
ICSI Station 1	11.04
ICSI Station 2	3.269
ICSI Station 3	0.284
ICSI Station 4	0.914
Practitioners	44.71
Embryologist and Practiotioner Pool	54.86
LFH Pool	9.042

Figure 60. *Resources utilisation means- one base case Simul8 run – Simul8 visual*

All resources mean utilisation during one year of simulation run are displayed in **Figure 60**. Having examined staff utilisation in details in the previous sections, the equipment was the next focus. The highest utilisation mean rate for equipment was for freezing station 1, but as there are two other freezing stations available and other stations can be converted if needed, the choice was to to focus on the next equipment in use which is Embryoviewer. Embryoviewer has an mean yearly utilisation of 15.1%. The simulation model base run was based on the availability of two embryoviewers. Observing the embryoviewer utilisation EVU over the year **Figure 61**, it starts by zero where the first week of January does not have scheduled workload and it increases gradually to reach a peak on Day 21. The highest point of EVU is at 40%. Most of the highest values were identified as Sundays.

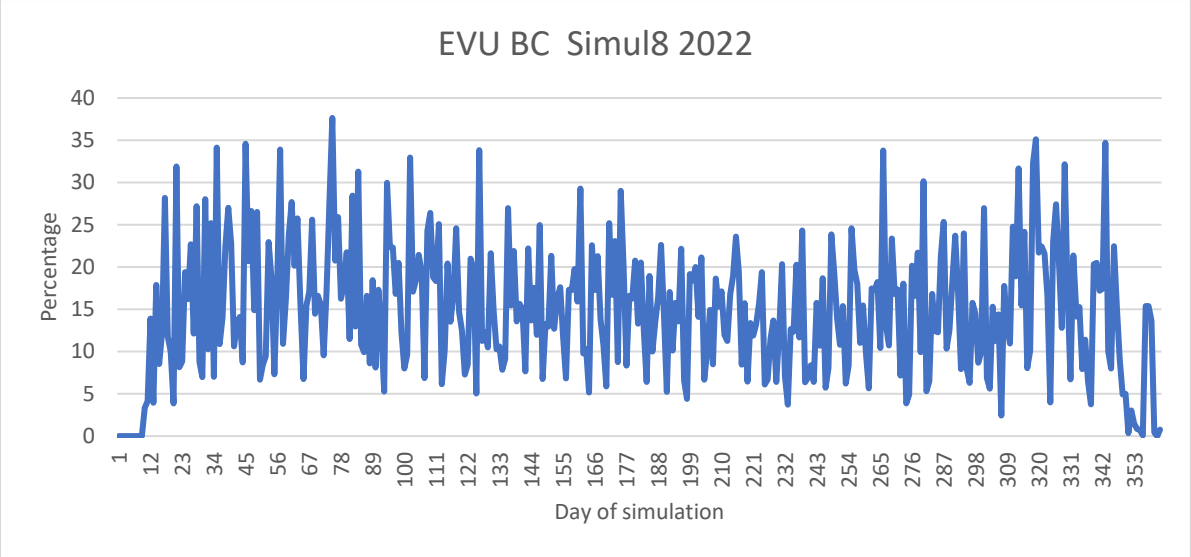


***Figure 61**. Display of EVU over a year: one base case simulation run*

5.2.4 Unfinished tasks/activities UT

Following running 5 simulation base runs, the number of unfinished tasks (UT) over the year was observed per weekday (**Figure 62**). The highest number of UT over the year were on Mondays and Fridays and this is confirmed by the boxplot display showing a detailed distribution (**Figure 63.** Box plot of daily unfinished tasks from the Base Case model simulation**Figure 63**).

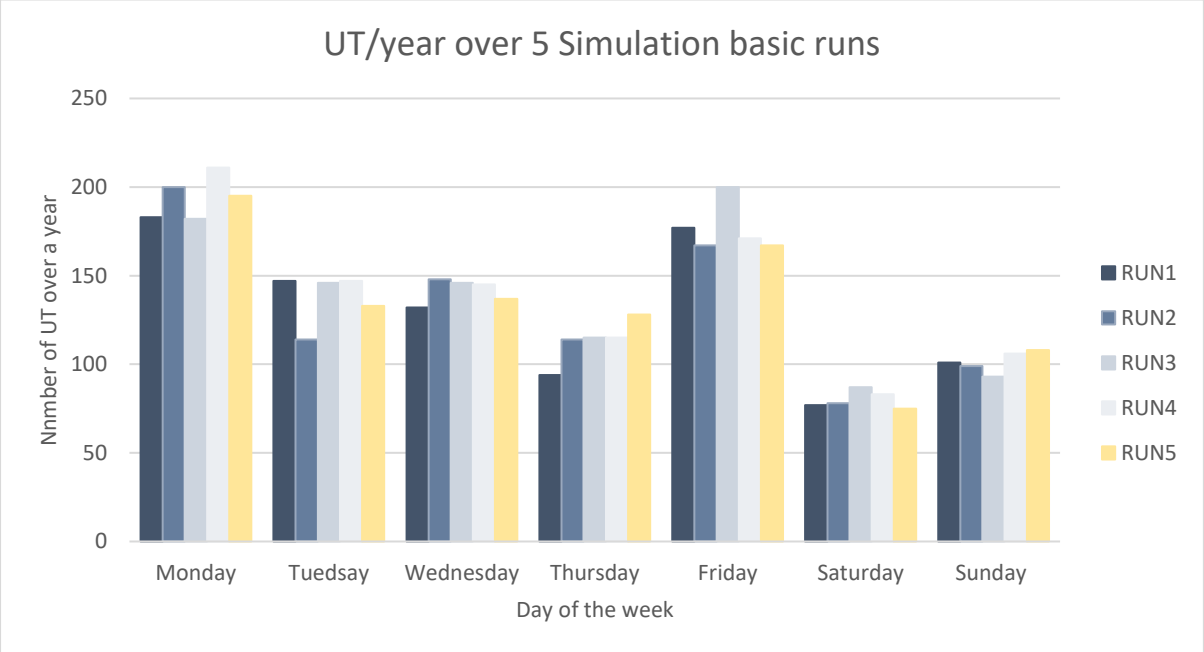


***Figure 62.** Total number of unfinished tasks (52 weeks, Base Case- Simul8)*

The number of unfinished tasks per day ranged from 0 to 12 with means (depending on the day) ranging from 2-4. When examining the list of unfinished tasks, some were recognised as critical (ICSI, sperm preparation) and are very unlikely to have stayed unfinished in real life and some were not critical and could have been left to the next day in real life (put frozen semen in dewars with a witness). Due to workarounds, unfinished tasks in simulations do not always reflect on what happens in reality but can be an indicator for high workload in accordance with staffing.

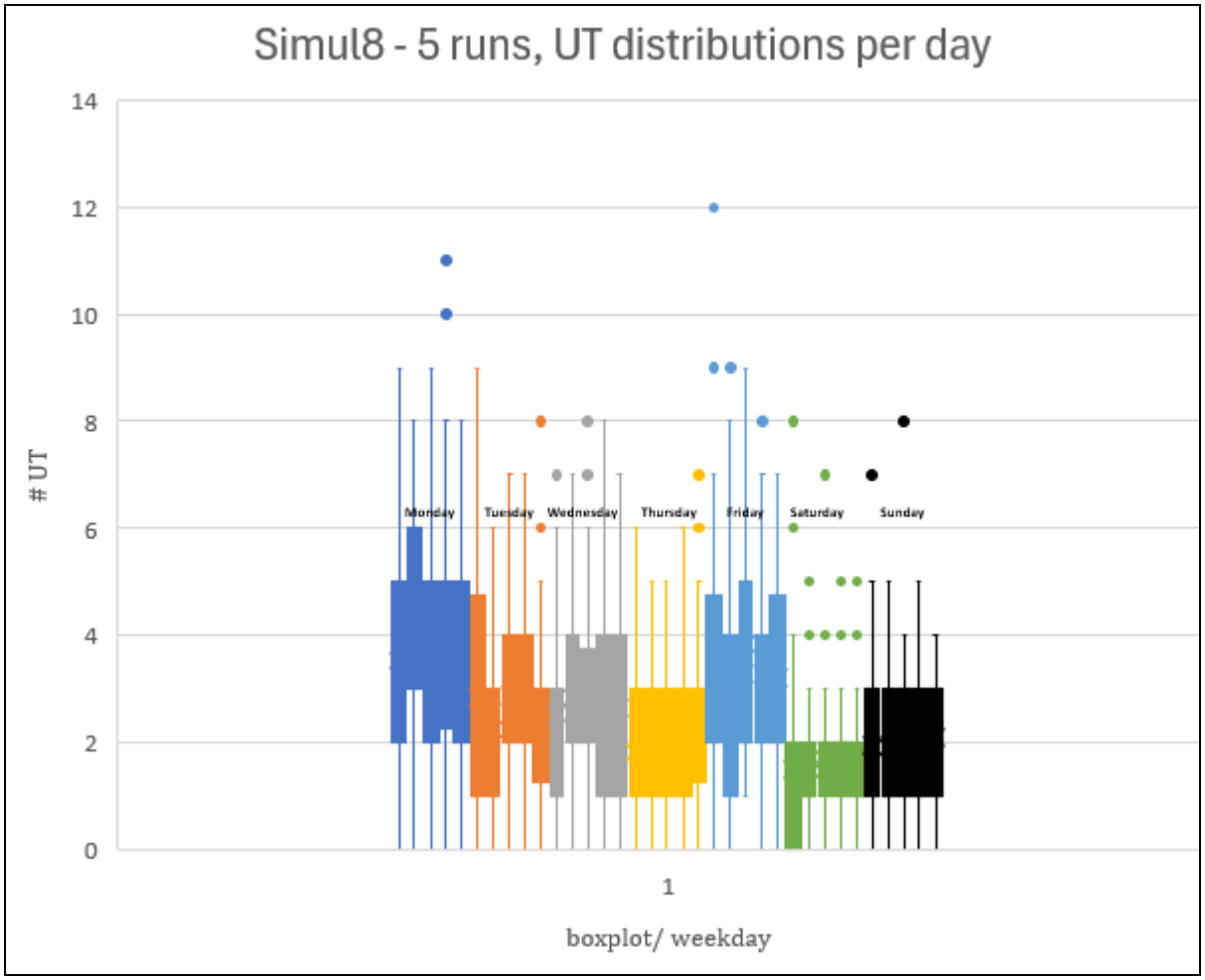


Figure 63. *Box plot of daily unfinished tasks from the Base Case model simulation*

The expectation was that no unfinished tasks are left at the end of a day shift so this idea was used that to map against EU and PU to identify the EU and PU allowing all workload to be done on time by the end of the day. **Table 27** showed that with the increase of UT, the staff utilisation increases which could be an indicator of high workload versus staff

available. If all procedures are completed by the end of the simulation day (UT=0), the EU is 44.5% and PU is at 22.8% that could be used as benchmark in the simulation model for "ideal" staffing utilisation to meet time requirements.

***Table 27**. UT and EU/PU*
Data from one Simulation BC run

mean # UT/day	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**>9**
EU	44.5	52.2	57.7	63.0	66.5	67.8	70.5	80.3	78.0	69.1	81.3
PU	25.8	37.2	43.2	47.7	50.1	56.2	53.9	65.9	NA	55.0	65.9

5.2.5 Queues

There are 81 queues in the simulation model created for GSTT-ACU IVF lab. Queues are displayed in results as the following: queue name, **average waiting** and **max waiting time** (in minutes). Some of the queues do not have added values or indications NAVQ (dummy tasks, overnight queue from Day 0 to Day1) and others have added value AVQ and significance in the interpretation of process workflows. If NAVQ is removed and queues are sorted by the longest average waiting time, the result is displayed in **Figure 64**. The queue times for the first 3 exceed 6 hours which in comparison to reality cannot be allowed to happen as workarounds are applied and some tasks are deprioritised on the day. In Simul8©, each queue can have added setting such as capacity, shelf life, minimum waiting time and expiry in addition to prioritization. In the model that was created for GSTT-ACU IVF lab, most of the queues did not have any settings changes.

In queuing theory, Kingman's formula also known as VUT equation is an approximation for the mean waiting time in a queue, the formula is the product of three terms which depend on utilisation (U) Variability (V) and service time (T) (Proudlove, 2020). A queue could be a way of identifying a bottleneck but it must be reminded that a queue is dependent on the parameters above which means that they can be analysed by their associations to all other variabilities.

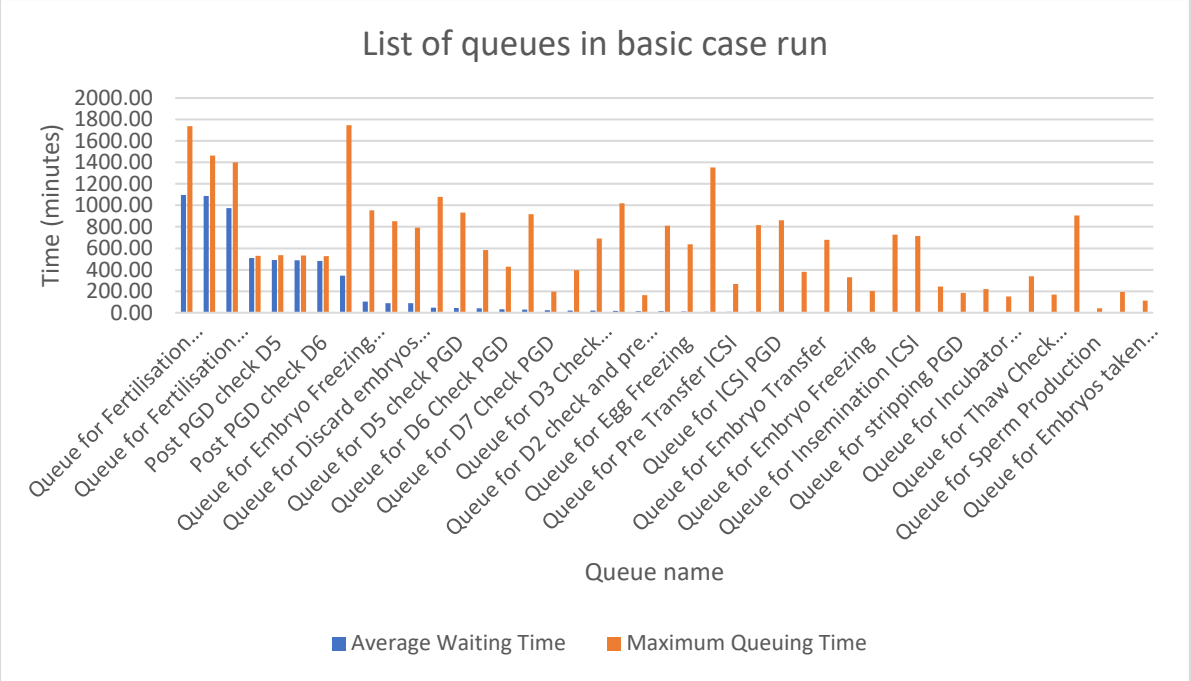


Figure 64. *AVQ sorted from the longest average waiting queue to the shortest*

The longest queues are displayed in **Table 28** and pointed to in conceptual model **Figure 65** to be able to visualise where the wait is mostly seen. The longest queues (**Figure 65**) even though the time is not concordant with reality showed that most queues are in tasks carried out by embryologists on embryoviewers (apart from IVF fertilisation check) so they are dependent on both resources and that could be the source variability.

Table 28. *Queues with the longest average waiting time*

Queue Name	Average Waiting Time (min)	Maximum Queuing Time (min)
Queue for Fertilisation check on screen ICSI	1097.32	1739.13
Queue for Fertilisation check PGD	1089.07	1463.44
Queue for Fertilisation check IVF	974.78	1400.97
Post PGD D7	508.93	529.23
Post PGD check D5	491.03	536.69
Post PGD check D3	487.58	531.92
Post PGD check D6	481.61	527.30

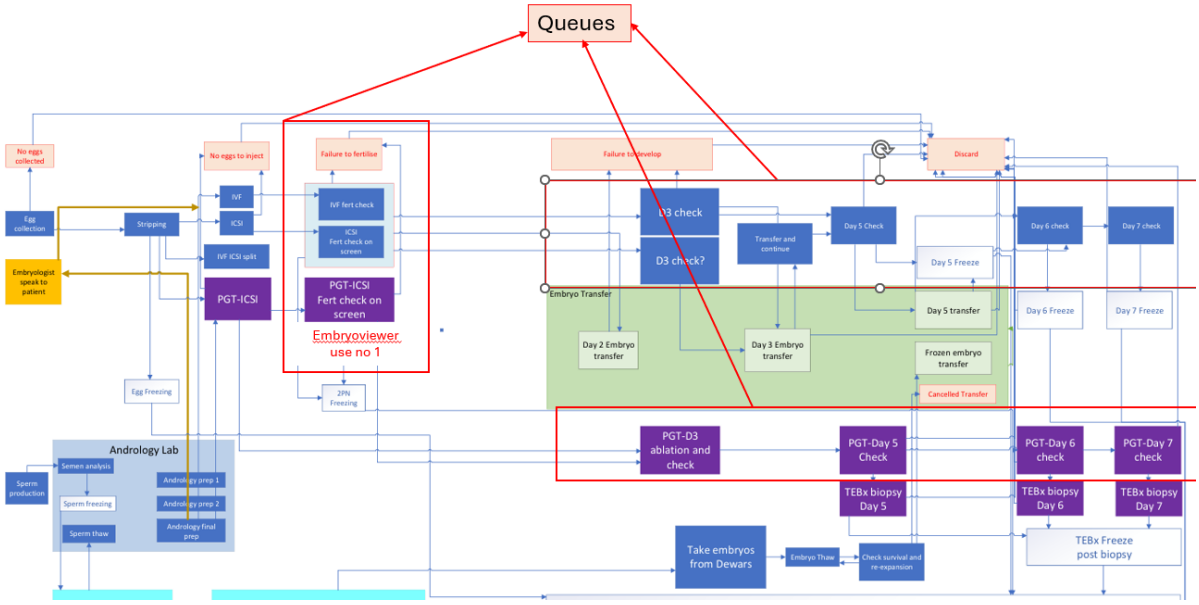


***Figure 65**. Conceptual model with a visual pointer to the longest queue location*

As a summary, even though the results given by the simulation model are not identical to reality (queue times for example), they give an insight into workload and staff combined rather than in separate numbers by showing resources utilisation, unfinished tasks and queues. There is no reference for resources utilisation to compare the model to, but all the data gives an insight on workflows and demand versus capacity that match with the variability seen in real life with OM1, OM2 and OM3 but also in OM generated by the base model. All the results show variability through the year that could be due to high workload or reduced staff numbers (due to annual leave, school holidays or work patterns). The model also shows two critical days in the model which are Mondays and Fridays where have seen in retrospective data deviations from procedures timing recommendations and consequently success rates.

The slow increase in all parameters from day 1 in the model (January) showed the reality of workload in the IVF lab that builds up on 7 day rolling basis: in fact workload does not come from the daily arrivals (egg collections) but from the current day arrival and the arrivals from the previous 7 days which is a concept that should be introduced in measuring workload in IVF.

The results retrieved confirmed the influence of contributing factors workload, resources along with processes durations on the results delivered by the model. Even if the model does not replicate reality 100%, it does give certain insights that generated some change ideas to test and apply to the secondary drivers **Figure 11** to check whether the ideas of improvements can have any effect on the results the simulation generates.

5.3 Do the scenarios tested suggest what the optimal working conditions are?

After validating the model, and identifying its limits, Mondays and Fridays were identified by the model results as the days requiring more staff (EU, PU and UT the highest). It was noticed that EU and PU especially for Mondays could have an influence on OM1, OM2 and OM3 so can be used as proxy for compliance to time durations and hence success rates of the system IVF lab. As far as equipment is concerned, embryoviewer was identified as an equipment linked to the longest queues. When looking into workload, to identify a task that can be removed : the andrology diagnostic service in **Table 23** (semen analysis, semen freezes) was identified as occupying 8% of embryologist tasks (competes for their availability) but is not part of the IVF processes so can be removed or moved from GSTT-ACU location. Queues are sources of bottlenecks and are dependent on Time processes so a change idea could be to change the time duration of a process.

Consequently, different change ideas were chosen to test or what is called "what if scenarios" in DES. The scenarios are described in **Table 29** applied to staffing (S1, S2, S3), to equipment (E1, E2), to a service (xA) and finally to a process duration (T). The effects of these scenarios were compared to the results from a base run model for OM : OM1, OM2 as proxy to success but also to staff utilisation.

***Table 29**. 7 "What if scenarios tested" using Simul8 model for GSTT-ACU IVF lab*

Base Case BC		2022 settings	Cost
Staffing	Scenario **S1**	All staff - 1h overtime	-119,282£ -30,390 £
	Scenario **S2**	Add one embryologist Monday & Friday	-33,540 £
	Scenario **S3**	Add one embryologist and one practitioner Monday and & Friday	-56,940£
Equipment	Scenario **E1**	Add one Embryoviewer	-9500£ + 905£/year
	Scenario **E2**	Add 2 Embryoviewers	-19,000£ +1,810£/year
Service	Scenario **xA**	Remove Andrology services	- 85,905£ - 199,000 £ +consumable savings + saving on staff time
Technology	Scenario **T**	Rapid Thaw	+Reduce staff time +Reduce consumables use

5.3.1 Staff Scenarios: S1, S2, S3

The expectation from staff scenarios was to improve compliance with procedure timings by increasing staff availability. The staff scenarios primary results ie Process Metrics PM such as number of egg collections completed and number of embryo transfers completed were unchanged from the BC to S1/S2/S3 which confirms that the model is working as expected (data not shown). In fact, the expectation was less pressure on staff and procedures completed on time rather than more procedures carried out. From the visual diagrams (**Figure 66**, **Figure 67**. **Figure 68**), adding overtime S1, did not influence OM1, OM2 and OM3 medians but the effect is seen on OM2 outliers. With S2 and S3 scenarios, there is a tighter distribution for OM1, OM2. None of the staff scenarios influence OM3.

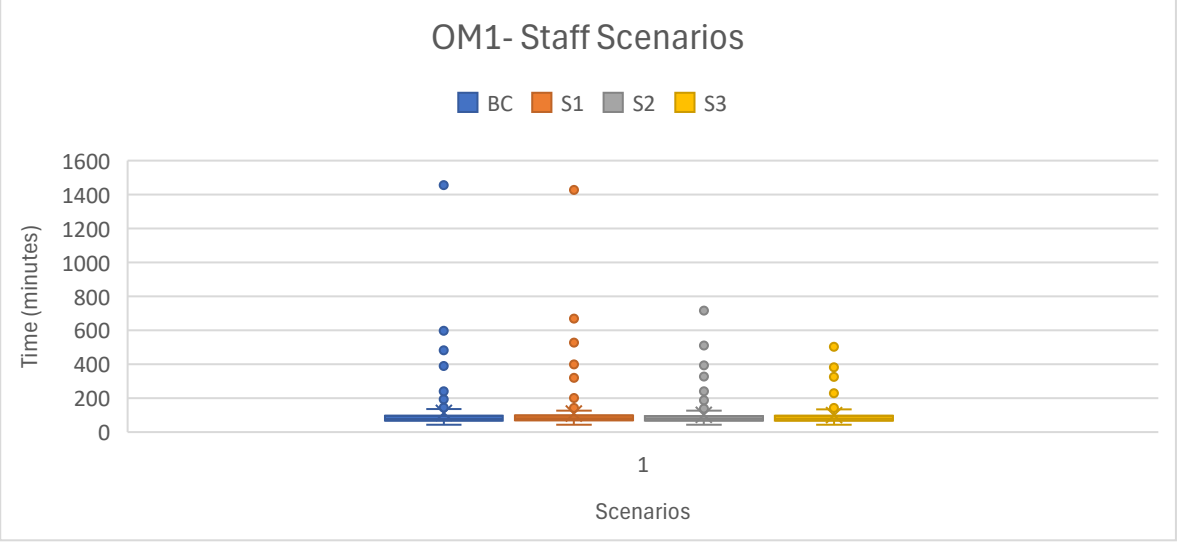


***Figure 66**. OM1 BC vs staff scenarios S1, S2 and S3 boxplot distributions*

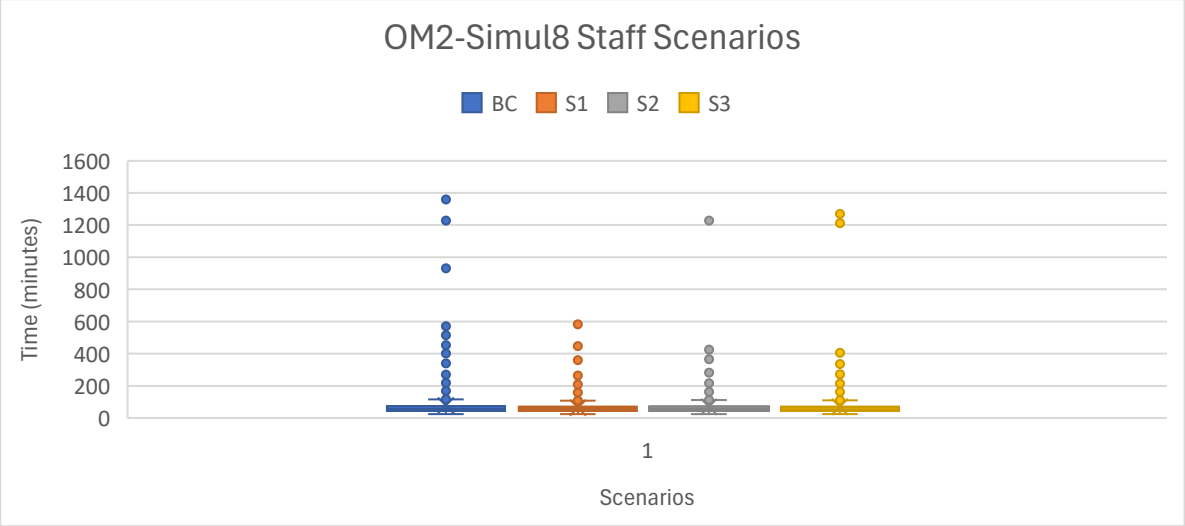


Figure 67. *OM2 BC vs staff scenarios S1, S2 and S3 boxplot distributions*

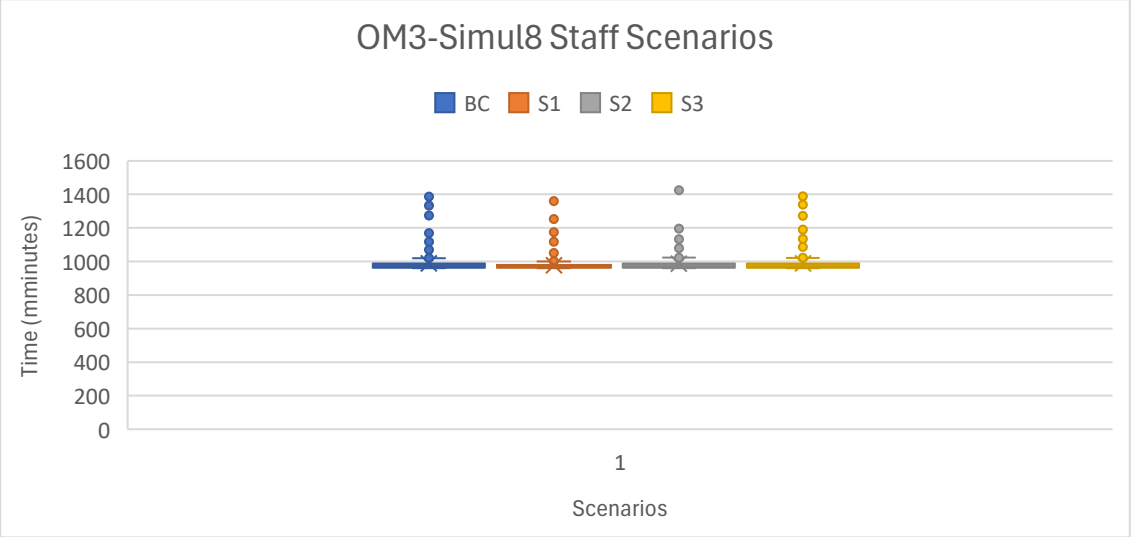


Figure 68. *OM3 BC vs staff scenarios S1, S2 and S3 boxplot distributions#*

Adding overtime reduces the median of staff utilisation (**Figure 69**, **Figure 70**) but the extremes are not affected. This is expected as the denominator is higher (staff is available by an extra hour). Adding embryologists on Mondays and Fridays does not reduce median of staff utilisation. The effect seen with staff scenarios is mainly when observing the specific days **Figure 71**. Adding overtime reduces the median of EU on weekdays but not weekends which is normal as overtime is only applied on weekends. S2 and S3 involve adding staff on both busiest days Mondays and Fridays which explains that the effect is mainly seen on these both days by reducing EU. It is actually with S3 where the model

can reduce EU to lower than 100%. Saturdays and Sundays do not benefit from the scenarios tested.

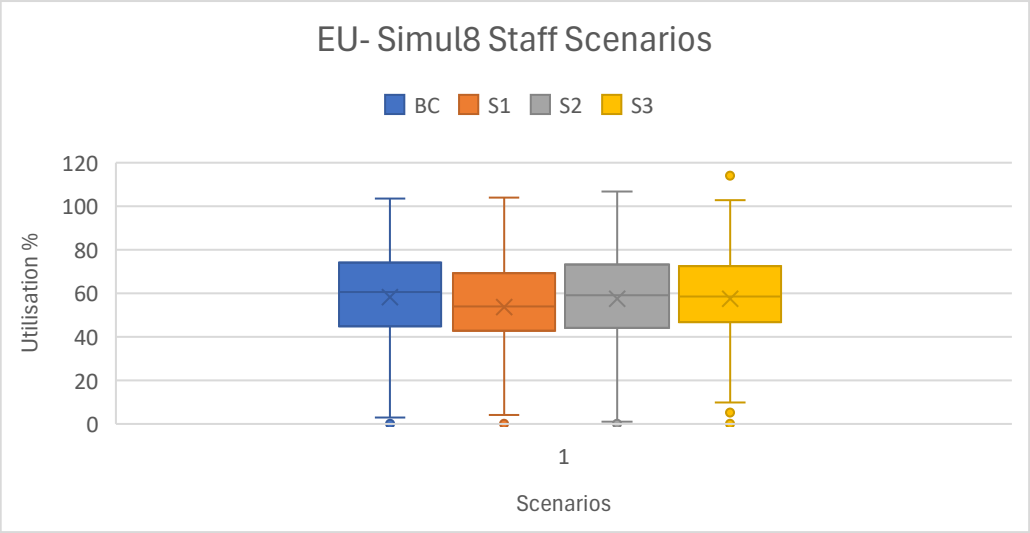


Figure 69. *EU BC vs Staff scenarios*

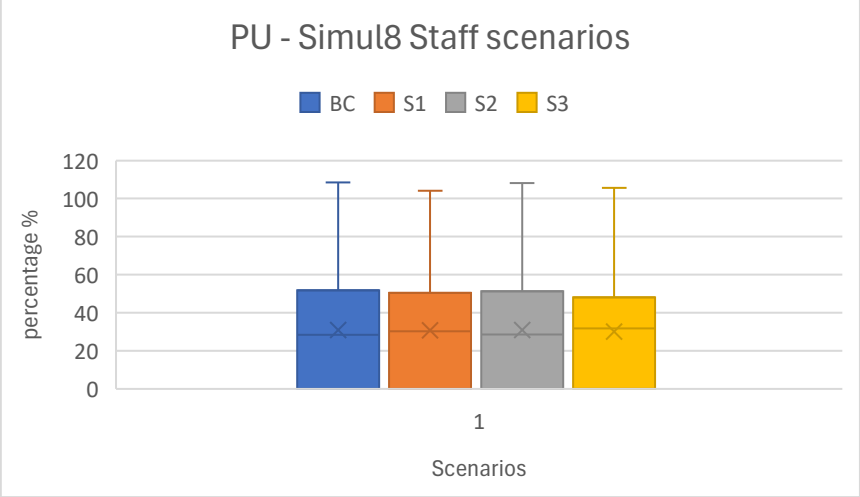


Figure 70. *PU BC vs Staff scenarios*

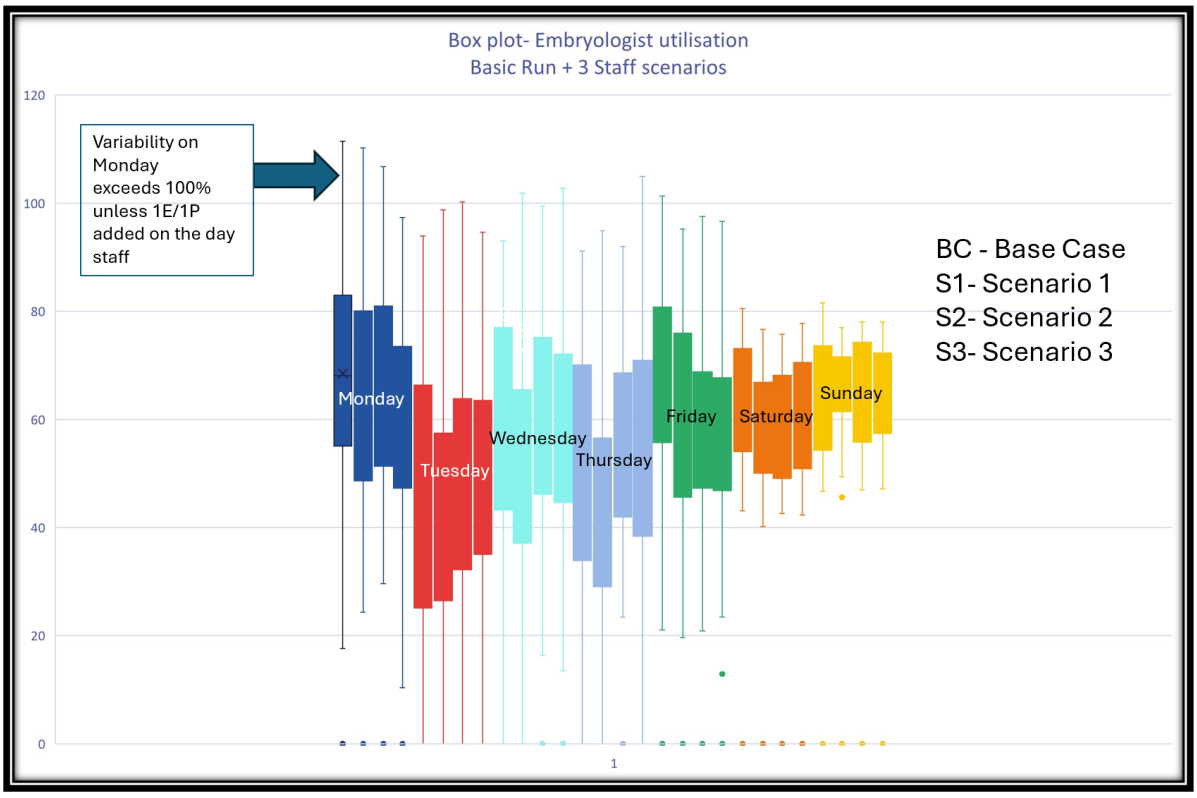


***Figure 71**. EU box plot of BC vs Staff scenarios per day*

The queues are unchanged in the staff scenarios in comparison with BC. The UT are reduced as a total per year in S1 only which can be explained by the fact the UT are mainly towards the end of the day and extending the working day by one hour is expected to reduce the UT. (data not shown). Staff scenarios showed that overtime reduced the number of UT and could probably contribute to completing time sensitive tasks earlier (no OM2 outliers). Adding staff on busy days reduces staff utilisation especially on these specific busy days (less pressure and need for overtime) and contributes to reducing variability in OM1 and OM2 to carry out ICSI and egg freezing closer to the mean time.

5.3.2 Equipment scenarios

Embryoviewer has been identified in the analysis of BC as the equipment linked to the longest queues. The BC model has been set up with use of 2 embryoviewers. The scenarios tested for equipment were focused on embryoviewer: adding 1 embryoviewer (E1) and then a second one (E2).

No changes were observed in PM, in terms of number of procedures completed by trying both scenarios which fits with the expectations. Adding equipment should not increase the number of procedures. The expectation by adding embryoviewers is to reduce queues and maybe therefore free time for staff to carry out other tasks that are time sensitive. No change was seen in the number of UT at the end of the simulation run in both scenarios in comparison to the BC. There was a reduction from 20-46% of the average queues displayed in **Figure 72**.

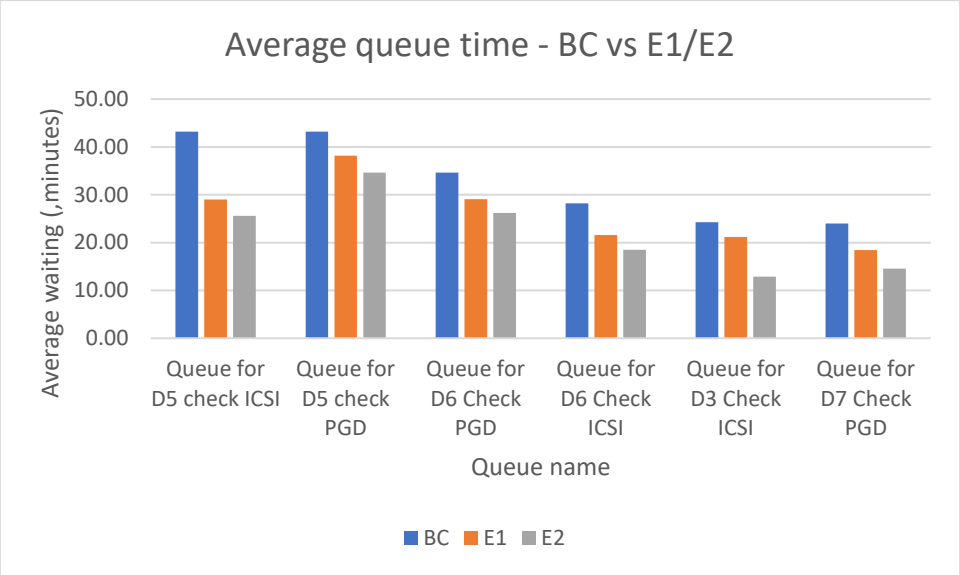


Figure 72. *Queues BC vs E1/E2 scenarios*

When analysing staff utilisation (EU, PU) , no change was observed in EU or PU by adding embryoviewers (**Figure 73** & **Figure 74**) . Detailed analysis of staff utilisation per weekday showed no change for EU or PU per weekday either. Analysis of OM time durations in both scenarios E1 and E2 versus the BC (**Figure 75**, **Figure 76**, **Figure 77**, **Figure 77**) showed no effect if this change idea on OM1, OM2 and OM3.

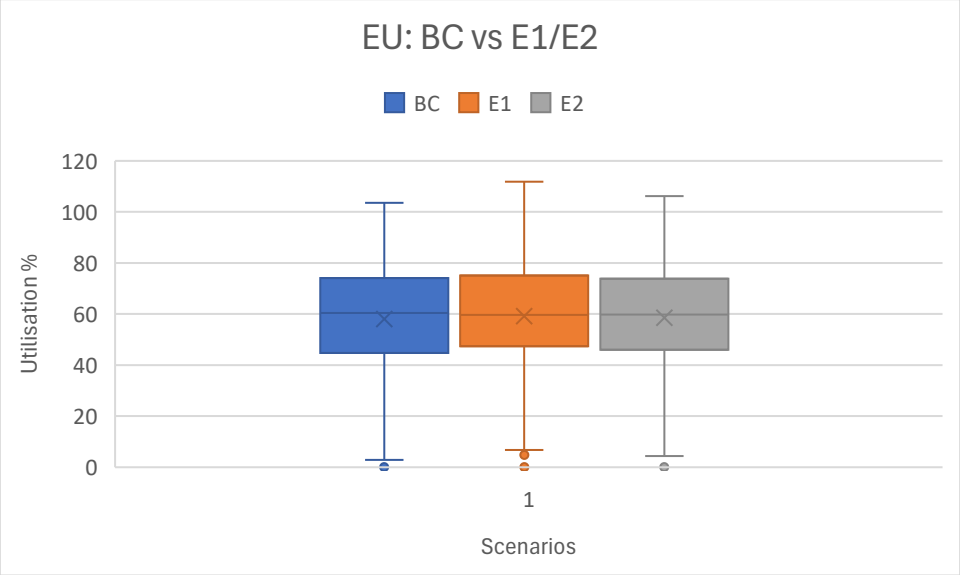


***Figure 73**. EU BC vs E1/E2 scenarios*

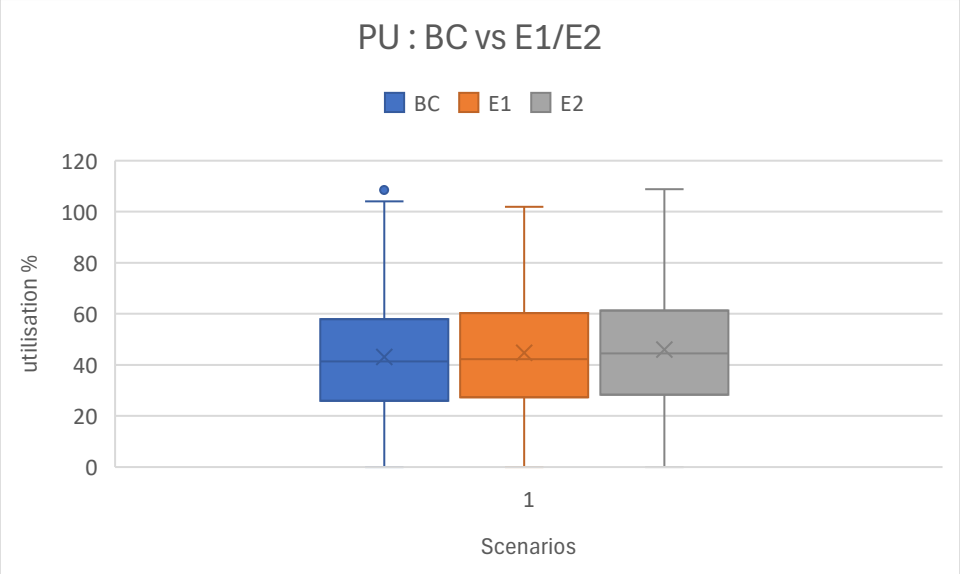


***Figure 74**. PU BC vs E1/E2 scenarios*

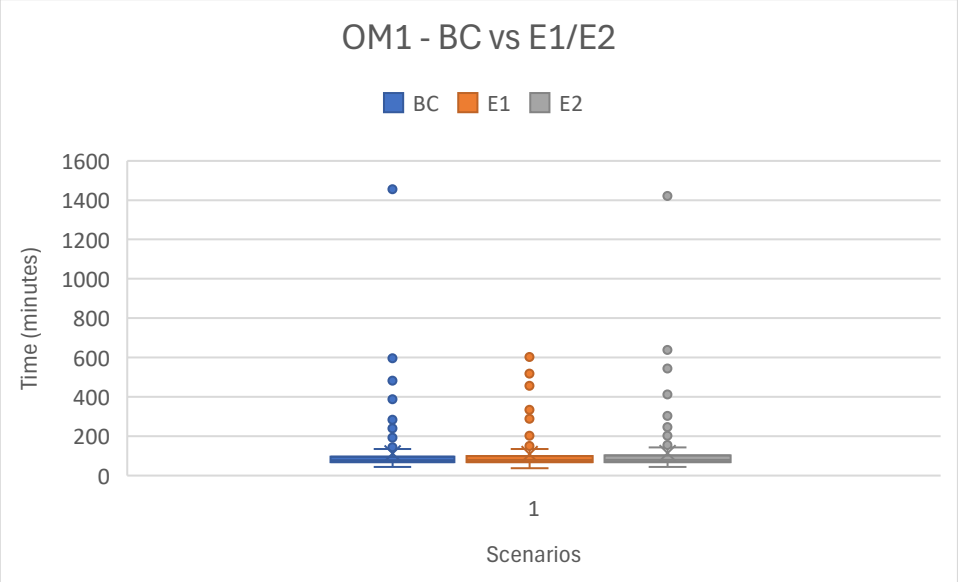


Figure 75. *OM1 BC vs E1/E2 scenarios*

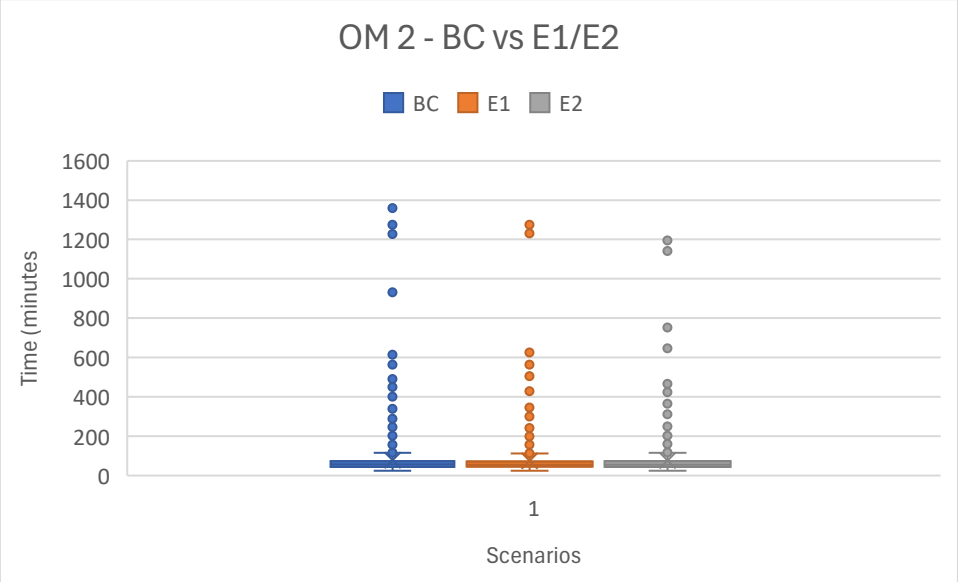


Figure 76. *OM2 BC vs E1/E2 scenarios*

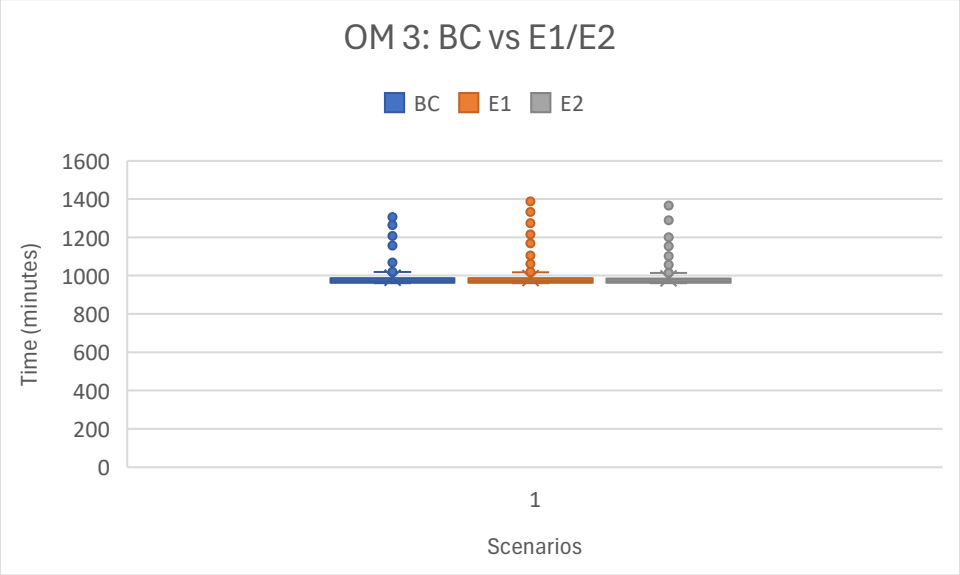


***Figure 77**. OM3 BC vs E1/E2 scenarios*

5.3.3 Service Scenario (xA)

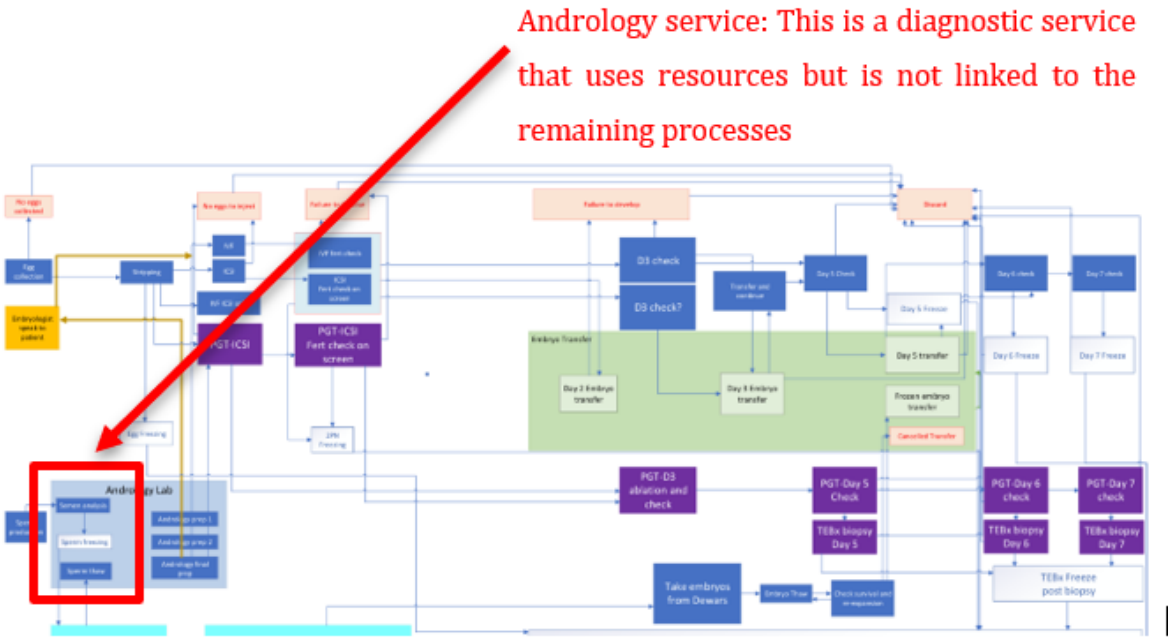


***Figure 78**. Simulation conceptual model GSTT-ACU IVF – xA scenario*
The diagram shows where xA scenario is applied

As expected, when xA scenario (**Figure 78**) was run in the simulation model, there were no more entries for semen analysis in the system, therefore, the only PM that changed were the number of **semen analysis** and **semen freezes** carried out at the end of the simulation : they were in fact reduced to zero which is a confirmation that the model runs

as expected. The expected effect of this change idea **(xA)** is to free staff to do other tasks so a reduction in UT and some improvements in OM and reduction in queues. The effect on EU and PU could be expected to be both ways : If staff is available to do other tasks, their time will be utilised so it would not necessarily change.

Following on a xA Simul8© scenario in the model, the number of UT was reduced in comparison with the BC from a total of 911 to 862 which represents -5%. The reduction mainly came from andrology diagnostic linked tasks (semen analysis, semen freezes) which is expected but it also from sperm preparation tasks which themselves allowed reducing ICSI UT. This will supposedly allow better OM2 distribution. The expected outcome from this is that OM1, OM2 and OM3 (**Figure 80**, **Figure 81**, **Figure 82**) can be reduced with xA but in effect only showed an effect on OM2 which is closely linked to the ICSI procedure (similar median value as the BC but a tighter distribution and less outliers which means that ICSI is not left to later thanks to the staff shift availability.

The most noticeable change with xA scenario is the change in queues (**Figure 79**) . Queue average waiting time and maximum waiting time for semen analysis and semen freezes were reduced by 100% to zero which is expected. The queues that benefited most from this scenario, were the queues for ICSI and insemination. These queues are closely linked to OM2 and OM3. This might explain the effect of this scenario on OM2 described above. The average time for theatre queue was also reduced from BC to xA which allowed egg collection to happen on time after trigger, a very important concept to not miss eggs before they are ovulated. This is probably the consequence of the sequence of events making staff available to talk to patients and free beds for the next egg collection. Theatre queue is closely linked to ICSI and insemination which also contributed in changing OM2 distribution.

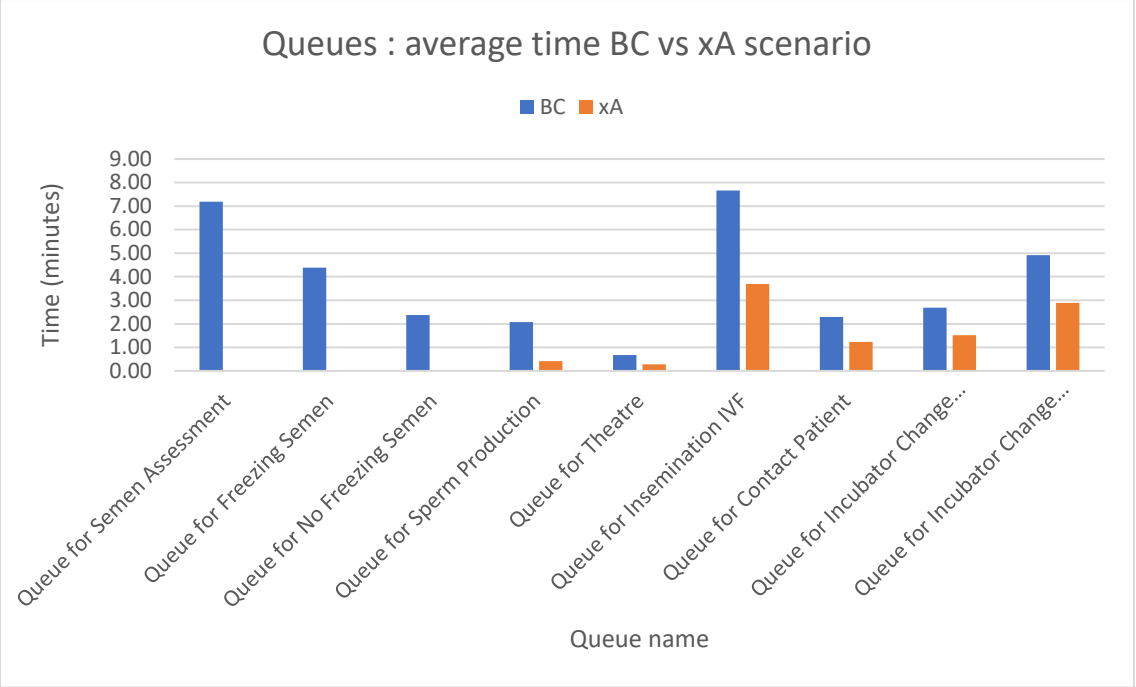


Figure 79. *Average queue times: BC vs xA scenario*

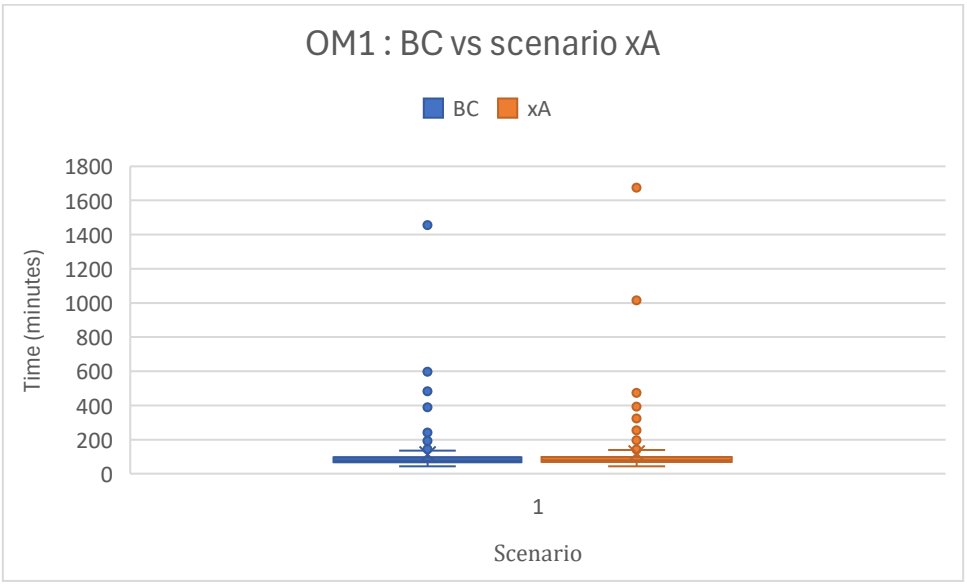


Figure 80*. OM1 boxplot BC vs xA scenario*

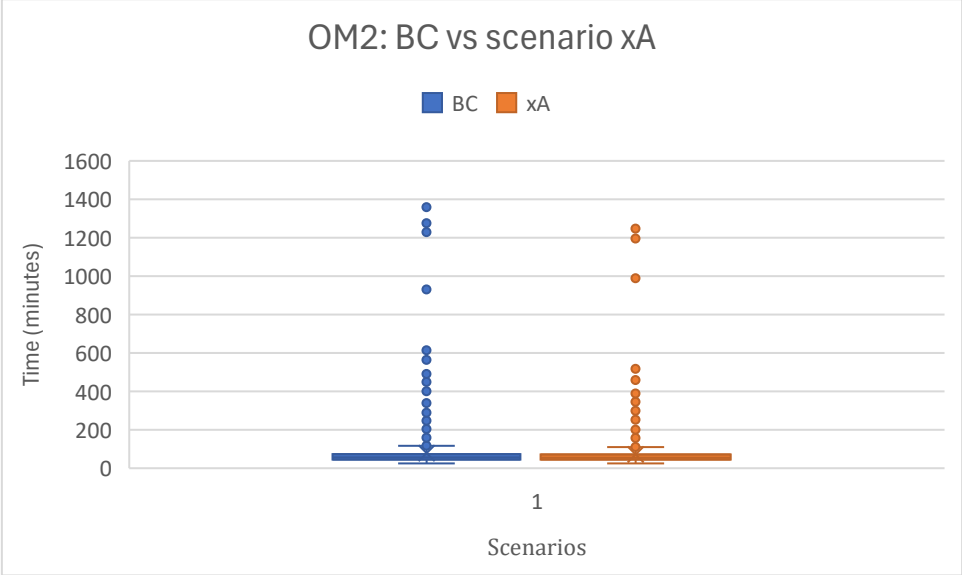


Figure 81. *OM2 boxplot BC vs xA scenario*

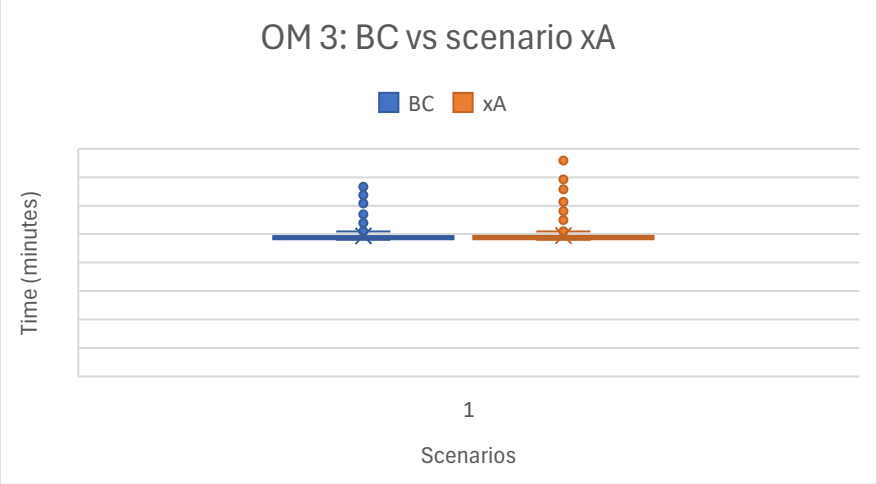


Figure 82. *OM3 boxplot BC vs xA scenario*

The xA scenario showed a slight reduction in EU and PU overall (**Figure 83, Figure 84**) but when looking into the detail of EU and PU on specific weekdays (**Figure 85**, **Figure 86**), there was a visible difference on specific days which are Monday and Friday for EU and PU but also Thursday for EU. In fact, Thursday is the andrology clinic day where most semen analysis are scheduled which can explain that.

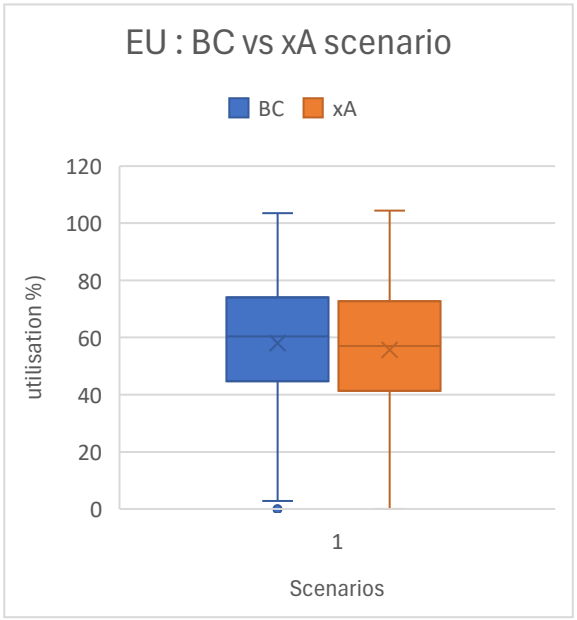


Figure 83. *EU boxplot BC vs xA scenario*

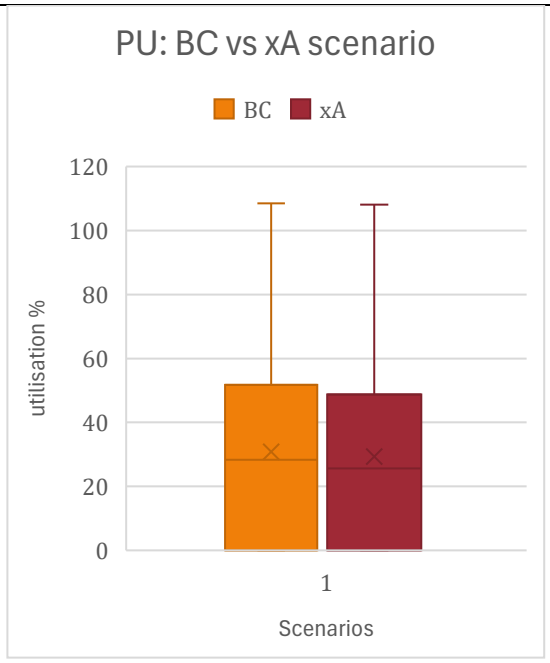


Figure 84. *PU boxplot BC vs xA scenario*

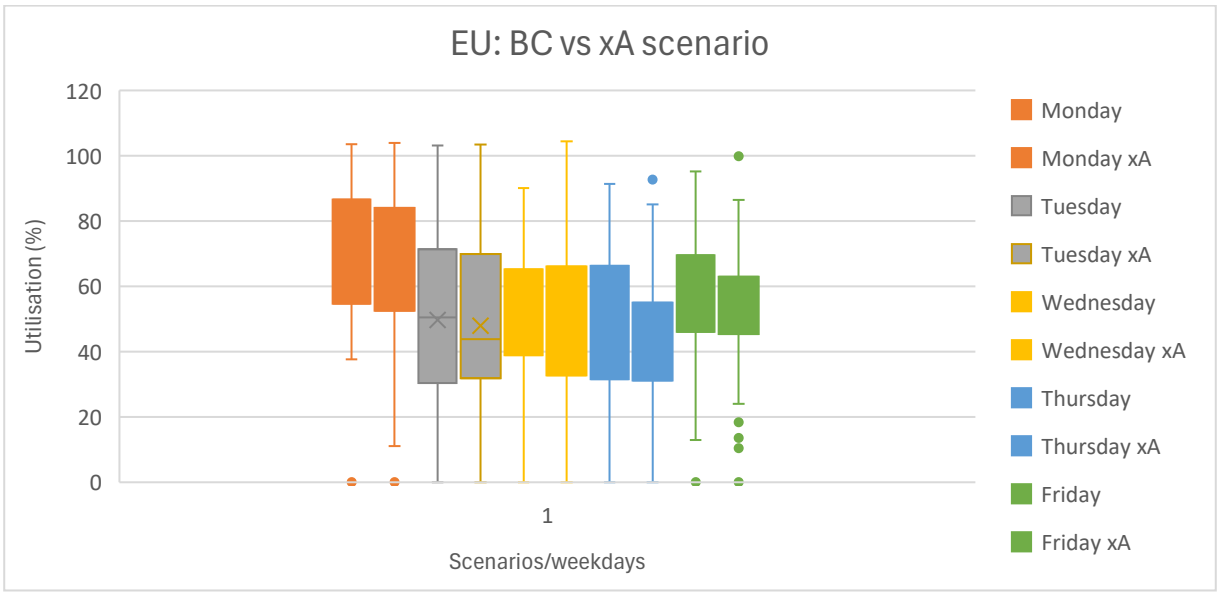


Figure 85*. EU BC vs xA scenario per weekday*

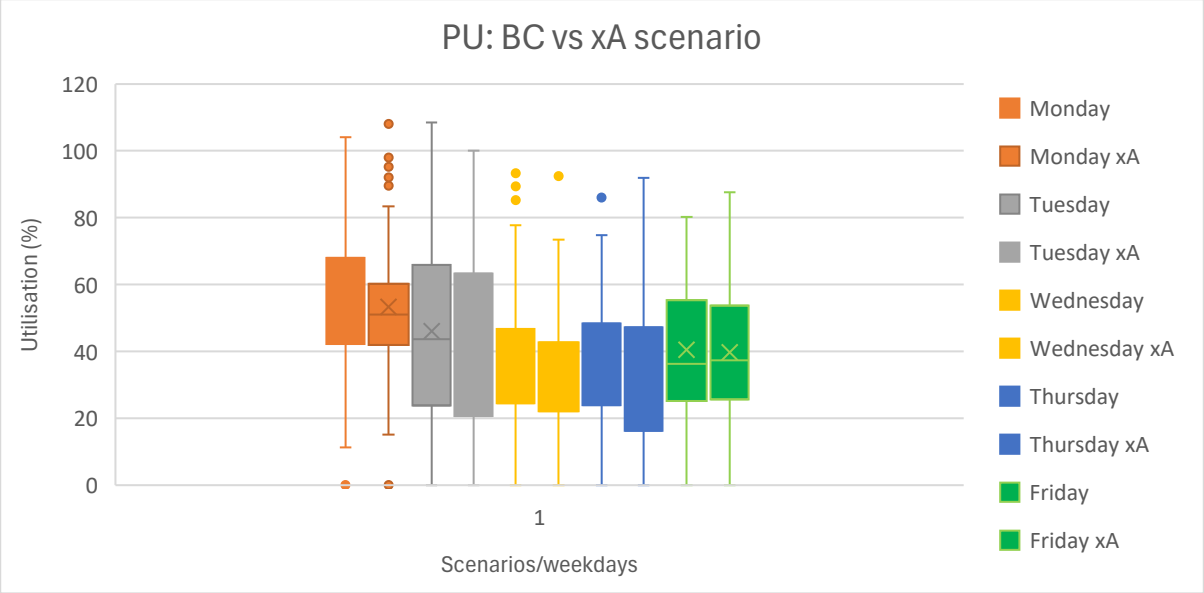


***Figure 86**. PU BC vs xA scenario per weekday*

5.3.4 Technology Scenario

With T scenario, the PM did not show any change which is what is expected. By changing the time duration of the process thaw, none of the completed tasks (egg collections, transfers, biopsy) changed. The number of UT as a total per year decreased by 15% per year going from a total of 911 to 782 between the two simulations scenarios. In terms of queues (**Figure 89**), the main queues that have seen a change in the average waiting times were the ones linked to the process changed which is the thaw: both tasks named "check thaw survival and check thaw re-expansion queues had a reduction in average queue time by respectively by 49% and 34% (on one simulation run). Other queues not linked to the process were surprisingly reduced : queues in the lab (ICSI, insemination IVF and embryo freezing) and queues in the andrology lab (semen assessment, semen freezing, talking to patient after egg collection). This probably explain the slight change in OM2 distribution with scenario T **Figure 91**. OM2 is the only OM that changed (less dispersed parameters and less outliers) following trying scenario T. OM1 and OM3 are unaffected by scenario T as shown in **Figure 90** and **Figure 92**.

In terms of staff utilisation, only EU on weekdays was looked at as the process of thaw is only carried out by embryologists and is mostly planned during weekdays. Overall EU was reduced **Figure 93** in T scenario in comparison with the BC. When examining EU per specific weekdays, **Figure 94**, there was a trend towards a decrease in staff utilisation even though the median is not that different and this is valid for most days. Friday shows a larger spread in distribution even though the median is very similar. The expectation from this scenario named T as a reference to the new technology is to free more time for staff to dedicate to other tasks. The expectation as a general outcome was also to reduce a certain number of queues.

Reducing the time for certain procedures can reduce variability around a process. Recent publications were encouraging towards introducing rapid warming (Liebermann *et al.*, 2024) or thawing of embryos which is a change idea to reduce the thaw process time from 20 minutes to 2 minutes as shown on the conceptual model to highlight where this step is within all processes (**Figure 88**) and drawn on diagram as an explanation (**Figure 87**).

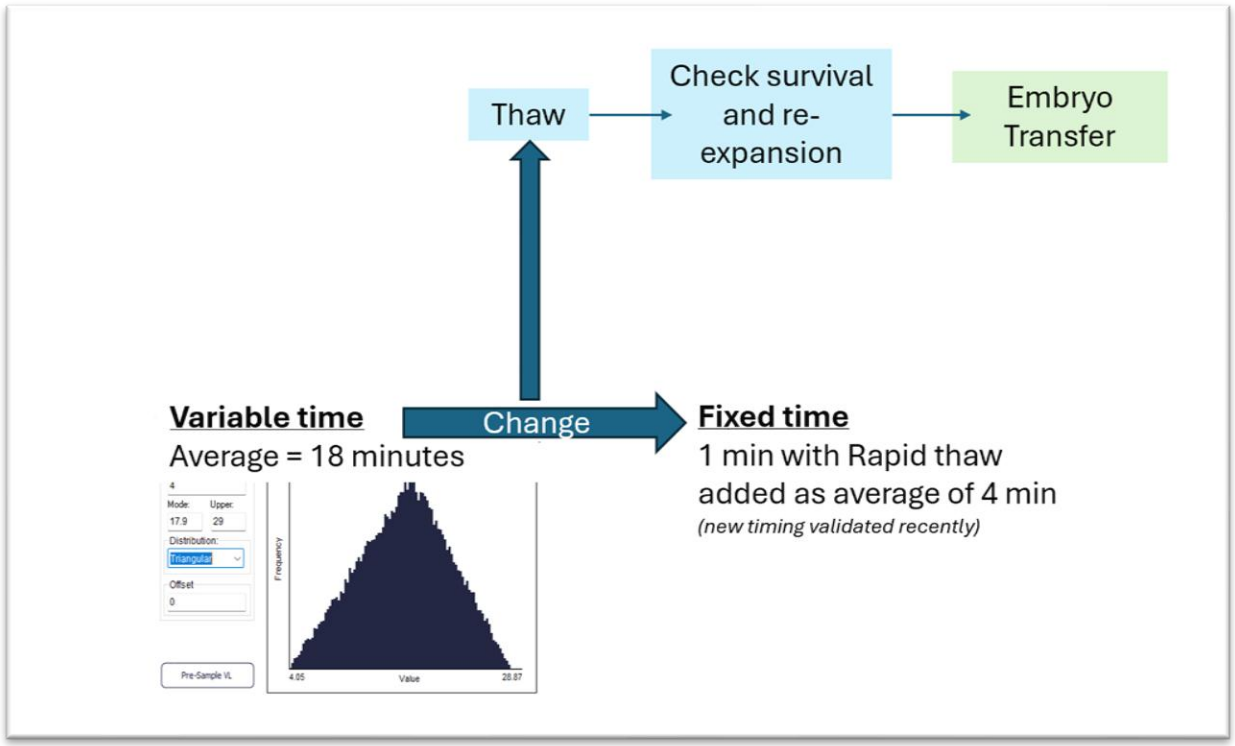


***Figure 87**. diagram description of the T change scenario*

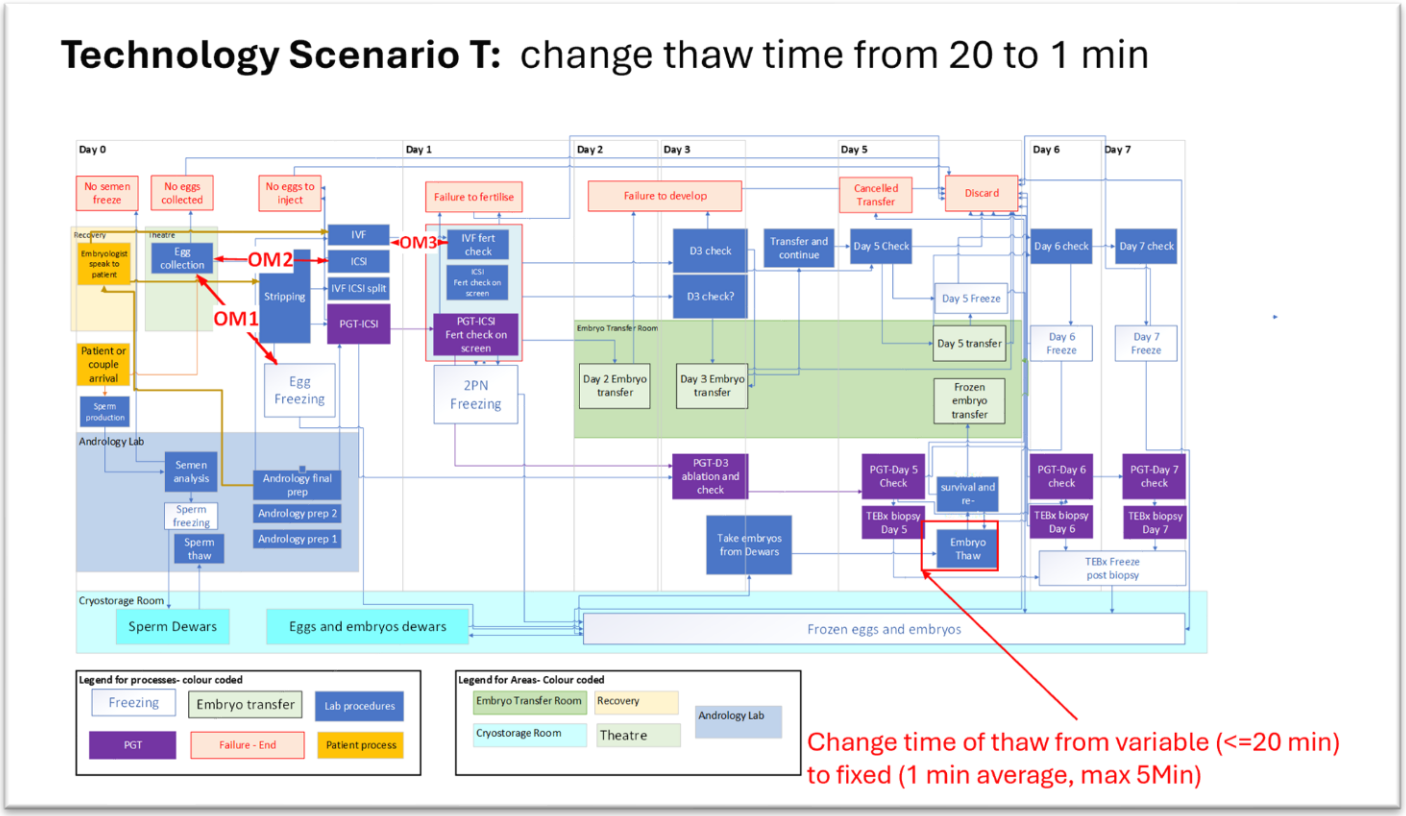


Figure 88. *Simulation conceptual model - Tscenario*

The simulation model is has a pointer to the T scenario (area of change idea)

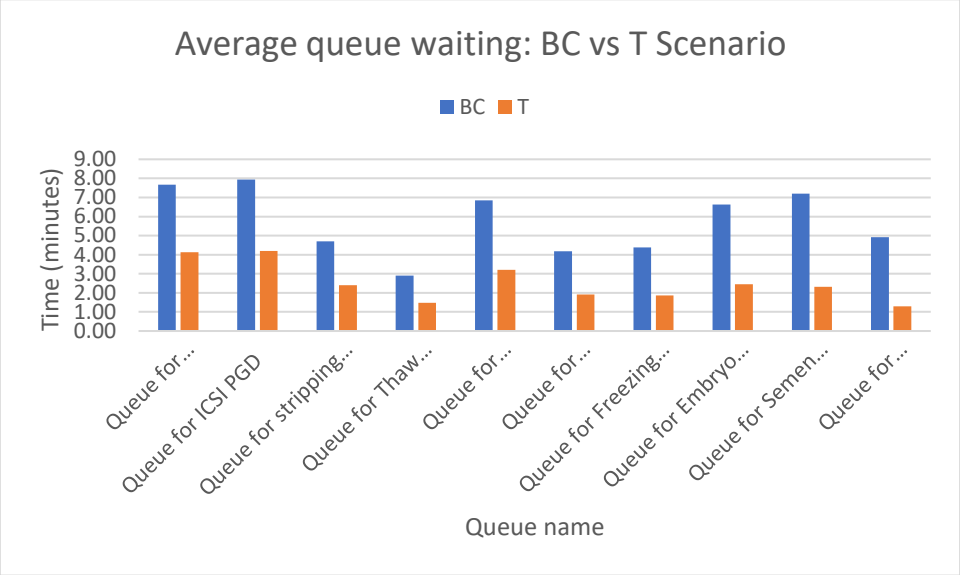


Figure 89. *Average queue waiting time : BC vs T scenario*

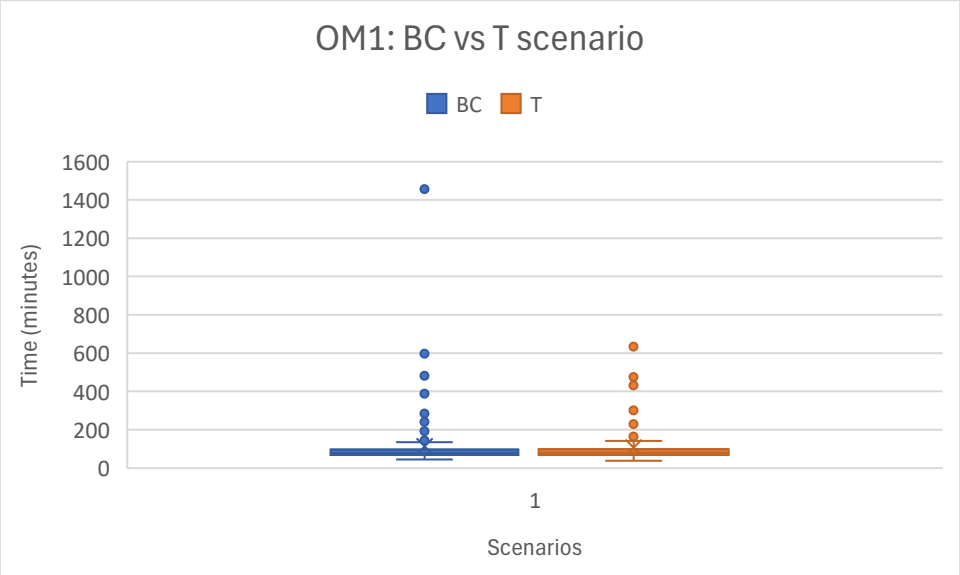


Figure 90. *OM1 boxplot - BC vs T scenario*

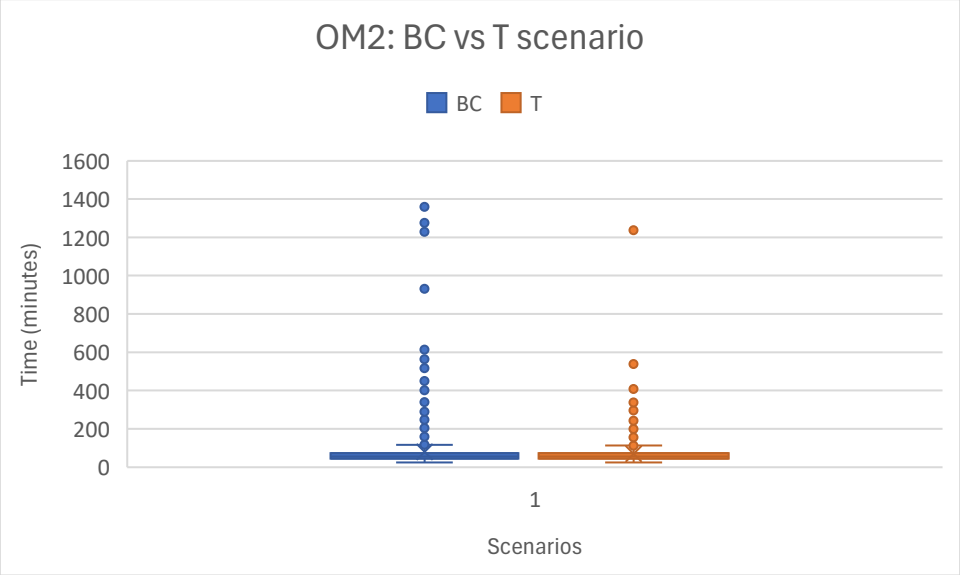


Figure 91. *OM2 boxplot : BC vs T scenario*

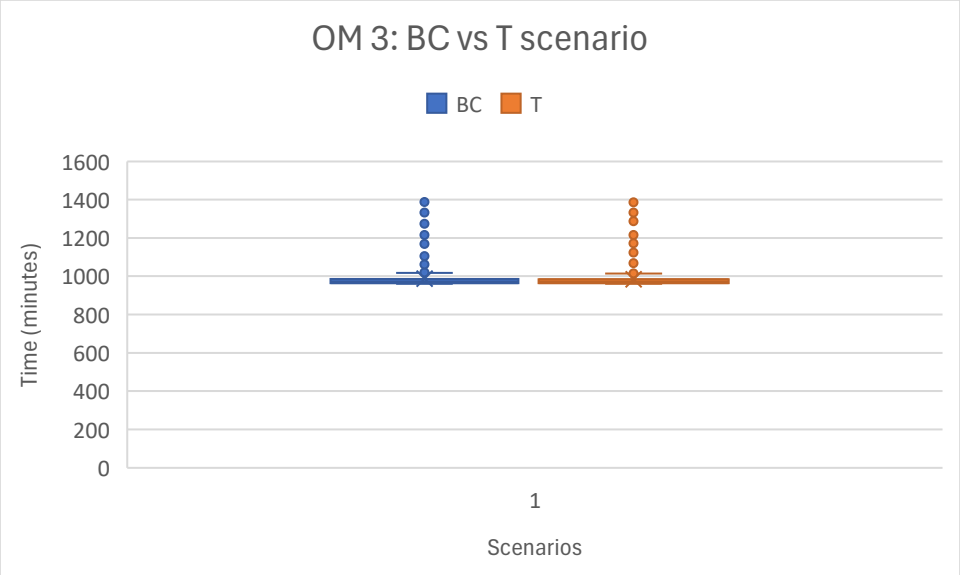


Figure 92*. OM3 boxplot : BC vs T scenario*

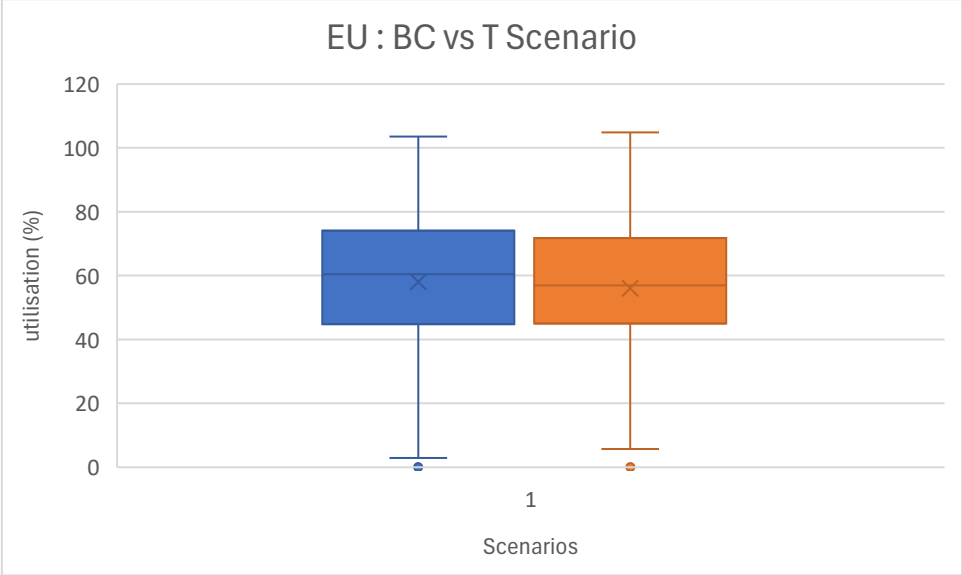


Figure 93. *EU boxplot : BC vs T scenario*

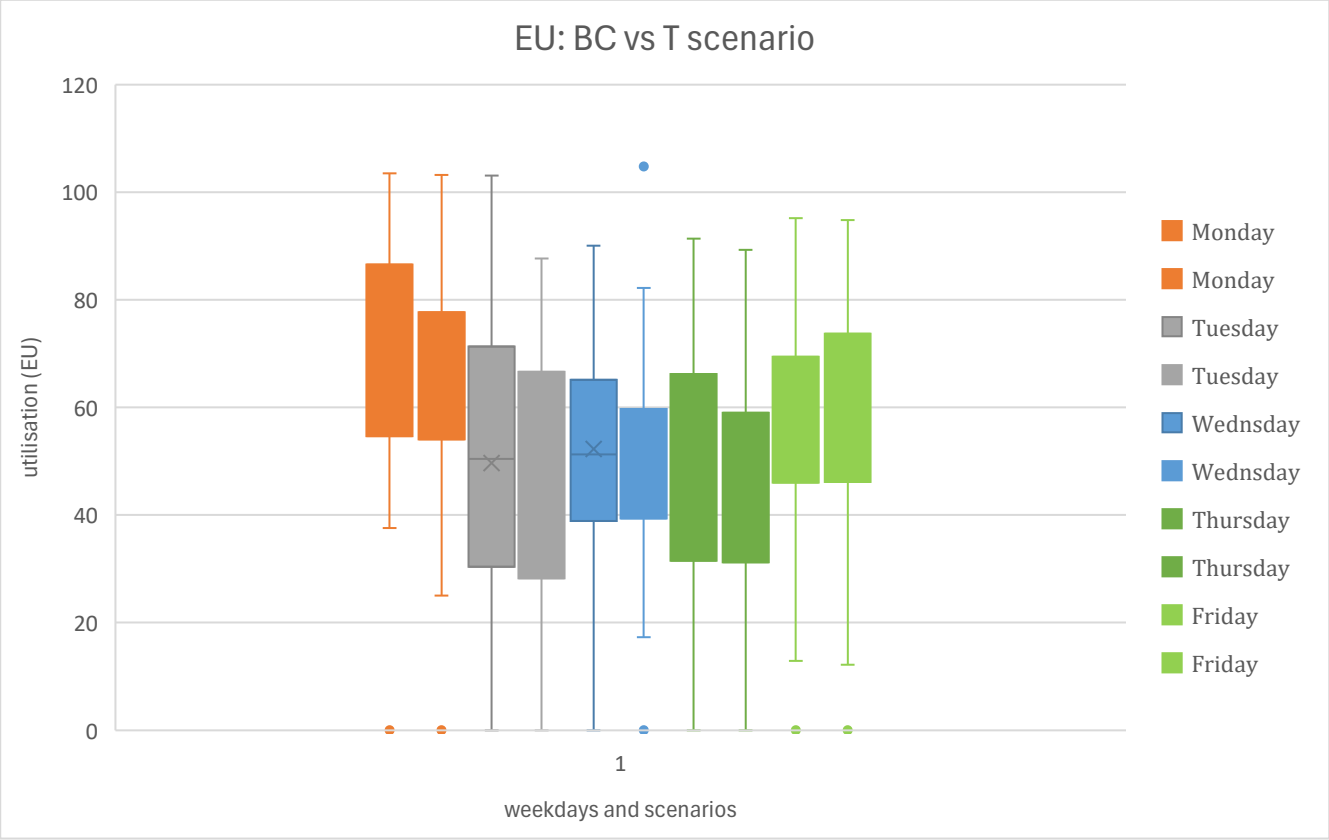


Figure 94. *EU boxplot per weekday : BC vs T scenario*

Conclusion from trying the change ideas / "what if scenarios" :

All the scenarios tested had a cost estimated globally on

Table 29. The cost was calculated from staff hourly rates, cost of equipment quoted in 2022. Cost is a parameter that can be added to the simulation model but wasn't in our case. Weighing the cost with the benefits of success improvement is an important parameter. The scenarios tested effect on OM from the simulation model are summarised in **Table 30**.

Table 30. *Summary of different scenarios results*
Simulation scenario in comparison with BC 91 run)

Scenario		description	effect
Staffing	Scenario **S1**	All staff - 1h overtime	OM2 no outliers UT reduced EU/PU reduced on weekdays
	Scenario **S2**	Add one embryologist Monday & Friday	OM1/OM2 no outliers EU and PU reduced for Monday and Friday
	Scenario **S3**	Add one embryologist and one practitioner Monday and & Friday	
Equipment	Scenario **E1**	Add one Embryoviewer (EV)	OM1/2/3 : no effect Queues on EV reduced
	Scenario **E2**	Add 2 Embryoviewers	
Service	Scenario **xA**	Remove Andrology services	OM2: less variability UT reduced Queues reduced for Andrology main lab (ICSI) and theatre (egg collection) EU/PU reduced Mon/Friday
Technology	Scenario **T**	Rapid Thaw	OM2 less variability UT reduced Queues reduced for thaw, main lab and andrology OM2 Queue time reduced for thaw but also gains for lab

Do the scenarios tried give the answer of what are the optimum working conditions ? Trying the different scenarios has given us an insight into improvements strategies and the possible gains on which areas. The scenarios tried show expected and unexpected changes of change ideas that also give an insight into how the associations between processes are so intricate and complex, showing a definite link between staffing level and timing of procedures.

- Adding overtime reduced the number of tasks unfinished at the end of the day but did not reduce bottlenecks (queues).
- Adding staff on busy days reduced staff utilisation (pressure on staff) but not queues.
- Adding access to an embryoviewer reduced bottlenecks and queues
- Removing the Andrology service improved staff utilisation and reduced queues and unfinished tasks (which can avoid unnecessary overtime).
- Reducing variability in certain processes (adopting a shorter time for embryo thaw) benefited the whole system by alleviating staff demand pressure and reducing queues.
- OM2 was the OM that benefited directly or indirectly from most of these change ideas. It was demonstrated previously the importance of OM2 for fertilisation rate.

There is no optimum idea that could be given but the change ideas and "what if scenarios" results could be used to combine in the future with balancing the cost as well. As an example, removing the andrology service or moving it as a separate service could be offered on the less busy days in terms of egg collections. Adding overtime for all staff could be an insight for changing shifts on busy days.

5.4 Stakeholder feedback

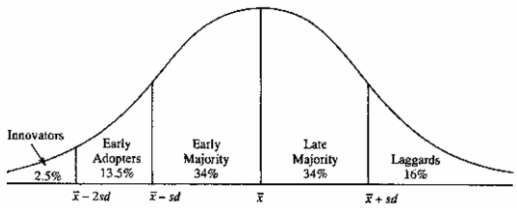


***Figure 95**. Adopter categorization based on innovativeness (Rogers, 2003)*

The project could be considered as an innovation and its adoption by stakeholders (embryologists at GSTT-ACU, the IVF community) will be discussed against Roger's categories for innovation adoption (**Figure 95**) using the communication channels as seen on **Figure 96**.

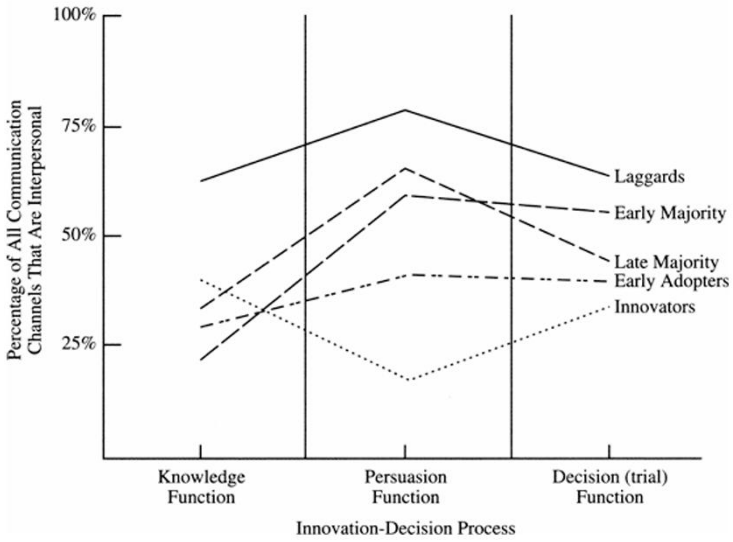


***Figure 96.** Importance of interpersonal communication channel (Rogers, 2003)*

The face-to-face feedback from the project presentation (17/09/2024) to the embryology team at GSTT-ACU IVF lab was very positive. 12 staff members from the embryology team out of 18 contracted attended and there was a general interest especially when the results section was presented and the data shown as validated. Validation from the embryology team was perceived by whether the model generates the same completed tasks from the arrivals. Workload has always been perceived by how many egg collections and how many transfers or embryo freezing are completed.

The impressions and ideas of the team were confirmed by the findings which is that Monday and Friday are the busiest weekdays with the highest utilisation rate, that there is a deviation from recommended timelines in certain timings and these are linked to staffing levels. The results confirmed the variability of staff utilisation over days due to workload distribution. The team confirmed that the andrology service tasks prevented them from allocating time to the Andrology preparation tasks and that was felt like a bottleneck by the whole team. The team confirmed that there is always a wait in front of the embryoviewer in the mornings and many of them confirmed that they tended to come early to avoid queuing. All staff members were fascinated by the possibility of trying different scenarios and started asking about different scenarios they suggest trying.

There was a general disappointment that the mean utilisation rate of embryologist was at 60% and practitioners at 40% while most of team members did overtime to be able to cope with workload but the team was reminded that the practitioners had mainly tasks that weren't mapped by the simulation (lab set up, paper set up and admin tasks) and only the lab clinical tasks were part of the simulation. Following on from that, the team was asked to participate by listing all the tasks they believe are part of embryologists and practitioners' roles and are not part of the simulation which they happily fed back by email following the presentation. **Appendix 23**. The feedback from the questionnaire was very positive and informative as the team used it to suggest workflow. Most of the members present responded to the questionnaire. Even though most of them never heard about simulation modelling, there was confidence in the simulation to identify bottlenecks and test different scenarios as a QI tool. Although all of them believed that the complexity of the healthcare pathways is the main hurdle to use simulation in healthcare (**Appendix 23**) There was a belief in the project to improve staff wellbeing as a first outcome but also cost saving and patient outcome. Many suggestions covered other parts of the IVF workflow that could benefit from simulation modelling. (Egg collection delays, Transfer delays…)

6 DISCUSSION

6.1 Main findings & research questions

6.1.1 Can the IVF lab be modelled into a DES "digital twin" as defined in the literature?

A digital twin is defined in the literature is a high computer representation of real systems running in close-to-real-time (Salehnejad and Proudlove, 2023). When translating the conceptual model created into the Simul8© software model, most tasks were modelled. The difficulty in building a model that could be a digital twin is the lack of data and lack of engagement from stakeholder. This project was initiated by an embryologist who had full access and understanding of the workflow dynamics, the databases used in the GSTT-ACU IVF lab. The demonstration of the simulation model with workplace supervisor, GSTT-ACU embryology team in a presentation and to the wider IVF community in a conference confirmed that the Simul8 model created in Simul8, mapped most IVF lab processes and could be considered as a "digital twin" for the list of lab processes mapped out. Some of the embryology tasks listed in **Table 6** were excluded (ordering, egg thaws, support tasks, meetings and auditing, intra uterine inseminations and all donor sperm management tasks). Some were excluded such as small equipment and dishes as well as the administrative team within embryology. It is in fact accepted that simulation models can be simplified (Tsioptsias, Tako and Robinson, 2023).

Simulation modelling relies on data and it is very important that the quality of the data used is reliable. The one advantage in this project that in IVF the time touchpoints are mapped in real time using RIW data (not affected by the need of data entry) and this bridges a gap in simulation modelling in healthcare. The model created was a digital interactive version where the data was not affected by the data entry limiting factor. The model created was shared with stakeholders as a read only video or as a 7 day interactive access to Simul8. (Kaffel, 2024a)

6.1.2 Can the model created in Simul8© give usefully accurate results and be validated?

The conceptual model and computer model created in Simul8© were continuously verified and validated using described methodologies (Robinson *et al.*, 2004). The specialised literature reported that there is no model that is 100% accurate but models created are ways to explore and understand reality. The process metrics (PM) and output metrics (OM) provided by the model were validated against real life data using white box and black box validation. The simulation model created has allowed a new way of displaying the IVF lab pathways and a new way of measuring workload, staffing and bottlenecks. Most articles in the literature represent the IVF lab workload by number of procedures carried out on a yearly basis (egg collections mainly) and estimate staffing as number of embryologists per number of procedures per year (egg collections) not accounting for variability across a year and or for complexity of each procedure. In addition, the simulation model allowed measuring all procedures linked to any resources (staff or equipment) answering the question, what are the main tasks of embryologists, or what is the equipment (ie, embryoviewer) mainly used for . Another feature of the simulation model created is the measure of time duration between procedures (OM1, OM2 and OM3) that were important for measure of success and measure of "what if strategies effect". These results are reviewed in the next section.

Process Metrics PM

Process metrics (egg collections completed, embryo transfers, egg freezing. etc) generated by the Simul8 model were validated against 2022 data. In the DES model created on Simul8, if arrivals are introduced in the model (planned procedures), the model allows prediction of PM (number of embryos biopsied, number of transfers, number of embryo-freezing or semen freezing). Therefore, it can allow to predict real workload based on scheduled workload and measure for example the cryostorage spaces needed. Once the model is validated, OM can be used for workload predictions based on day-to-day arrivals instead what is always used in the literature which is yearly and monthly number. In this case, generating a model took around a year and validating it lasted 3 months. A model can age and deviate from reality because of a change in parameters in real life (workload, resources).

However, the same changes can be modified easily in settings, the model can follow reality and aging does not become a problem. In IVF, an arrival for egg collection can generate workload for up to 7 days later. The model created in Simul8© allows to account for the variability that happens in real life with different workloads on different days instead of having mean**s over weeks and months.**

OM1, OM2 and OM3 between simulation model and real-life data

The black box validation of the model created for GSTT-ACU IVF was carried out by comparing 3 time-sensitive procedure durations (OM1, OM2, OM3) between the simulation base case (BC) and real-life data. The validation showed that the simulation model runs faster than real life for OM2 and OM3. This validation revealed the number of workarounds that embryologists apply to fit procedures within the timeframes required. In fact, workarounds and prioritisations were not added in the settings: The simulation model showed similar OM1 to real life data confirming egg freezing duration. The only difference is that the model had outliers where OM1>2hours which is when staff was available carry out the procedure. This would never be allowed to happen in the lab as the recommended time is less than 2 hours. In these situations, embryologists will prioritise this task over another. Similarly, the model runs faster for OM2 and has outliers that would not be allowed in real life : despite staff being available, ICSI is always done later than what the model has shown. OM2 rarely exceeds 4 hours and should be completed by the end of the working day, but as the workarounds are not modelled, the data displayed by the model shows how much workarounds are done. This shows that there is probably a window where staff are available for ICSI but as this is not ideal physiologically, the procedure is not done, which could be an area for reflection on staff rota management. OM3 which is the time duration linked to fertilisation check starts later in the model than real life. The model was built on the base of SOP knowledge that it can only be carried out 16 hours onwards but real-life data showed some outliers <16h.

Even though the DES Simul8 model created for GSTT-ACU IVF lab did not behave exactly as expected, creating the model itself was a learning process. The fact that the simulation did not work the way the real-world works raised awareness with the modelling team that there are many workarounds embryologists do without even thinking (Johnson,

Burgess and Sethi, 2020)and highlighting factors contributing to embryologist mental load, cause of stress and anxiety around workload management in the IVF lab (Priddle, Pickup and Hayes, 2022; Kasraie and Kennedy, 2024).

Number of unfinished tasks (UT)

*The analysis of unfinished activities or tasks (UT) at the end of a shift in the BC model allowed to signpost the need for overtime to fulfil workload needs. When UT is high, it means that workload surpassed staff capacity. In real life some of the tasks are left to the following day (witness to put embryos or sperm in the dewar) or sometimes staff shorten their breaks to fit the tasks within a working day (a workaround not accounted for). Monday and Friday are the days where there are the most unfinished tasks at the end of the shift which are the same days where the staff utilisation is the highest (**Figure 62**,* **Figure 63**). The simulation model allows to signpost situations where the workload is high in comparison with staff capacity by accounting for number of tasks and their time duration.

Staff utilisation at the end of each working day (EU, PU)

The analysis of EU and PU has shown variability over the year with peak periods that match with school holiday periods. Staff utilisation over a year (**Figure 51**, **Figure 56**) ranged in the simulation results from 0 which is when the lab is closed during Christmas to over a 100% especially on Mondays. Staff utilisation values over a hundred mean that the tasks that needed to be carried out need more than the staff available which indicate discrepancy between capacity and demand. There has always been feedback from staff in the lab at GSTT–ACU that Mondays and Fridays are very busy and there aren't enough people for the workload This was confirmed by the simulation model analysis. The highest EU was mainly on Mondays and Fridays and the highest PU was on Mondays. The question is here what is the ideal staff utilisation rate to avoid overtime or deviation from processes time recommendations. There is no reference in the literature neither from the Simul8© as a company or from literature in the IVF field about lab staffing utilisation rate threshold. If the created model incorporated every single activity in a setting, , it would be normal to expect a staff utilisation rate of 100% but only the clinical lab work was modelled in this study (as per **Table 6**), the expectation was that staff utilisation would never reach 100% otherwise the staff would only be doing lab procedures with no time

left for all tasks not mapped in the simulation. When asked HSST trainees in reproductive science what proportion of lab work is done by embryologists in a day most of the answers that came were 50-70%. The choice was made to focus on the number of unfinished tasks at the end of the working shift as a measure of ideal staff utilisation. Ideally, if workload and capacity are correlated, there shouldn't be any tasks unfinished at the end of a working day. The measure of "ideal staff utilisation" would be when unfinished tasks = 0 (**Table 27**). This gives EU= 44.5% and PU= 25.8%. If these two values were considered as target values and mapped on the cumulative EU and PU, (**Figure 54** and **Figure 59**), 75% of the EU values are > 44.5% and 70% of PU values are over 25.8% which indicates that most of the time, staff utilisation is higher than this targets in the results delivered by simulation.

Queues: Queues are a very complex concept that is often misunderstood (Proudlove, 2020). They are dependent on 3 parameters Utilization (U), Variability in arrival and service (V) and mean service time (T). It is not expected to have all tasks to flowing without any queues. Some queues are expected and do not represent an issue in the workflow. The waiting time is some queues was so high that it did not match with real life but it was mainly used in our results to identify bottlenecks in a workflow or improvements in the workflow when testing scenarios. Bearing in mind the VUT equation can help identify improvement ideas to reduce queues. The longest average queues identified in the BC model were all linked to both resources embryologists and the equipment embryoviewer. The queues identified were probably linked to the unfinished tasks at the end of the shift day. The scenario test increasing the number of embryoviewers reduce queues waiting times.

6.1.3 Does the analysis of the model data show any link between staffing levels – duration of procedures and clinical outcomes?

The empirical work examining the time durations between egg collection and ICSI (OM2) and IVF insemination and IVF fertilisation check (OM3) suggest a significant link between these durations and the FR outcomes at GSTT-ACU setting. Some OM2 results in the literature are comparable to our results (Wang *et al.*, 2021) and OM3 results are concordant with what has been published (Coticchio *et al.*, 2025). OM2 is the sum of two periods, time from egg collection to stripping called OPU-DN in the literature in addition to time between stripping and ICSI called DN-ICSI. There are conflicting results in the literature about optimum timings for OM2 especially that most studies focus on one of the components mentioned above rather than both. In addition, there are differences between studies for the time of egg collection in relation to hCG trigger (Wang *et al.*, 2021). In summary, the recommendation in the literature is to incubate eggs with the cumulus cells before ICSI and ICSI (around 2 hours minimum) should not be delayed for too long (no longer than 6h) because eggs can age and deteriorate which can affect fertilisation. With regards to OM3, the current Istanbul recommendation is for OM3 to be 17+/-1h for optimum results (Coticchio *et al.*, 2025). It is to be noted that all studies and timings do not account for the ICSI procedure length that can be affected by the difficulty of the procedure, the number of eggs available or the operator's experience.

Analysis of OM2 and OM3 per weekday suggested a deviation from ideal time durations for OM2 on days where staff utilisation is the highest so supposedly the busiest days. Staff utilisation is a parameter given by the simulation that gives an indication on two measures: number of staff available and workload. On the high staff utilisation days, OM2 tends to be shorter which is linked to lower FR results. This has been confirmed by stakeholders (embryologists) as they confirmed that on busy days, they try to do ICSI as soon as possible to be able to cover all the workload. On the same days, embryologists confirmed that on busier days there tends to be egg collections at the end of the day (at 4pm) which means ICSI is carried out straight away to cover the work-shift and not end in doing more overtime. There is a definite link between staffing and timing shown by the model, but it would be demonstrated much more clearly when the model is improved to add prioritisation.

6.1.4 Can the scenarios tested point towards the answer of what the optimum working conditions are to carry out all the IVF tasks on time ?

The model allowed to test different scenarios to try change ideas and observe effects. This is one of the most important parts of using simulation modelling. The findings were summarised in **Table 30**. Given the link between staffing, timings (Output Metrics) and unfinished tasks and the results from the scenarios, it can be suggested to change staff shifts to allow cover at the end of the day (tested by the overtime scenario), change staff working days or recruit more staff on the busier days (Monday and Friday). Adding access to an embryoviewer (which can be done remotely) can reduce bottlenecks and queues.

The scenario testing suggested to remove andrology diagnostic service to improves staff utilisation and reduces queues and unfinished tasks, which can avoid unnecessary overtime. Adopting technologies for new processes to reduce time variability was also a change idea that made improvements in workflows. The change ideas tested are improvements for workflows that can improve outcomes (for patients) by allowing better timings in relation to physiology but they should always be balanced with costing and benefits to staff which are the other stakeholders of the system.

As reported in the literature, simulation did not give an answer but gave possibilities to try ideas. There is no optimum idea that could be given but the change ideas and "what if scenarios" results could be used combined in the future with balancing the cost as well.

6.2 Strengths of simulation in IVF

Collecting the data to build the simulation was a learning process itself. It allowed analysis of the time durations versus outcomes (page 67) and analysis of time distributions for each process while creating the conceptual model (page 62, page83) Using DES allowed implementing time spent carrying out tasks as a distribution based on real life data rather than an means which is closer to reality. Examining the staff available every day allowed measuring it effectively 78% of embryologists contracted are present every day 75-80% of contracted practitioners are available every day with a variability

across days and after adding absences (annual leave, study leave, time off in lieu and sick leave).

DES use in the IVF lab can be classified as a data science project where scientific, mathematical, statistical algorithms are used to find patterns in data to support patient care, staff in their work and organisational improvement: 3 wins (Salehnejad and Proudlove, 2023). As full automation of tasks is not feasible in IVF yet, working on data science using mathematical projections and predictions is an alternative for making improvements on pathway improvements and outcomes in addition to achieving three wins. A simulation can in fact deal with many interconnected input data can exceed the reach of computational power to try and make predictions. The outcome here is that the simulation portrayed an entirely different picture of the IVF lab from the static data to a dynamic visualisation. The model results (EU/PU/UT) allowed to demonstrate the variability in workload and how the workload builds up. The general assumption is that the workload is calculated from the number of egg collection on the day while workload comes from the current day but also from previous EC as embryo culture can last up to 7 days. This effect is observed on EU, PU and UT the first 3 weeks of the year.

The NHS and many healthcare providers use the FTE/WTE (Full time equivalent/Whole time equivalent) for staffing measurement to map them to workload (BSA, 2025). The Association of Reproductive and Clinical Scientists in the UK (ARCS) recommends that centres should employ one state registered clinical scientist (embryologist) for every 80–100 cycles of treatment undertaken, the assumption being that it is a whole-time equivalent embryologist (Kasraie and Kennedy, 2024). The HFEA code of practice does not give a specific required number but states that "personnel in the centre must be available in sufficient number and be qualified and competent for the tasks they perform" (HFEA, 2023).

Different recommendations were published about required number of embryologists as shown on **Table 26**. Each group built the recommendations differently, some including andrology activities and quality control checks in addition to complex treatments (Lee *et al.*, 2023) while others were more general, whether not including andrology services

(Alikani *et al.*, 2014) or not adapted to all laboratories (Veiga *et al.*, 2022). In all scenarios, the number of FTE at GSTT-ACU 12-15 fell below all recommendations published showing understaffing but it is to note that all calculations do not include support staff (practitioners and lab administrators). WTE counts the number of staff contracted regardless of annual leave, sick or study leave and workload. Building the simulation allowed us to see from the data that only 73-80% of contracted staff are available every day and it showed variability in staff available every day. The WTE count does not account for variability. In the simulation model, staff utilisation accounts for workload and staff in addition to workload including all procedures in the lab while the most common staffing calculations in IVF labs account for contracted staff members per number of egg collections and FET scheduled. Results generated from the simulation model showed the discrepancy between the two types of association staff-workload measurements. As observed in **Table 25**. EU and PU which is based on number of staff available and actual workload demand, varied considerably between February-March vs September-October while the variation was not observed using the WTE/workload ratio. Staff utilisation from the simulation model gave more information on how the staff time is utilised daily in comparison to literature publications. It could be used as a closer to reality measure to make sure that the lab is correctly staffed to comply with time constraints.

This is the first time an IVF lab is modelled into a DES model to represent all tasks involved and the resources utilized, including staff and key equipment. This model aimed to visualize the complexity and intricate dynamics of laboratory processes (Basar, Unsal and Ergun, 2024). It was confirmed in this study that the simulation model created showcased as much as possible the complexities of the IVF lab and has been an eye opener on workarounds done to fit the time constraints. This concept is called workarounds but can be labelled as creativity, flexibility but the embryologist mind is constantly working to priories tasks that are competing for attention.

The IVF lab staffing has always been modelled the same way by everyone considering number of procedures (Input metrics) regardless of the process metrics (pathways and percentages) to be able to set up the resources needed (equipment and staff). The concept of staff utilisation demonstrates that the IVF lab could be resourced differently if different metrics were used. Operational researchers have good insights and understanding of how

DES can be used. Contribution from specialists in the field could make considerable improvements on all 3 fronts : patients, staff and organisational.

6.3 Challenges/limitations and risks in simulation

The challenges that were encountered in this project were similar to what has been reported in the literature (Robinson, 2014a): Firstly the high cost implications of the project: some of it tangible (Software, hardware, consultancy with Simul8©: **Appendix 11**, **Appendix 12**, **Appendix 13**) and a considerable proportion of it intangible (time spent to extract the data and build, verify and validate the model). This goes into the second challenge that simulation is time consuming while time is one of the most important factors for its success and implementation: The project timeline highlights that the model has been built with 2022 data and was only ready to be used in 2024. In simulations, creating a model can take months (mean is 3 months), very rarely years. Creating a model took a year (2023 to 2024) which is longer than expected and 2022 was the closest full year data to 2023 to be able to validate the model. Changes in the IVF lab processes are very often applied to a small section. IVF is such a sensitive field that changed in the lab must be applied carefully. Therefore, if the model was to be applied to 2024, or 2025 or later, only adjustments need to be added in settings to make it transferrable.

In a data science projects, the time needed to collect, process, and validate the data can impede the overall effectiveness of the simulation: a model to help in a current state be to help plan/forecast is hard to achieve which can be frustrating and means that the benefits cannot be immediate. The current model was in continuous validation up to mid November 2024 which delayed the generation of valid results.

Simulation modelling has been labelled as data hungry which has been confirmed by this project : The project pathways needed data for number of processes but also duration of each process and proportions for each pathway. Most of the data needed in the project was available and collectable. The fact that a lot of the data in this project (time distributions of procedures) was collected automatically via RIW as part of the normal pathways and legal requirements, it allowed real time recording of processes and reliable

data available. The data needed to be processed though to calculate time duration between steps and due to patient data confidentiality, this could only be processed by a GSTT-ACU staff and could not be delegated. Some of the processes were not tracked on RI Witness ™ (embryo checks on embryoviewer, taking embryos out of dewars, talking to patients) so they needed to be monitored and recorded by staff which is subject to variability and error recording as it is a manual process. Some IVF clinics still use manual witnessing only for all their processes. This project can highlight the importance of RFID witnessing in time saving but also in auditing and also improving processes and outcomes for clinics that only have manual witnessing.

Simulations require substantial amounts of data for both construction and validation. Many healthcare processes lack reliable recorded data but the data extracted from PMS-BBS was relatively reliable as it went through monthly checks of data entry for all embryology tasks as part of monthly and yearly KPI generation SOP: all data relative to number of procedures (egg collections, embryo transfers, sperm freezing) and proportions in each pathway (% of embryo transfers, % of D5/6/7 freezing, % of biopsy..) was verified regularly.

Building the conceptual model, validating it and understanding the statistics behind the simulation modelled required expertise. At the start of the project, the initial idea was to build the model by building knowledge of Simul8© from Simul8© training academy courses (**Appendix 11**). This was quickly abandoned in favour of an expert help from a simulation consultant (S8C) from Simul8© company to speed up the project and build a model confidently with meeting time constraints. Simulation modelling is more than use of a software package and even having a software package requires a lot of time investment to understand the possibilities provided by the software and how the model is built to rectify it following verification and white and black box validation. The conceptual model was created by an embryologist and conveyed to the simulation consultant but there was always a risk of misinterpretation. This demonstrated the need for investing in complementary organisational and technological assets and skills if an organisation wants to use a data science tool (Salehnejad and Proudlove, 2023). The need

for expertise from a simul8 consultant created some dependency on it to make modifications in a secure way and change parameters and that was a limiting factor to the project progress.

One of the other risks associated with simulation modelling is the potential for creating an incorrect model. However, the definition of what constitutes a "wrong" model can be subjective and challenging to evaluate (Tsioptsias, Tako and Robinson, 2023). What constitutes a valid model is a concept very hard to determine. The validation processes can increase confidence in the model but cannot confirm validity. The concern with simulation is that a model, even if flawed, may convey a false sense of over-confidence by presenting interactive process workflows, which can lead to erroneous conclusions being drawn. It is impossible to prove that a model is valid so verification and validation are processes to increase confidence in the model to the point that it can be used in decision making. In this model, some parameters were validated but there was not enough time to verify and validate everything. Furthermore, statistical analysis, when possible, will only provide a probabilistic approach but no definite answer.

Several problems were highlighted in trying to validate a model: the absence of workarounds in the model for example but any model is only validated with respect to its purpose. One of the Simul8© model purposes in this project was to have a better understanding of staff in respect to processes timing in addition to identifying bottlenecks in the system. The aim was to suggest change ideas linked to the investigated parameters. In contrast , it is not a simulation model to understand how much space is needed for cryostorage or to understand the admin tasks covered by the embryology team (not integrated in the model).

One of the challenges in creating a simulation model was the need of time to train on the software and understand the technology from the perspective of a clinical scientist. This project raises awareness of investing in data science training by healthcare professionals. Training should be offered to healthcare professionals or integrated as part of a healthcare organisation. The cases where DES implementation is successful is where there is involvement from stakeholders and these projects involve healthcare

professionals that are part of the process to analyse and improve. Introducing data science tools requires investing in complementary organisational and technological assets and skills and a fundamental rethink of the organisation of production

The national school of healthcare science in the UK offers now a clinical data science funded programme targeted at healthcare professionals. A programme as such is an encouragement for clinical scientists to learn, train and integrate data science into their practice to work on improvement projects such as simulation modelling. There is no feedback on the programme yet as it started in 2023 (Science, 2024) and it would need a few years to audit and see an impact of such a program.

Aside from the general simulation challenges identified in this project and reported in the literature, there were limitations and challenges specific to the model created for the IVF lab. Some general assumptions were made by the modelling team to make the model easy to create such as time travel between tasks that was not mapped out. Other challenges were real life problems such as no access to RIW data due to an IT issue (Hosea, 2022), impossibility to include unpredictable variability such as workarounds (prioritising egg freezing over ICSI, doing the ICSI in the order of difficulty, assigning tasks according to staff experience). One of the limitations is that the data extracted from RIW was calculated and used on the assumption that all practitioners follow the RIW pathways and logic, there is no way to identify deviations from SOP. The model was created on the base that the processes times would have the distribution assigned so if there is any change in the process time, it must be applied to the whole year: The model as it is, have no capacity to integrate changes of SOP unless applied to the whole year. As an example, if egg freezing takes 10 minutes and it has changed mid-year to take 20 minutes, it can be added but two different runs need to be created to match with the historical change. As not all the processes carried out by the embryology team were mapped into the model, this has needs to be taken into consideration when interpreting results.

In the model and in real life, practitioners do not work weekends but the results generated from the model assign a PU on Saturday and Sunday which was a copy from

Friday results. To analysing the results, all PU had to be changed on Saturdays and Sundays to zero with all risks of manual data manipulations.

In August 2024, Simul8© software did an upgrade of the version and with the upgrade, all the results delivered by the model changed which raised concerns. This was raised with the Simul8 development team that found a bug in Simul8 software built which was then resolved. This raises the issue of relying on any software and the need of analysing results carefully.

One issue was raised with the results is the very occasional negative EU and PU values in certain runs. Some model runs give occasionally negative values (1 value per run that would be >-8%) The values were exclude by being rounded to zero as it was one value in 365 values. This was raised with Simul8© development team and is still waiting for investigation.

Time being a limiting factor, all "what if" scenarios results were based on comparing one scenario run to one BC scenario run. Running 5 runs on each side would give more confidence in results but as time was limited, only one run was tried.

It is to be reminded that this simulation model has been created by an embryologist. It has the advantage of having a SME involved but also the bias coming from a preconception that the issues are in mainly in staffing.

6.4 Reflections on simulation in IVF

Simulation in healthcare in general has always been reported as very complex and difficult to map which was confirmed with the project and validated by the difficulty of mapping workarounds (Proudlove *et al.*, 2017). As any use of data science technology, t**here is always a learning curve which in this situation has affected timings of project delivery and time dedicated to data analysis.**

Reflections and limitations

As a reflection for the future, when embarking on a journey of creating a DES simulation model, unless being a simulation specialist, one does not know exactly how the model works in the setting and you do not know what the limitation are in results. There is a need if anyone embarks on this journey to read all documentation relevant. Ideally is to work on it as a team one from the clinical background and what is called SME in the literature, one person proficient in building the model in Simul8. Analysing is a very important part but so much effort is spent on the simulation built that no time is left for the analysis. The knowledge of simulation modelling is important; but the results quality of the model cannot be proved useful until it is used. By the end of the project , when the results generation was understood, the model needed rectifying. The current simulation model created for the IVF lab would still benefit from some adjustments for future improvements such as adding workarounds and priorities in addition to adding staff specific competencies (such as biopsy practitioners). On reflection the project could have been limited to one area in the lab to meet with timeline constraints of the project but that would not allow an overview of the whole IVF lab.

Adaptability of DES modelling in IVF

Using simulation modelling at GSTT-ACU to analyse, help decision making and forecast was the first aim but ultimately the project was investigating to use of this tool in other IVF units in the UK or worldwide. The question is would that be possible or feasible and if feasible, how can it be made possible. According to Robinson (Robinson, 2014a; Robinson et al.; Robinson et al., 2004), a model created can be used in a variety of ways : throwaway (single use), ongoing use, regular use, generic and reusable or reusable components. The expectation is that the model created could be reused. It is not for ongoing use as it has been presented to GSTT-ACU team, raised interest among the clinical team, senior leaders and strategy teams but would still need to go through total approval to be used which will be discussed below in innovation adoption. The model created is specific to GSTT-ACU lab as it has been built with great details of pathways. This means that it can't be generic (used across a number of organisations) unless the pathways are exactly the same across organisations.

The reuse of the model for the same IVF unit is possible but requires regular data updates to make sure it behaves similarly to the current system. In fact, all parameters in the model were based on 2022 data. If there is a change in SOP, it must be reflected in the model to adapt it to the current state. The model has multiple settings that are open to changes to allow adjustments and adaptability over time: Input metrics (number of egg collection, number of semen analysis, etc.) in addition to resources (staff, certain equipment) and Process metrics (pathway proportions and time duration). If the model is validated and updated regularly, it can become a model for regular use but that would require expertise from the modeller and is not possible unless GSTT chooses to invest resources and training. The model can also be used in the same unit for different purposes such as cost.

Can the model be re-used or adapted to other units? GSTT IVF lab is one of the largest in the UK. It covers most services offered by IVF units and the model covers most of the clinical processes in the lab. Re-using the model or one of its components for other IVF units could be possible to save time and money. Robinson (Robinson *et al.*, 2004; Robinson, 2014a) raised several problems with the use of simulation models and components: economic and validity. Robinson claims that the producer of the model pays the cost of writing, documenting, verifying and validating and as there is no charging mechanism for sharing models, there is very little incentive for sharing them. One could argue that sharing a model initiates a learning outcome and allows the model to be improved. The validity part is to answer the question how can the model validity for another context is ensured and whether it would save time. This raises the question of databases where models can be shared.

This project has identified that reusing the concept of simulation modelling in IVF is possible and using the previous expertise of modellers to save time on a new project but no lab in IVF is identical to the other, unless the labs belong to the same healthcare groups and even so, the staffing structure is different.

A single model can take one or more of the types cited above. The model created in this project is reusable locally (GSTT-IVF) as an ongoing tool or for regular use but that will

depend on the updates that are fed into it. It is not generic as it has all the process specificities of GSTT-ACU lab but some components of the model can be re-used and adapted by other units for a quick model built. The model can also be re-purposed locally for cost use. The most important parameter in re-using a model is to know exactly how it works, which means that it must come with a user guide, which was developed here by the simulation team (Appendix 15).

6.5 Patient and staff feedback on simulation in IVF

Raising awareness of the IVF lab complexity was the first objective. The presentations of the project to the GSTT-ACU team at the start (December 2021) and after having preliminary results (September 2024) were received very positively overall. There was a concern from the embryology team in 2021 that any dynamic model could possibly manage the challenge of representing the complexity of the IVF lab but all staff members were keen to have the lab complexity and workload-staff effect on outcomes demonstrated in a tangible data format especially after feeling the pressure from workload. The team felt the disjointed demand and capacity in IVF compromised timing of procedures and patient's treatment outcomes, but also staff own mental health. This was demonstrated in the embryology stress survey at GSTT-ACU (**Appendix 24**. GSTT embryology team stress survey 2020 – unpublished)and reported in the literature (Murphy *et al.*, 2023; Priddle, Pickup and Hayes, 2022). The clinical team members present at the beginning of the project (2021) were fascinated by the idea and found it reassuring that it was previously used in A&E departments but were very sceptical about modelling patient pathway in an IVF clinic claiming that it is too complex to model. The preliminary results were then presented to GSTT-ACU in 2024 and as demonstrated in the feedback questionnaire (**Appendix 4** & **Appendix 23**) was very positive. All staff who attended were engaged and participated actively in the discussion to understand how the simulation model was built and what the results can give but also the limitations. Presenting the project to the GSTT-ACU embryology was a very important milestone. Building a DES model that can make an impact is important in the life of the project. Creating the simulation model is not the purpose, it is a tool to be used. Including the team that is mostly affected by the workflows is important to give stakeholders an opportunity to voice ideas and opinions, give feedback and participate with change ideas. Including

the embryology team meets the essential point of inclusion which can be benefit from the project into the simulation experience to move into implementation. The last change idea (T) was adopted from the discussion with the team. The literature review of simulation projects has shown limited implementations of simulation in the clinical healthcare setting due to the project coming from academia and not from the clinical team.

There was a slight disappointment from GSTT-ACU team that staff utilisation rate was lower than their expectation : In fact, everyone felt overworked and had to do overtime hours. It was reminded at this point that not all the embryology responsibilities were included due to lack of time information and that could be a project for the future. It was an opportunity to discuss the importance of data entry to identify improvements. The team recognized that most lab processes were mapped and were fascinated that data from OM1, OM2 and OM3 is confirmed to be linked to outcomes and staffing. Due to time constraints, improvement ideas tried in "what if" scenarios could not be implemented but were well received by management and raised interest from SMT at GSTT and as well as with the strategic planning team. The project was presented to a strategic team focusing at demand and capacity at GSTT-ACU and the simulation display was shared with the strategic planning team as a video (Kaffel, 2024a) along with the simulation Simul8© model (a link to the simulation model base case can be shared to see the simulation as a read only for 7 days). The plan is to attend a SMT meeting to present the data and back change ideas for an implementation phase.

As part of diffusing the idea in the IVF community, the project was also presented to Evewell clinic embryology team where I am currently lab manager (July 2024). It was received very positively and the team offered ideas of scenario trials and asked whether it is possible to do the same at the Evewell clinic. The project preliminary steps were shared on Simul8© website as a case study (Simul8, 2023) and the experience using simulation modelling for GSTT-ACU IVF lab was also presented in a drop-in session organised by Simul8. Participants were interested to hear the experience from a healthcare user and the challenges encountered during the project. The preliminary results were presented at an international conference (ALPHA conference meeting, June 2024) as an oral communication (**Appendix 3**) and was well received by the audience

and the organising committee. The attendance found the subject very interesting especially that any lab manager would like to find a balance between demand and capacity to meet the physiological constraints and with rising concerns over embryologists' wellbeing a very demanding role. The presentation was selected as as oral abstract winner. Following on from ALPHA conference, a meeting was organised with an author that has interest in the subject (Alikani *et al.*, 2014) that expressed interest in the use of DES to update the recommendations published in 2014. The overall feedback is a confirmation that the model is a first that could realistically map the IVF lab complexity and give tangible information that could allow moving away from the count of number of embryologists per number of procedures.

6.6 Innovation adoption and perspectives

The use of DES in IVF is a new concept. Its diffusion as an innovation is part of its life cycle. Rogers (Rogers, 2003) defined innovation diffusion as the process by which (1) an innovation (2) is communicated through certain channels (3) over time (4) among the members of a social system. Rogers (Rogers, 2003) also classifies adopters of innovations depending on the speed of adoption as (1) innovators, (2) early adopters, (3) early majority, (4) late majority and (5) laggards (**Figure 95**). GSTT-ACU is one of the largest NHS IVF units in the UK and the largest PGT centre in the UK. From the unit's historical publications, GSTT-ACU falls into the early adopter or early majority definition depending on how the innovation to adopt impacts the unit's reputation. Introducing DES into GSTT-ACU IVF lab has been welcomed to start with as it is considered as a service improvement project that falls within the GSTT objectives (Trust, 2024) the unit wants to be seen as innovative but the continuous adoption will depend on how the diffusion process would flow. This project has also raised interest with the SMT and strategy team.

The characteristics of this innovation (Rogers, 2003), will determine its adoption :

Relative advantage: by superseding arbitrary workload planning and staff rota management relieving the lab manager from a task that is mainly based on their knowledge of each member's expertise, experience, knowledge of the processes. The very few articles published on the subject are based on "expert opinions" (Alikani *et al.*, 2014;

Go, 2015a; Cohen *et al.*, 2018b). This will benefit embryologists with a proactive planning assuring better work conditions to achieve staff retention (Robinson et al., 2012) . It will also benefit managers by allowing a simpler and data-based staff and workflow management. Leaders of the unit would be able to claim the notoriety of being the first implementing this innovation. The IVF field is competitive, being the first in the field for adopting an innovation or publishing on it is a tool for publicity/notoriety. Leaders would benefit from cutting costs and reducing waiting time, hence improving patients' satisfaction and achieving financial targets.

Compatibility: The innovation would be an analytical tool to test different hypothesis/strategies for workflow improvement without affecting quality of care which allows less resistance to change.

Complexity : Simulation is complex to set up as it requires a good knowledge of process mapping. Having advanced on the project and created the model, the unit would only need to adjust for its use (Mohiuddin et al., 2017; Simcore, 2019).

Trialability: Trialling the simulation could be accessible to anyone to try any change idea, very much like a video game. Simul8 software offers easily understandable dynamic visualisations to test "What if" scenarios, even the most complex ones (change of bed numbers, addition of working stations, addition/removal of staff or equipment) to predict outcomes, without changing practice or disturbing the clinic dynamics.

Observability: Having presented the preliminary results for the team offered observability. One of the scenarios tested was already implemented by the time the results were presented (adding an embryoviewer) and the team confirmed the outcomes

Innovation characteristics are associated with the social context and how the innovation interacts with it (May, 2013): Diffusion of innovation in IVF relies on understanding the social system in the field and using the right communication channels. Previous simulation studies in healthcare were mainly published in management and healthcare economics journals. Using the IVF network communication channel is compulsory for its diffusion (conferences, publications, meetings) and approval from governing bodies such as the HFEA and scientific societies (ESHRE, ARCS, the American Society for Reproductive Medicine ASRM) are essential for effective dissemination. Utilizing conference meetings

(which was done during Alpha meeting 2024) to raise awareness of issues everyone faces (staff shortages, lack of planning in the lab) and presenting an innovation that could possibly solve these challenges has been good opportunity to disseminate an idea within a likeminded community (homophilous as defined by Rogers). The lack of implementation and diffusion of simulation is probably due to previous studies were mainly led by academics for research purposes. Taking innovation beyond research would need to see implementation as a continuous, inclusive process and understand the social and psychological social system.

The IVF world is a niche discipline where interpersonal channels work better for communicating a new idea to the specialised audience (the IVF community). Interpersonal channels are very important for persuasion especially for early and late majority innovation adopters (**Figure 95**, **Figure 96**). Mass media channels are the most rapid and efficient mean to create awareness-knowledge of an innovation (Rogers, 2003) but in the case of IVF, it is only the last step to communicate to the larger public. Over the last 30 years, with improvements of ovarian stimulation, embryo culture media, devices, introduction of new embryo freezing techniques, fresh IVF and frozen embryo transfer success rates (live birth rates) have nearly tripled in the UK (HFEA, 2021; HFEA, 2024). As the technical improvements are currently slowing down, and research on human embryos is increasingly difficult, IVF units are looking into new non embryo invasive methods to improve their results and reduce costs (Campbell *et al.*, 2021).

Computer simulation modelling comes as an innovative approach to address a dynamic and complex system : the IVF laboratory in a time where there is increased interest in studies including data scientists and IVF practitioners (Curchoe, 2022). DES could offer cost savings strategies in a time where there is pressure to work cost effectively to enable patients to access treatments given that NHS funded IVF cycles have declined drastically (HFEA, 2024) and the mean cost of IVF treatment is 5000£ and up 20000 £ in the UK (CMA, 2022; HFEA, 2025). Moreover, there is pressure in IVF units to increase the number of patients treated without changing staffing or even with reduced staff numbers. There is such a shortage of embryologists (I3, 2022) that many IVF units had to create a

financial retention scheme to recruit and retain embryologists. The innovation proposed (DES in IVF) would improve staff retention and wellbeing in a time where there is increased interest in embryologists' work conditions (Campbell *et al.*, 2022; López-Lería *et al.*, 2014; Sunderland, 2021).

7 CONCLUSION

This project was overall a first trial to use an operational research concept (DES) in the field of IVF. The novelty of the project is the use of new measurement tools to analyse efficiency in the IVF lab, suggest and try improvements virtually before implementing or investing in new tools.

This can be considered as a data science project as well as a QI initiative in a field that needs structured improvements to improve patients outcomes where pathway duration is key to success but also improve organisational efficiency and ultimately benefit embryologists, the power house of the IVF lab in a time where embryologist mental wellbeing and workload pressure has been raised as a limiting factor to train and retain staff.

Simulation and modelling in IVF are novel approaches to understand processes workflow, have some marginal gains in the IVF laboratory where time and staff are the main constraints facing an ever increasingly complex workload. Data collection could be a limiting factor to DES modelling but as IVF laboratories have a duty to record procedures witnessing (electronically) and IVF processes results to the regulator (HFEA in the UK), IVF labs could be a good candidate for this innovation to improve outcomes but also in workforce planning and staff wellbeing and retention. Implementing this innovation will be a challenge in a sector that has always worked with approximations while there is mainly a hype for AI and all derived AI technologies.

Using this tool would require investment from healthcare organisations in data science and operational research knowledge building and training to make informed decisions. It also requires time investment and interest in the field in addition to engagement and involvement from teams that are involved. The purpose of creating models should not be academic only but it must make an impact in the clinical settings to create tangible improvements.

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9 APPENDICES

***Appendix 1**. Abstract from Alpha Conference*

Using simulation to optimize IVF lab resources and meet physiological time constraints

Aida Kaffel[1], Jon Taylor[1], Llwyd Orton[2], Jessica Aiani[3]
[1]Assisted Conception Unit, Guy's and St Thomas NHS Trust
[2]Department of Life Sciences, Manchester Metropolitan University
[3]Simul8 Corporation

BACKGROUND AND AIM:IVF laboratory procedures are dynamic and increasingly complex. Time spent carrying out procedures and timing in relation with oocyte retrieval are closely linked to performance (ICSI, cryopreservation, embryo survival) but there is very little published data on the subject. Labs are resourced using estimations and often reliant on workarounds that are challenging to plan.
The aim of this project is to use a manufactural concept to:
1. design a simulation model for IVF lab processes using a discrete event simulation software (Simul8©),
2. use the simulation model to improve patient outcomes and efficiency.
METHODS:database (BabySentryPro©) and timings from the electronic witnessing system (RI Witness©):
1. To model and map the IVF laboratory processes: replicating every touchpoint of the patient or their gametes/embryo journey,
1. Use retrospective data to validate the model,
2. Identify bottlenecks and deviations from optimal physiological timings,
3. Test strategies (workload and staffing) to take to mitigate against deviation.
RESULTS:Key vatiables generated were:
- Number of processes completed; using a timetable and determined by resources available within a timeline.
- Dynamic input in time (e.g. egg collection, semen analysis, embryo thaws) compared to dynamic output (embryo/egg freezing, embryo transfers, number of spaces utilised in dewars).
- Bottlenecks identified by queuing times in procedures vs a set target.
- Staff time utilisation (expressed in percentage).
- Timing of procedures vs set targets.
Currently at the validation stage, preliminary results show a clear dynamic visualisation of processes (inputs and outputs with a timeline). Challenges and limitations identified were representing deviations from set behaviours or unpredictable human choices.
CONCLUSIONS:Traditionally, IVF laboratory workload/resources are measured by number of weekly egg collections/full-time embryologists in post. Preliminary simulation allowed a dynamic understanding of workload and resources in real time and raised awareness with stakeholders of complexity.
Once validation is completed, the aim is to model and identify bottlenecks and test "what if scenarios" to improve patient outcomes and optimise workflow.

Keywords: IVF, embryology, simulation, workload

Appendix 2 *Certificate of attendance ALPHA meeting 2024*

Appendix 3 *Acceptance of oral presentation- ALPHA meeting June 2024*

Details

Status	:	Accepted:Oral Presentation
Presentation Type	:	E-Poster
Abstract Category/Topic	:	Clinical Quality
Language	:	English
Saved:	:	29.01.2024 12:02:30
Submit:	:	06.02.2024 15:48:14

Confidential to Author and Editor

Note to Editor	:	This is a project that is part of a DClinSci study at MMU university in collaboration with Guy's ACU. The case study is on https://www.simul8.com/case-studies/guys-and-stthomas-optimizes-IVF-lab-resources-using-simulation
Presenter	:	Aida Kaffel (aida.kaffel@evewell.com)

***Appendix 4**: Stakeholder engagement questionnaire*

1. Did you attend the presentation about simulation in IVF 01/12/2022

YES/NO/ Maybe I can't remember

2. Did you attend the presentation about simulation in IVF 17/09/2024

YES/NO / Maybe I can't remember

3. Have you ever heard about simulation modelling before

YES/NO

4. Simulation modelling is a quality improvement technique that works from a real world problem to create its digital twin : It works in industry, in shipping, airports café… do you think it has its place in healthcare.

YES/NO/MAYBE

5. What do you think are the challenges of simulation modelling in healthcare (tick as many as you think are applicable)
   - Data reliability to create a model
   - Complexity of healthcare pathways and processes
   - Oversimplification of processes to create the model
   - Other…… (free text)
6. If simulation works efficiently, I think the advantages include
   - Create knowledge and understanding the process flow
   - Identifying bottlenecks and process flow issues
   - Visualization and communication: Raise awareness of system complexity
   - Possibility to do try different scenarios without incurring extra costs: buying equipment, hiring staff
   - Other: (free text)
7. Do you think simulation modelling will be a tool for
   - cost saving
   - Improving staff wellbeing
   - Reducing unnecessary overtime
   - Improving patient outcome and/or experience
   - Research only but not applicable to clinical settings
   - Other:…..
8. How long do you think it takes to create a simulation model for example for a Gynae clinic workflow
   - Hours
   - Days
   - Weeks
   - Months
   - variable depending on the size of the project

Stakeholder Engage
SIMUL8 Manchester Metropolitan University 2

9. Can you think of an example of a process/pathway in IVF that you would like to see modelled to run different scenarios
10. After the presentation and hearing about Simulation, this a first trial of Simulation modelling use in IVF, would you like to see this developed further and adjusted for future use.
    Definitely not
    Possibly
    Definitely
11. Do you have further comments or feedback

Appendix 5. *MMU ethos application outcome*

Manchester Metropolitan University

10/09/2024
Project Title: The IVF laboratory : Using a computer simulation model for lab processes to adhere to physiological time constraints.

EthOS Reference Number: 69416

Ethical Opinion

Dear Aida Kaffel,

The above application was reviewed by the Science and Engineering Research Ethics and Governance Committee and, on the 10/09/2024, was given a favourable ethical opinion. The approval is in place until 30/09/2024 .

Conditions of favourable ethical opinion

Application Documents

Document Type	File Name	Date	Version
Additional Documentation	NDA_Simul8_Corp_Signed_AK Guys ACU	23/03/2024	v1
Letter to Gatekeeper	Service audit authorisation 16169 GSTT	21/05/2024	V1
Project Protocol	Project 16169	31/05/2024	v1

The Science and Engineering Research Ethics and Governance Committee favourable ethical opinion is granted with the following conditions

Adherence to Manchester Metropolitan University's Policies and procedures

This ethical approval is conditional on adherence to Manchester Metropolitan University's Policies, Procedures, guidance and Standard Operating procedures. These can be found on the Manchester Metropolitan University Research Ethics and Governance webpages.

Amendments

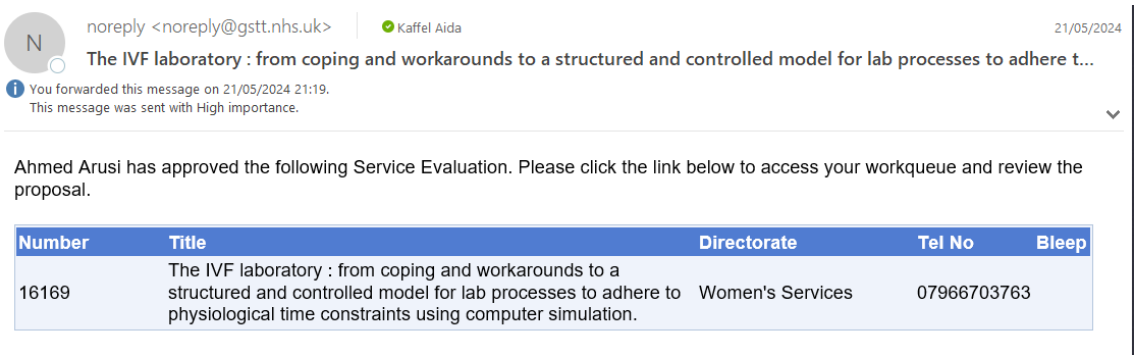
If you wish to make a change to this approved application, you will be required to submit an amendment. Please visit the Manchester Metropolitan University Research Ethics and Governance webpages or contact your Faculty research officer for advice around how to do this.

We wish you every success with your project.

Science and Engineering Research Ethics and Governance Committee

For help with this application, please first contact your Faculty Research Officer. Their details can be found here

Appendix 6*. GSTT Audit application outcome*



N

noreply <noreply@gstt.nhs.uk> | Kaffel Aida 21/05/2024

The IVF laboratory : from coping and workarounds to a structured and controlled model for lab processes to adhere t...

You forwarded this message on 21/05/2024 21:19.
This message was sent with High importance.

Ahmed Arusi has approved the following Service Evaluation. Please click the link below to access your workqueue and review the proposal.

Number	Title	Directorate	Tel No	Bleep
16169	The IVF laboratory : from coping and workarounds to a structured and controlled model for lab processes to adhere to physiological time constraints using computer simulation.	Women's Services	07966703763	

Appendix 7*. GSTT Audit procedure*

Guy's and St Thomas' NHS Foundation Trust

Quick guide:
Setting up a clinical research study

A: If you are leading the research and you are employed by Guy's and St Thomas' NHS FT (GSTFT) or King's College London (KCL):

It is likely that GSTFT and/or KCL will be the Sponsor for your research. A Sponsor is the institution that takes on responsibility for initiation, management and financing (or arranging the financing) of the research. The Sponsor is usually the employing organisation of the Chief Investigator. **All research in the UK must have a sponsor confirmed prior to assessment by the Health Research Authority (HRA).**

For GSTFT and/or KCL to take on the role of Sponsor, you are required to submit your full study documentation for sponsorship review to R&D@gstt.nhs.uk **before** you can proceed to electronic HRA submission via IRAS. This is to sign off your application; to ensure that your research is designed and set up in line with all applicable research governance requirements; and to guide you through submission to the relevant regulatory bodies. Please note that confirmation of sponsorship is not approval to start your research, but is the first stage towards obtaining all the approvals you will need. Please follow the flow chart below.

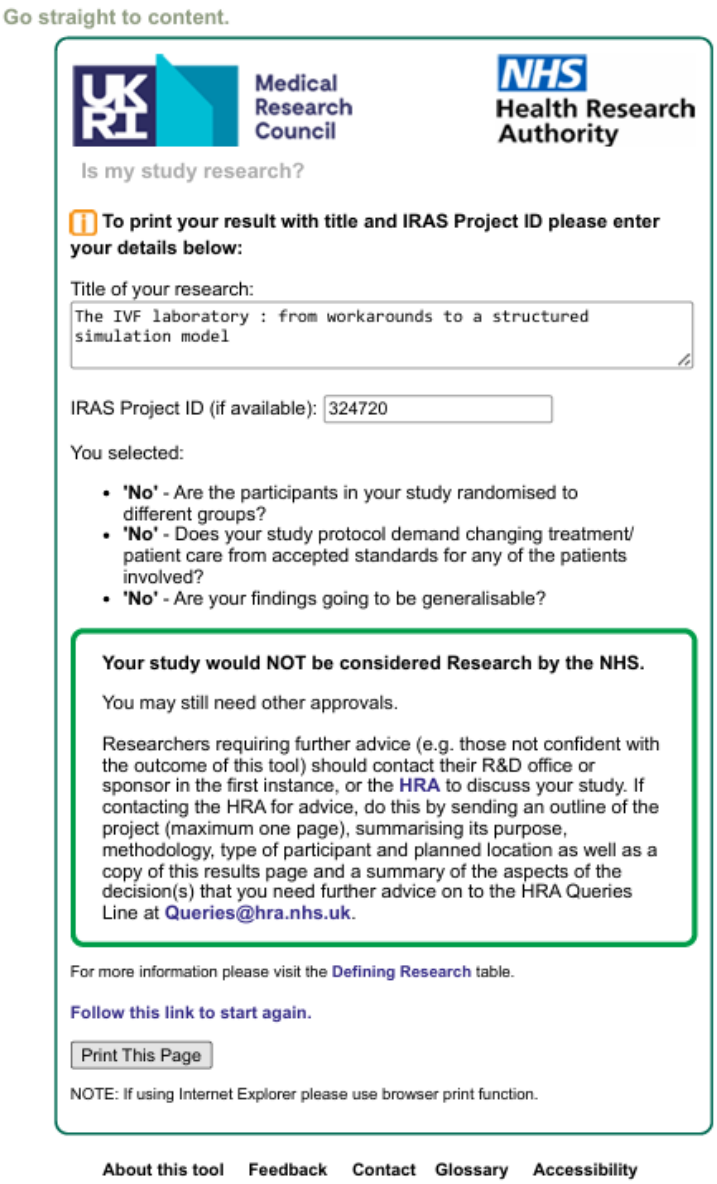
1. Is your project research? Or is it service evaluation or audit?
Please refer to http://www.hra-decisiontools.org.uk/research/ and the 'defining research' document within that page.

2. Set up your project in IRAS
https://www.myresearchproject.org.uk/

- Complete the Project Filter Questions
- The IRAS Form should then be available for completion. Click on 'Navigate' and then 'Project Forms'.
- An IRAS step by step completion guide is available here.

2. Is your project service evaluation or clinical audit? If so, the Trust Quality Improvement and Patient Safety (QIPS) Team will support you.
Email: ClinicalAudit1@gstt.nhs.uk
Tel: 02071881346
There is an online Trust registration process available through this link.

Appendix 8. *HRA outcome*



Go straight to content.

Medical Research Council

NHS Health Research Authority

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

The IVF laboratory : from workarounds to a structured simulation model

IRAS Project ID (if available): 324720

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the HRA to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at Queries@hra.nhs.uk.

For more information please visit the Defining Research table.

Follow this link to start again.

Print This Page

NOTE: If using Internet Explorer please use browser print function.

About this tool Feedback Contact Glossary Accessibility

Appendix 9. *GSTT Audit application*

Service Evaluation 16169 Printed By: AKaffel on 21/05/2024	
Project Number:	**16169**
Project Tile:	The IVF laboratory : from coping and workarounds to a structured and controlled model for lab processes to adhere to physiological time constraints using computer simulation.
Proposer:	Aida Kaffel
Added Proposers:	Jon Taylor
Tel No/Mob No:	07966703763
Email Address:	Aida.Kaffel@gstt.nhs.uk
Bleep:	
Lead Specialty:	Assisted Conception
Specialty Lead:	
Responsible Person:	Aida Kaffel

Reason for carrying out this project:	
Very frequent service	
Of local concern	
Identified as a problem	
Quality Improvement	
Measure compliance with local guideline	
Note:	Time spent carrying out procedures and timing in relation with oocyte retrieval are closely linked to the processâ€™s performance (ICSI, cryopreservation, embryo survival) and to molecular aging or changes in the oocytes and embryos as gametes and embryos are exposed to ambient conditions where temperature, pH and light can fluctuate. The novelty of this project is exploring new ways of improving work patterns and outcomes to match to physiological timelines as well as staffing with better embryo culture conditions and outcomes for patients undergoing IVF treatment.

Objective(s) of this project: What do you intend to achieve by carrying out this activity?

The aim of the investigation is to use a manufactural concept : 1. To design a simulation model for IVF lab processes by using a discrete event simulation software (Simul8Â©) that has been used in other healthcare settings (Mohiuddin et al., 2017) and allow a visual/dynamic understanding of the IVF laboratory. 2. To use the simulation model that integrates multiple data factors to: â€¢ Identify bottlenecks and process traffic issues. â€¢ Identify number of procedures that could be done with the available premises and staff within the desired timeframe (eg number of egg collections, number of embryo thaws) â€¢ Identify deviations from recommended process timings that are crucial in IVF. â€¢ Test â€œwhat ifâ€• scenarios to be able to plan pro-actively. â€¢ Improve efficiency (increase capacity, reduce waiting times), lab flow, minimise bottlenecks, enhance service quality and clinical outcomes.

Stakeholders and their involvement (maximum of 5). List the individuals or types of staff who will be involved in or affected by this activity and indicate how they will be involved

Stakeholder	Design	Data Source	Review	Plan Action	Other
Embryologist	✔	✔	✔	✔	✘
service manager	✘	✘	✔	✔	✘
patients	✘	✔	✘	✘	✘

Will the project involve Patients/Carers? e.g. advise on data collection/planning action

Yes

Please describe how they will be involved:

Data will be collected from RI witness and Babysentry for procedure timings and number of procedures carried out Outcomes (fertilisation rates and pregnancy rates will be collected from Babysentry) All data won't be identifying patients but rather amalgamated data
Population (Patients, Service Users, Events or Situations):
Include:
Patients who had egg collections, frozen embryo transfers, semen analysis, semen freeze at Guy's ACU All staff present within the embryology team was accounted for : embryologists and reproductive science practitioners
Exclude:
Export and import procedures of gametes and embryos and all admin procedures relating to this
Additional data to be collected for information only (specify):
number of incidents reported in the lab during the same time period
Population or Sample
Number of Cases:
Over 1000
Date From:
01/01/2022
Date To:
31/07/2024
How will they be selected:
All patients having treatment at ACU and registered on babysentry and RI witness during the retrospective analysis (2022) All patients having treatments in ACU during the proposal of QI measures
Data collection strategy:
Retrospective
Prospective
Data sources to be used:
Patient or service user records
Other
Please specify other data sources to be used:
staff availability from the staff Annual leave spreadsheet
Identifying problems and finding causes: Describe how you plan to address any problems revealed by the audit to find the root causes so that effective action can be taken

Standard	Evidence	Exceptions	Definitions
<80%	Process measure = Staff utilisation (embryologist and practitioners)	no admin time would be included	Number of hours staff utilised for procedures/Number of hours staff employed
65-70%	Outcome measure: fertilisation rate with the staff available and timing dedicated	separate IVF and ICSI	fertilisation = 2PN/ number of eggs collected
IC in literature	Outcome measure : egg Stripping timing when bottlenecks identified	none	from RI witness: time spent to do stripping and time from egg collection to stripping

IC in literature	Outcome measure: ICSI timing : time spent and time from egg collection to ICSI	none	Time from RI witness : egg collection to ICSI and time spent doing ICSI
1 per 200 per year	Process measure: Number of fresh procedures per embryologist available	weekends	ratio: Number of embryologist available/number of egg collections carried out per time period
	Process measures : Outcome measure: Resources utilisation	preparation time is not accounted for	Number of hours resource is used(equipment)/number of hours resource available
IC vs real data	Process measure: simulation vs real life data	admin tasks	Number of procedures carried out in 2022: simulation vs real life data to confirm if the model created is validated

Time plan	
Data collected by	31/05/2024
Findings reviewed by	30/06/2024
Report submitted by	31/10/2024
Identifying patients or carers	
Data collected WILL NOT include:	
Name	✔
Date of birth	✔
Hospital or patient number	✔
Other easily linked identifiers	✔
Identifying Healthcare or other professionals	
Data collected WILL NOT include:	
Names	✔
Professional registration or PIN numbers	✔
Other easily linked identifiers	✔
Reports or representations will not include any of the above (including initials)	✔
Storing information	
Code sheets or lists to protect identity will be used	✔
Code sheet will be kept securely and separately from main data	✔
Data (in any format) will be stored in a secure place	✔
Patient records or any other identifiable information will not be removed from GSTT site	✔
No patient identifiable data will be kept on laptops, memory stick or other removable storage device	✔
NO patient identifiable information will be emailed to a non NHS email account (e.g. Hotmail, Yahoo, Google etc.)	✔
Data will be accessed by the auditing team (or those specifically authorised by the lead clinician) only	✔

Password protected databases or spreadsheets will be used	✔
Data sheets (electronic or hard copy) will be kept and disposed of in accordance with Trust Information Governance policy	✔
Is Audit on forward plan	
No	
Specialty Lead Comments	
approving for "SL" as unclear who current lead is for ACU	
Directorate Lead Comments	
Is Azar really the responsible person? This should be the person responsible for completion of the audit cycle, which is either the lead proposer or supervisor/sponsor	
It says the data sample will be 01/01/2022 to 31/12/2022, but also says it will be both retrospective and prospective. Surely this is retrospective only?	
Please state in the wording on the first page that this is a quality improvement project (it is not an audit)	
The information governance checklist is completed incorrectly. You have stated that you are anonymising data. Therefore you need to put a tick (i.e. the statement is correct) in these boxes. Otherwise, if professional or patient identifiable information is used, you will need to explained how you will be obtaining consent to do this.	
Please can you email the supporting documents, as the system has a glitch and does not allow me to open any attachments.	
When you are analysing your findings, please present these measures in terms of standard QI methodology, e.g. outcome measures, process measures and balancing measures	
CG Comments	
No comments	

Appendix 10. *Evidence of Section HSST completion : FRCPath part 1 & 2 examinations*

The Royal College of Pathologists

By these letters make it known that

Aida Kaffel

having undertaken the required training and
after having passed the Part One examination in

Reproductive Science

has been awarded

Diplomateship of
The Royal College of Pathologists

In witness whereof the Seal of the College and the signatures of the proper Officers have been affixed this thirteenth day of February 2020

LONDON

President *Registrar* *Member of Council*

The Royal College of Pathologists
Pathology: the science behind the cure

College Reference Number: 20010797
Candidate Number: 367

22nd November 2024

Dear Mrs Kaffel

FRCPath Part 2 Practical and Oral Examination in Reproductive Science– Autumn 2024

I am pleased to inform you that you have satisfied the Examiners in the Part 2 Examination.

However, as you are aware, you are not yet eligible to become a Fellow of The Royal College of Pathologists as your Part 2 Project has not yet been approved.

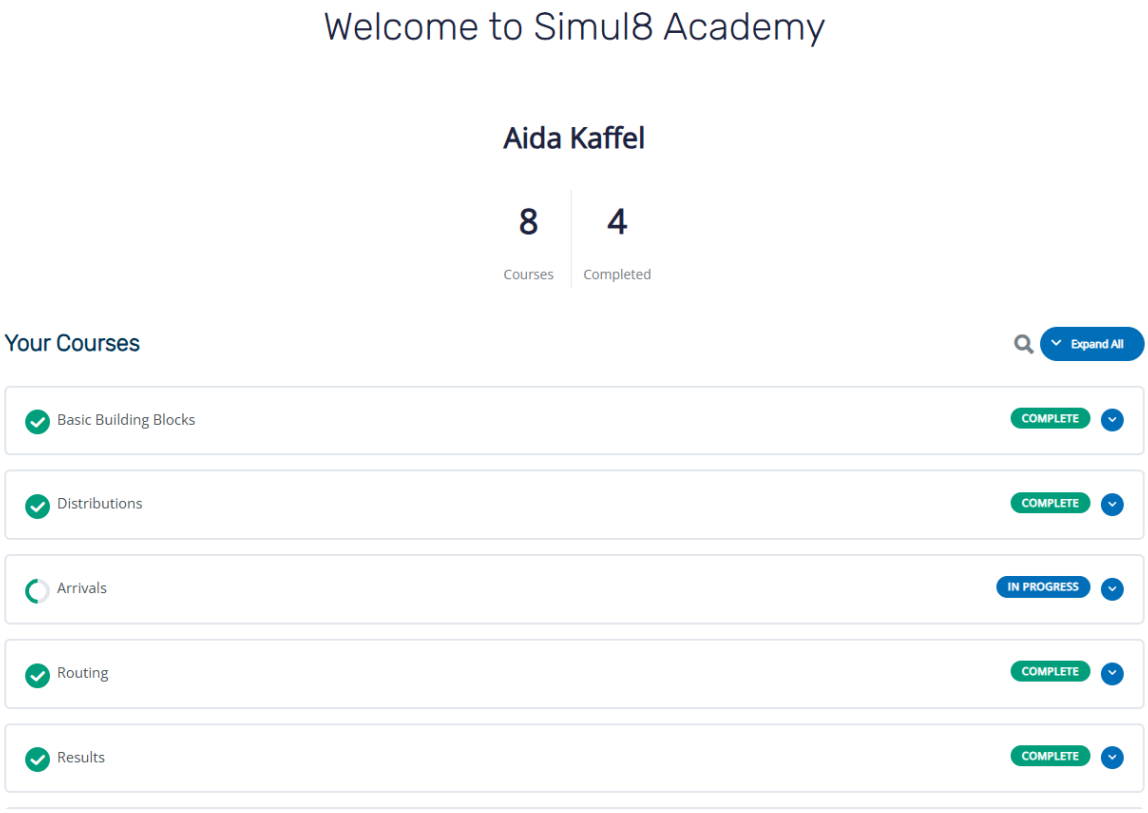
We look forward to receiving the project in due course. If you have any queries about your project, please contact exams@rcpath.org.

Congratulations on your success in this examination.

Yours sincerely

Professor Nicki Cohen
Clinical Director of Examinations

***Appendix 11**. Simul8© academy training course*



***Appendix 12**. Financial implications of the Simulation modelling project for GSTT-ACU-IVF*

The costs associated with the simulation project encompass various components, including software, hardware, and time investment:

Software Costs: This includes the purchase of software licenses as well as ongoing maintenance fees.

Simulation Software Training: Costs for training sessions on the use of the simulation software.

Training in Simulation Modelling: Expenses for specialized training in simulation modelling techniques.

The software, training in simulation and maintenance were covered by HSST budget from HEE to cover 5035£.**Error! Not a valid bookmark self-reference.**

Hardware Costs: Expenses related to the purchase and maintenance of necessary hardware. This was covered by access to GSTT computer that was part of Aida Kaffel contract of employment.

Personal Time: This encompasses the time spent on modelling, data collection, experimentation, project management, and attending meetings. (one study day a week as per HSST training contract)

Consultancy Support: Fees for consultancy services provided by Simul8. (14996£)

Additional Costs: Extra expenses incurred for supplementary scenarios requested from the software company, Simul8. (6370£ **Error! Not a valid bookmark self-reference.**) All expenses incurred were covered by the HSST annual budget to trainees 13000£ per year and the personal time needed was covered by the study time given through the HSST training contract between the employee (AK) and the employer (GSTT and the Evewell).

***Appendix 13**. GSTT Simul8 licence, model assistance and scenarios*

SIMUL8 CORPORATION

Client Name	Aida Kaffel
Organisation	GSST
Date	10/08/2021
Issued by	Karen Walker
Quote Number	GSST_KW100821
SIMUL8 Tel:	0141 552 6888
SIMUL8 Fax:	0141 553 2331

Quotation

Quantity	Item Description	
1	Simul8 Professional Perpetual license 2021	£2,995
	Includes Simul8 software for desktop & web	
1	Annual Maintenance	£540
	Includes online training, priority support & annual upgrade	
10	Online coaching with a simulation expert (hours)	£1,500
Total		**£5,035**

Comments:

1 Quote valid until 31/08/21
2 System requirements can be found at www.SIMUL8.com/products/system_req
3 Online Coaching is delivered remotely by our consultants using telephone, email and web-presentation technology
4 Quotation Currency £GBP
5 Payment terms are 30 days and payments can be made via Credit Card or Bank Transfer only.
6 Please include Tax Exempt Certificate if applicable with the order
7 Training/coaching dates will only be confirmed on receipt of a purchase order or payment.
8 All purchases of SIMUL8 Services, including Training, Online Coaching and Coaching, will expire 1 year after purchase
9 Purchase of Annual Maintenance entitles the user to upgrades and priority feature support issued from date of purchase for 1 year
10 All taxes, levies, rates, charges, duties and the like shall be paid by the purchaser. The above prices are not inclusive of any such payments
11 Service terms can be found at www.SIMUL8.com/service_terms

Simul8 Corporation
Clockwise Offices
77 Renfrew Street
Glasgow, G2 3BZ
Tel: +44 141 552 6888
info@SIMUL8.com www.SIMUL8.com

Client Name	Aida Kaffel
Organization	GSTT
Date	28/11/2022
Issued by	Tom Stephenson
Proposal Numbe	GSTT_TS150722_JSB
SIMUL8 Tel:	0141 552 6888
SIMUL8 Fax:	0141 553 2331

Proposal

IVF Lab Pathway
Simulation project delivered remotely

Objective
To allow understanding of how to maximise throughput in the IVF laboratory process at Guys and St Thomas NHS Foundation Trust without compromising service levels that can maximise fertilisation and pregnancy rates. The simulation will add intelligence to the configuration of available resources to maximise efficiency, or indicate areas where capacity needs to increase to prevent bottlenecks.

Deliverables
1) A Simul8 model with a user interface that allows quick changing of scenarios, with a results output that can be easily interpreted
2) Training and handover to be able to run the simulation

Simul8 model inputs
1) Appointments per day, demand for appointments and waiting list size
2) Timing of all processes
3) Staff numbers
4) Lab opening times and shifts when different processes and workers run
5) Capacity of different rooms and processes e.g. slots available to freeze
6) Effectiveness expectation of process including when service targets are not met

Simul8 model outputs
1) Appointments delivered and demand
2) Freezer Stock
3) Successful/unsuccessful outcomes

Delivery
It is expected that this project can be completed within a 3 week time period if all data is immediately available. We expect there could be discussion and information gathering requirements which extends this timeline.

SIMUL8 Corporation
Clockwise Offices
77 Renfrew Street
Glasgow, G2 3BZ

Tel:(+44) 141 552 6888
info@SIMUL8.com www.SIMUL8.com

Costs Quantity	Item Description	
1	Simulation model build	£14,996
	Funding to be split into 2 orders as requested 50% of overall cost - second installment	-£7,498
Total		**£7,498**

Comments:

1 Quote valid for 30 days
2 Quotation Currency £GBP
3 Commencement of project will begin upon receipt of contract and / or purchase order. Payment terms are on a single invoice in advance, single payment basis
4 Payment can be made via Credit Card or Bank Transfer only
5 Please include Tax Exempt Certificate if applicable with the order
6 All taxes, levies, rates, charges, duties and the like shall be paid by the purchaser. The above prices are not inclusive of any such payments
7 Purchase of Annual Maintenance entitles the user to upgrades and priority feature support issued from date of purchase for 1 year
8 Online Coaching is delivered remotely by our consultants using telephone, email and web-presentation technology
9 Training/coaching dates will only be confirmed on receipt of a purchase order or payment
10 All purchases of SIMUL8 Services, including Training, Online Coaching and Coaching, will expire 1 year after purchase
11 System requirements can be found at www.SIMUL8.com/products/system_req
12 Service terms can be found at www.SIMUL8.com/service_terms

SIMUL8 CORPORATION

Client Name	Aida Kaffel
Organization	GSTT
Date	08/08/2024
Issued by	Corinne Freeman Neish
Proposal Number	GSTT_CFN01082024
SIMUL8 Tel:	0141 552 6888
SIMUL8 Fax:	0141 553 2331

Proposal

Adding Scenarios to Existing IVF Lab Simulation £ 5,375

Delivered remotely
This proposal is in relation to current project delivered under Proposal number:
GSTT_TS150722_JSB

Objective

Through the delivery of the current IVF Lab pathway project, the constructed simulation provides a reliable baseline for validating the current performance of the IVF Laboratory. This proposal outlines the necessary modifications to the baseline simulation to conduct further scenario testing. The goal is to assess available resources (shifts & overtime), maximize efficiency, and identify areas where capacity needs to increase to prevent bottlenecks.

Scenarios that can be tested within the current simulation

1) Changing to a 7-day arrivals schedule for egg collections and frozen embryo transfers
2) Increase and decrease staff numbers and test effects
3) Add or reduce dewar capacity
4) Change proportions of egg freezing and IVF
5) Change proportions of ICSI and IVF/ egg freezing
6) Carry out whole weeks of PGD
7) Change timing proportions
8) Change semen analysis distributions
9) Change time spent to carry out procedures

Scenarios that require additional time for modification and testing

1) Allowing overtime for both practitioners and embryologists
2) Adding an embryoviewer
3) Changing staff rota to have different shifts

Assumptions

1) All Simulation input data to be provided by GSTT
2) Overtime for practioners and embrylogists will be set to extra time up to 3 hours each day within the working week (Monday-Friday)
3) All equipment is available during the set overtime duration
4) No optimisation algorthims will be developed as part of this phase of work

Results

No additional results will be collected from the scenarios, but the existing results sheets (Process Metrics and Queueing Results) will be updated to allow comparison of KPIs between runs (staff and equipment utilization, dewars results, arrivals and processed completed, queues' waiting times). This will help identify areas where additional capacity may be needed to meet physiological time constraints.

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Tel: 0141 552 6888
info@SIMUL8.com www.SIMUL8.com

Deliverables

1) Simul8 will implement the 3 scenarios that require additional time for modification and testing
2) Simul8 will provide a handover document to key user Aida Kaffel, detailing how to run the scenarios that can be tested within the current simulation, as well as the additional scenarios that require modification and testing.

Software Renewal benefits

7 Day Share - Share your Simulation for 7 days with Stakeholders (Can be renewed after 7 days)

Share function direct from Software with no requirement for additional viewer licences

Simul8 2024 Upgrade - Internal Spreadsheets Improvement

Costs

Quantity	Item Description		
1	Scenarios that require additional time for modification and testing	£	5,375
1	Renewal of Simul8 Annual Subscription per user per year	£	995
Total		**£**	**6,370**

Comments:

1 Quote valid for 30 days
2 Quotation Currency £GBP
3 Commencement of project will begin upon receipt of contract and / or purchase order. Payment
4 Payment can be made via Credit Card or Bank Transfer only
5 All taxes, levies, rates, charges, duties and the like shall be paid by the purchaser.
The above prices are not inclusive of any such payments
6 Please include Tax Exempt Certificate if applicable with the order
7 Service terms can be found at www.SIMUL8.com/service_terms
8 All purchases of SIMUL8 Services, including Training, Online Coaching and Coaching, will expire 1 year after purchase

Appendix 14 *. GSTT NDA with Simul8©*

SIMUL8 CORPORATION

NON DISCLOSURE AGREEMENT

This Agreement is made the

Between:

1) SIMUL8 Corporation (Company Number SC147795) whose registered office is Clockwise Offices, 77 Renfrew Street, Glasgow, G2 3BZ, UK.

And:

2) Guy's ACU_____ (Company Number _____), whose registered office is Guy's Hospital NHS trust_____

WHEREAS:

The "Disclosing Party" shall mean either party disclosing Confidential Information.

The "Recipient Party" shall mean either party receiving Confidential Information.

The parties are willing to disclose to and receive from each other proprietary or confidential information under suitable terms and conditions as to confidentiality set out herein, and these terms and conditions are acceptable to both parties.

AGREEMENT:

1. Confidential Information

For a period of three (3) years from the date hereof, any Confidential Information given by the Disclosing party will be kept in confidence by the Receiving Party and will not be disclosed to anyone without the Disclosing Party's prior written consent, other than to its employees who need to know the Confidential Information for the purposes for which it was disclosed. The Receiving Party will not use the Confidential Information, or permit others to use it, for any purpose other than that for which it was disclosed. Also, the Receiving Party will notify its employees of its obligations and ensure that they understand and abide by this agreement. For purposes of this Agreement, "Confidential Information" means any information that the Disclosing Party supplies to the Receiving Party about the Disclosing Party's computer programs, research, technology, existing or future products, sales processes, customers, business plans, financial information and other proprietary or confidential information which is marked or otherwise identified as confidential or proprietary at or near the time of disclosure.

2. Authorised Disclosure

If the Disclosing Party authorises the Receiving Party to disclose its Confidential Information to someone other than the Receiving Party's own employees, the Receiving Party will take all necessary action to ensure that the Confidential Information is kept confidential, including, but not limited to, requiring that the recipient agree to be bound by this agreement. This includes disclosures that are made by the Receiving Party to consultants, agents and to any parent or affiliate company.

3. Exceptions

Confidential Information will not include and this Agreement will not apply to: (a) information that was in the Receiving Party's lawful possession before it was disclosed, without confidentiality restrictions; (b) information that the Receiving Party obtains

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101 Federal Street, Suite 1900
Boston, MA 02110
T 1-800-547-6024 (F 1-800-547-6389)
Clockwise Offices, 77 Renfrew Street, Glasgow
G2 3BZ, UK
T +44 141 552 6888 (F +44 141 553 2331)
info@SIMUL8.com http://www.SIMUL8.com

from a third party on an unrestricted basis without breach of this agreement or breach of any other obligation of confidentiality by the Receiving Party or the third party; (c) information independently developed by the Receiving Party without any use of Confidential Information; or (d) information which the Receiving Party is required to disclose by any court order or government action, provided that the Receiving Party gives the Disclosing Party advance notice of such order of action and cooperates with the Disclosing Party to limit the scope of the required disclosure.

4. No License

All Confidential Information will remain the Disclosing Party's property. This agreement does not grant the Receiving Party an express or implied license, or an option on a license, under or to any patent, copyright, proprietary right, products or Confidential Information of the Disclosing Party.

5. Return of Confidential Information

When either party requests and, in any event, when the business dealings between the parties that required the disclosure are concluded, the Receiving Party will return promptly to the Disclosing Party all tangible material relating to Confidential Information. This includes material the Disclosing Party supplies as well as material the Receiving Party created.

6. Remedies

Each party in its capacity as a Receiving Party acknowledges that unauthorised disclosure or use of the Confidential Information of the Disclosing Party could cause irreparable harm to the Disclosing Party for which monetary damages may be difficult to ascertain. Accordingly, each party agrees that the Disclosing Party shall have the right, in addition to its other rights and remedies, to seek and obtain injunctive relief from breaches of this Agreement by the Receiving Party. The prevailing party in any action to enforce this Agreement shall be entitled to recover its reasonable attorneys' fees, court costs and expenses incurred in such action.

7. Miscellaneous

This Agreement is the entire agreement between the parties relating to Confidential Information. Neither party may assign all or any part of this Agreement. Subject to this restriction, this Agreement is binding on and for the benefit of each party and their respective successors and assigns. This Agreement will survive and remain in full force and effect even if the parties end the business dealings giving rise to it. This Agreement shall be governed by European law without reference to its choice of law principles.

SIMUL8 Corporation

101 Federal Street, Suite 1900
Boston, MA 02110
T 1-800-547-6024 (F 1-800-547-6389)

Clockwise Offices, 77 Renfrew Street, Glasgow
G2 3BZ, UK
T +44 141 552 6888 (F +44 141 553 2331)

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Company Name: Guy's and St Thomas ACU

Sign: [signature]

Name: Aida Kaffel

Title: Senior Clinical embryologist

SIMUL8 Corporation Ltd.

Sign: [signature]

Name: Laura Reid

Title: CEO

Appendix 15. *IVF lab simulation model user guide*

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IVF Lab Simulation Model

US
101 Federal Street, Suite 1900
Boston / MA / 02110
t: (800) 547 6924 / f: (800) 547 6389

Europe
Clockwise Offices, 77 Renfrew Street
Glasgow / UK / G2 3BZ
t: +44 (0)141 552 6888 / f: +44 (0)141 553 2331

1

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Table of Contents

2

***Appendix 16**. MMU Research integrity certificate*

Appendix 17. *The context of the C2 research project within the wider context*

Doctor of Clinical Science (DClinSci) - Programme overview (Details taken from MMU Doctor of Clinical Science Network handbook 2024-2025)

Programme context

The HSST is a five-year, practice-based education and training programme supported by an underpinning part-time professional doctorate and, where appropriate, external body qualifications. All HSST curricula were developed by national working groups, including input from academia, practicing healthcare scientists and where appropriate, the Medical Royal Colleges. Curricula are quality assured, owned and accredited by the NSHCS. As such, Manchester Met has little control over curricular content, however the mode of delivery is flexible within the overall curricular framework provided by the NSHCS, which allows for individual trainees to take control and lead their own learning journey. All published curricula, as approved by the NSHCS, share a common structure:

- **Section A:** Leadership and Professional Development (120 credits)
- **Section B:** Specialist Scientific and Clinical Programme (150 credits)
- **Section C:** Research, Development and Innovation (270 Credits)

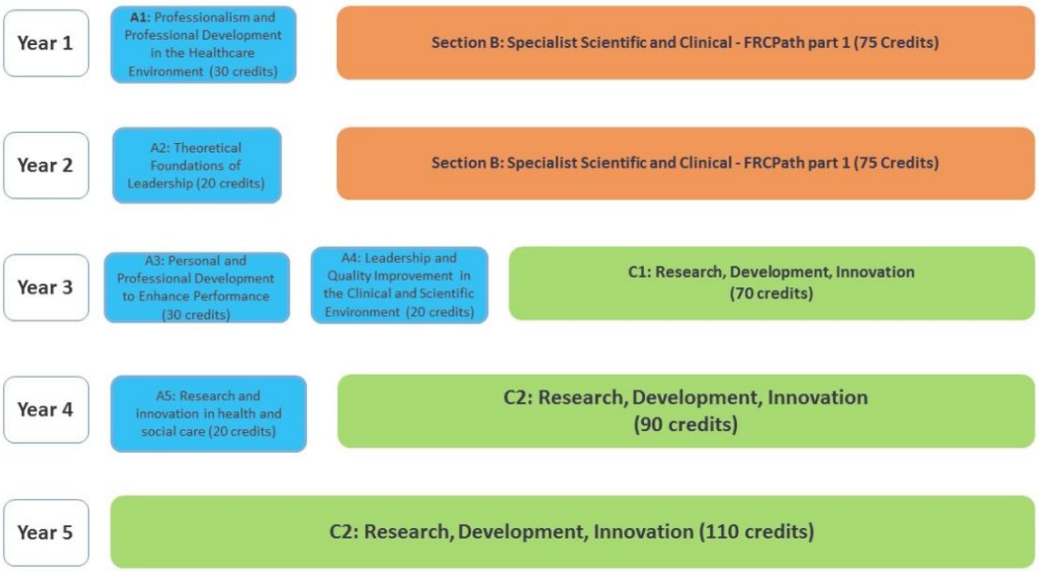
The purpose of these professional doctorates is to formalise and facilitate the learning of Clinical Scientists in HSST as they:

- Create and interpret new knowledge, through original research and scholarship, requiring advanced academic enquiry.
- Systematically acquire and apply a substantial body of scientific and clinical knowledge at the forefront of their specialism and embrace the future scientific and technological advances within the field.
- Systematically acquire, develop and apply the qualities and transferable skills necessary for employment as a Consultant Clinical Scientist (or equivalent), requiring the exercise of personal responsibility and taking largely autonomous initiative in complex and unpredictable situations.
- Develop the knowledge, skills, experience, behaviours and attitudes required of a clinical leader in an evolving and rapidly developing health and life sciences sector.

A key purpose of these degrees is to facilitate the opportunities for learning by those undertaking HSST by providing a structure within which they can obtain underpinning knowledge, skills and learning to support their progression through the programme. The programme you are enrolled upon is run through the Department of Life Sciences and administered through the Manchester Met graduate school, with overarching support from MAHSE.

All specialisms within the HSST cover higher scientific skills and knowledge, as well as clinical competency. Throughout the programme, trainees are required to innovate/improve service delivery, patient safety, care, outreach/patient and public involvement & engagement and quality management. The programme delivers a blend of personal and professional development, spanning leadership & management, teaching, values, attitudes and behaviours as appropriate for higher professional practice in the NHS. There is some flexibility within the programme and it is encouraged that as your studies progress, you work with the team here at Manchester Met to make the programme bespoke to your needs, which we will facilitate as much as possible.

The Doctorate in Clinical Science (DClinSci) is a multi-year, part-time programme. Your final thesis submission date is 30 September, five years after you started (barring any periods of interruption from your studies or extensions). The programme is 540 credits on the DClinSci pathway, or 370 credits on the Innovation Project pathway (i.e. for Trainees using their previous PhD for equivalence who are not completing the full research project as part of their programme of study).



A units (blue) are coordinated by The University of Manchester. FRCPath qualification is used for equivalence to section B (orange). The research, development and innovation units are coordinated at Manchester Met by Dr Llwyd Orton. Manchester Met unit codes are shown in superscript next to the associated unit (e.g. 6ACPXXXX). Some trainees may opt to take the A units over a different timescale to balance workload related to the RCPath exams/assessments for their specialism.

Appendix 18: *Evidence of HSST Section A Conpletion, University of Manchester.*

The University of Manchester
Alliance Manchester Business School

PGDip Leadership & Management in the Healthcare Sciences
Unit marks ratified by Board of Examiners, November 2022

Trainee name: Aida Kaffel

Student ID: 10428693

Award: PG Credits

Unit	Unit Title	Mark	Credits
BMAN73511	Unit A1 Professionalism and Professional Development in the Healthcare Environment	63% **Pass**	**30**
BMAN73522	Unit A2 Theoretical Foundations of Leadership	51% **Pass**	**20**
BMAN73531	Unit A3 Personal and Professional Development to Enhance Performance	53% **Pass**	**30**
BMAN73542	Unit A4 Leadership and Quality Improvement in the Clinical and Scientific Environment	62% **Pass**	**20**
BMAN73550	Unit A5 Research and Innovation in Health and Social Care	50R **Pass**	**20**
			120 / 120

Appendix 19: Royal College of Pathologists email approval for C1

Hi Aida,

I'm just contacting you to inform you that the RCPath have contacted us to say they have approved your DClinSci C1 Full Project Porposal.

Many congratulations on this, you should by now have received your feedback on the proposal and your Lay Presentation and be proceeding with your research project as part of the C2 unit Please do let me know if this isn't the case!

If you have any questions, please do get back in touch and let me know.

Best wishes,
Callum

Guy's and St Thomas' NHS Foundation Trust

Vitrification of Oocytes using Irvine Method

Risk Review

Risks specific to this procedure are as follows:

R.1 Cryopreservation of oocytes from viral positive patients, risking cross contamination of other patient samples

R.2 Vitrified oocytes on straws held temporarily in Dilvac of liquid nitrogen are not collected from the pass-through hatch and transferred to final storage location in dewar

R.3 There are no straws / media available for the vitrification

R.4 The oocytes are vitrified outside of the 2 hour optimal window post egg collection

R.5 There is not an appropriately trained embryologist rostered for the procedure

The control measures to minimise these risks are:

C.1 For R1; oocytes cryopreservation section

C.2 For R1; See L-RISK-D8: Hep B Embryo Storage

C.3 For R 2; Dilvac is not placed in pass-through hatch until a colleague is waiting to collect it in the Freeze Room

C.4 For R3; weekly traceability/stock check will minimise this risk. The contingency is to contact other local IVF units as per ACU BCP.

C.5 For R4; although within 2 hours is ideal we have expert advice (Laura Rienzi) that this is not critical to the outcome

C.6 For R5; we do not vitrify oocytes every day so BBS should be checked for oocyte vitrification cases and an embryologist rostered for the procedure

Oocyte cryopreservation

MII oocytes are cryopreserved by vitrification with up to 3 oocytes per straws with consideration for allowing split location of fertility preservation patients. Oocytes for vitrification should be stripped and vitrified within 38-39hrs post hCG (approximately 2 hours post Egg Collection).

Work in an IVF Witness workstation without a heated stage/ on an 'Ambiplate' throughout.

Preparation

Check the Egg Collection laboratory worksheet to confirm HFEA storage and ACU freezing consents are in place. Check that the patient has been screened for HIV, Hepatitis B (surface Ag and core Ab) and C as per HFEA Code of Practice.

Only one patient's oocytes should be vitrified by any one embryologist at a time. Ensure a witness is present to verify identity of oocytes as well as straw labelling / ID.

Oocytes from patients who screen positive for HIV and/or Hepatitis C will not be vitrified as the ACU does not have dedicated storage tanks for this purpose.

Where the patient screens positive for Hepatitis B, oocyte storage is possible but there are additional requirements:

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Intracytoplasmic Sperm Injection (ICSI) Procedure

Risk review

See L-RISK-D9: ICSI

Risks specific to this procedure are as follows:

R.1 The wrong reagents may be used for a procedure resulting in a failed treatment

R.2 Dishes may be incorrectly labelled resulting in gamete mix ups

R.3 Sperm motility could be compromised due to exposure to suboptimal temperatures and pH

R.4 Samples may become microbiologically contaminated

The control measures to minimise these risks are:

C.1 For R1; staff must not rely on using coloured caps to distinguish reagents, as the same colour coding is used for different reagents. Operators must check the written reagent labels at every step to verify correct reagent type before use.

C.2 For R2; Use of RI IVF Witness system, labelling of dishes e.g. step 4 (See L-RISK-D9: ICSI for full risk assessment).

C.3 For R3; use and recording of appropriately buffered media, incubators / heated plate / heated stage at key points throughout

C.4 For R4; step 22 (use of holder and SOP L-MAN-P21 Samples to Microbiology when appropriate)

Purpose

This SOP is to ensure that ACU Embryology staff, equipment and media are correctly prepared in order to perform cumulus dissection (stripping) and intracytoplasmic sperm injection (ICSI) in the approved manner. This acts to ensure the safety and security of personnel and gametes while maintaining conditions that maximise the potential for normal fertilisation of oocytes and subsequent implantation post Embryo Transfer (ET).

Applicability

ICSI is a micromanipulation technique used to inject immobilised, but previously motile, sperm into mature oocytes. ICSI has become the first choice of treatment for patients with severe male factor infertility, where the chances of achieving a pregnancy with routine IVF were considered extremely low or impossible. Ejaculated or even surgically retrieved spermatozoa may be used. ICSI is also the treatment of choice for patients with normal semen parameters who have undergone a previous IVF treatment with low or complete failure of 'normal' fertilisation, egg donation or those patients who present with unexplained infertility and who have failed to conceive for 3 years or more (after discussion with clinician/colleagues) see L-ICSI-P1 ICSI Criteria for more information.

Under the 9th edition of HFEA code of practice it is only permissible to perform ICSI on 'mature oocytes'. Mature oocytes are defined as those that have reached metaphase II in development and are identified by the presence of one polar body. Eggs that are yet to extrude the polar body (metaphase I) are returned to culture for several hours and re-examined for extrusion prior to injection. Eggs remaining at either metaphase I or germinal vesicle stages are not injected.

Personnel Qualifications / Responsibilities

All embryology staff that have been approved by the Consultant Embryologist to perform ICSI.

ICSI PROCEDURE

Timing

Oocytes are routinely injected from 1200hrs on the day of egg collection. Precise timing is dependent on time of oocyte collection, oocyte 'stripping' and status of the oocytes**. Optimal time for ICSI is currently 38-41 hours post hCG[1] [2], with injection ideally occurring within 1 hour of stripping.** If a cohort contains a high proportion of immature oocytes, injection may be delayed but this should always be confirmed with a senior embryologist. There may be cases where all oocytes are immature. The oocytes should be re-checked regularly up to the end of the working day. The consultant embryologist or senior embryologist may decide to continue monitoring beyond the end of the normal day in certain cases. Only when an oocyte has undergone maturation to metaphase II is it injected. Injection of 'aged oocytes' is not permitted under guidelines issued by the HFEA. An oocyte is considered 'aged' when 24 hours have elapsed after collection.

Preparation of injection dishes

- The injection procedure is performed in ICSI dishes.
- These dishes should be made up 0.5-2 hours prior to the ICSI on a cool surface, the lid replaced and then the dish placed in the warming oven/non-gassed MINC until required.

- Prepare dishes using media and oil from the laboratory refrigerator: **Do not use a combination of pre-warmed and cold media / oil.**
- There are a number of dish configurations possible and each operator may have different preferences. All should be prepared with the same considerations in mind.
- Label each dish with the date and time of preparation.

For standard ICSI sperm preparations:

[1] 'The optimal time for intracytoplasmic sperm injection in the human is from 37 to 41 hours after administration of human chorionic gonadotropin' Fertility and Sterility, Vol. 82, No.6, December 2004
[2] Optimal Timing for Oocyte Denudation and Intracytoplasmic Sperm Injection', Obstetrics and Gynecology International, Volume 2012, Article ID 403531

Appendix 22. *Page1-2 GSTT-ACU fertilisation check SOP*

Guy's and St Thomas' NHS Foundation Trust

L-EGG-P2: Fertilisation Checks SOP

Risk Assessment

See L-RISK-D7: Fertilisation Check

Risks specific to this procedure are as follows:

R.1	Early fertilised eggs may not be moved from one culture medium (G-IVF) to another (G-TL) on Day 1 after egg collection
R.2	Following fertilisation check, the patient is not added to the lab white-board for the next step in their treatment
R.3	Culture dishes may be placed in an incubator that is switched off or only heated rather than gassed
R.4	Potentially viable (diploid) embryos are discarded
R.5	Triploid or multi-nucleated zygotes are included in culture and used in treatment.

The control measures to minimise these risks are:

C.1	For R1; Normally fertilised IVF eggs must be moved to an embryoslide containing G-TL.
C.2	For R2; Ensure the patients are added to the white-board, there is a tickbox on the worksheet to prompt this.
C.3	For R3; If an incubator is not fully functional, an out of use sign must be placed on the top
C.4	For R.4; Timelapse culture enables multiple review points for final decision on unclear PN status eggs post ICSI / IVF
C.5	For R.5; The default is to culture all eggs post ICSI, and zygotes identified as '2PN' (cIVF cases) in an Embryoscope if there is sufficient capacity. In some instances, this is not possible due to a high volume of cases. Utilisation of aneuploid embryos is an inherent risk of ART procedures. This is due to asynchronous or non-visible PN. Use of time-lapse; where possible, mitigates this.

Scope and purpose

This procedure describes the tasks that need to be undertaken to perform a fertilisation check within the Embryology Laboratories at Guy's ACU

This SOP can be performed by all appropriately trained staff, however, for pre-registered embryologists, embryology practitioners and medical lab assistants this is under the appropriate supervision.

Responsibility

The Consultant Embryologist is responsible for ensuring the implementation and maintenance of this procedure.

Guy's and St Thomas' NHS Foundation Trust

General information for checking fertilisation

- Before starting fertilisation checks, collect the plastic pockets from D1 tray in the lab, check that all egg collections from previous day are included (minus egg freeze, no
- eggs). Arrange in priority order to ensure prompt check of 2PN freeze cases and also any cases being cultured in MINC incubators. This is to avoid missing PN observations due to Syngamy / PN fade.
- For 2PN freeze cases; move zygotes to an Embryoslide for ES+ culture prior to cryopreservation. Complete PN status confirmation on the Embryo Viewer before proceeding with cryopreservation. If the ES+ are at capacity, complete PN assessment and return the culture dish containing the zygotes to the benchtop incubator.
- 'Cleaning' of oocytes is carried out initially using a 170µm denudation pipette followed by a 140-145µm denudation pipette as necessary. Care should be taken to avoid stress and potential damage for slightly larger than average eggs / zygotes.
- Denuded eggs should be handled using a 170µm pipette.
- Ensure only the minimum volumes of medium are transferred.
- Care must be taken not to catch or 'flick' the end of the denuding pipette when transferring eggs / zygotes from well to well.
- A new pipette must be used for every patient.
- Pipettes should be discarded immediately at the end of the procedure.

Timescale for checking fertilisation

Oocytes should be checked in the morning following egg recovery:

- IVF - 16-20 hours post-insemination.
- ICSI - 14-18 hours after injection as pronuclei may appear earlier. Oocytes cultured in the EmbryoScope can be checked at any point in the morning but the patient call should be before 12pm.

It is important to consider time of insemination or ICSI completion prior to undertaking fertilisation checks. Procedure timings on day of egg collection should also reflect staffing cover and shift start time on the following day.

Checking for fertilisation following ICSI

Following ICSI, the injected oocytes are placed in the Embryoscope and assessed for fertilisation the following day using Embryoviewer software. The only exceptions are scenarios when there is no free location in the ES+ units or eggs were cultured in a microdrop '2PN Dish'. For all routine ICSI cases the eggs are cultured in a pre-equilibrated Embryoslide immediately post injection. PN 'scoring' should be undertaken on Day 1.

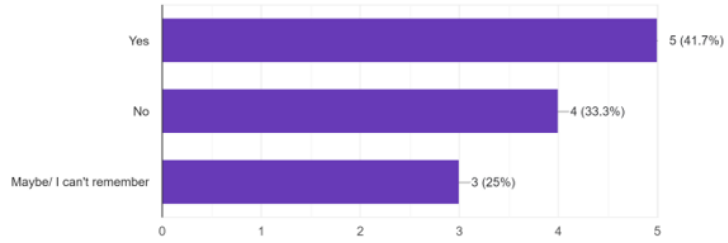
- Remove the plastic folder of worksheets for the first patient whose eggs are to be checked, from the 'Fert Check' tray.
- Select the ICSI case to be checked from 'View Running' tab and open the slide images

Appendix 23. *GSTT Feedback from stakeholder questionnaire*

Responses from Embryologists at ACU 17/09/2024

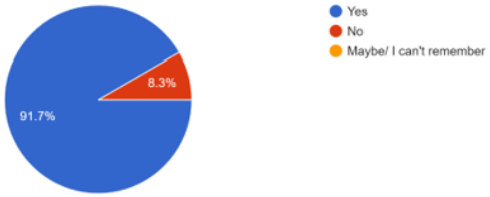
Did you attend the presentation about simulation in IVF 01/12/2022

12 responses



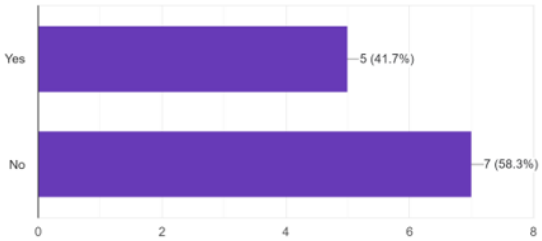
Did you attend the presentation about simulation in IVF on 17th September 2024

12 responses



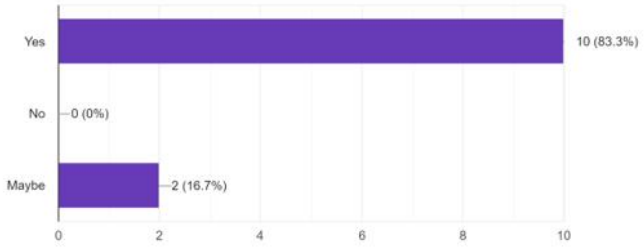
Have you ever heard about simulation modelling before

12 responses



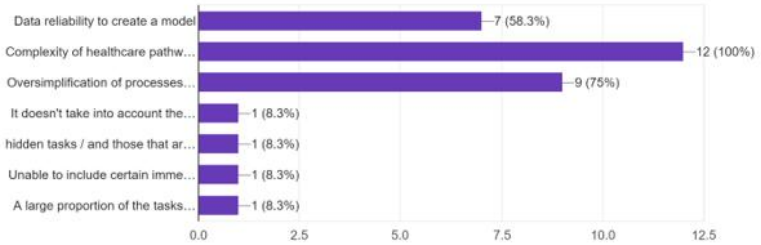
Simulation modelling is a quality improvement technique that works from a real world problem to create its digital twin: It works in industry, in shippi...s, cafes... do you think it has its place in healthcare

12 responses



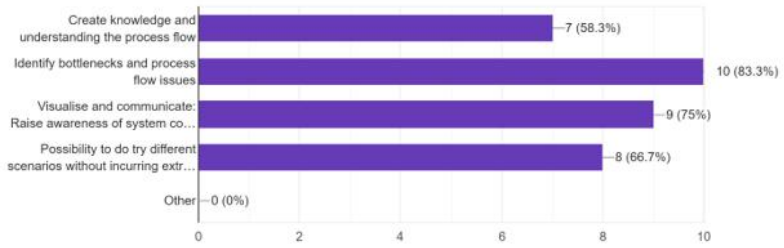
What do you think are the challenges of simulation modelling in healthcare (tick as many as you think are applicable)

12 responses



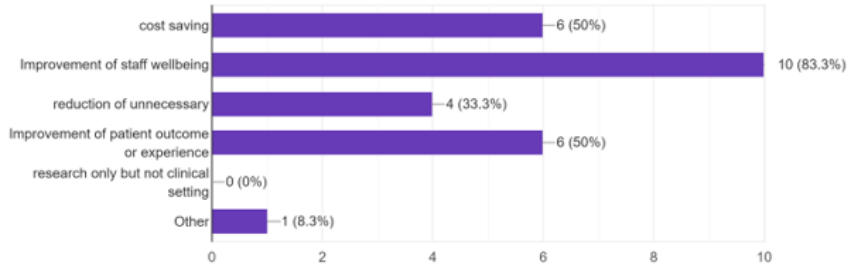
If simulation works efficiently in healthcare and most specifically IVF, I think the advantages include

12 responses



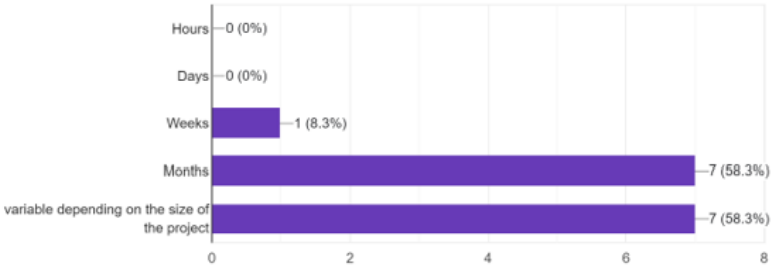
Do you think simulation modelling could be a tool for

12 responses



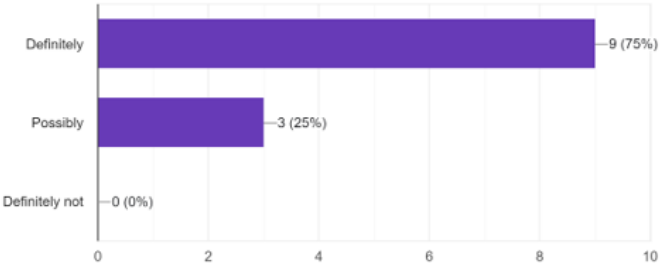
How long do you think it takes to create a simulation model for example for a Gynae clinic workflow

12 responses



After the presentation and hearing about Simulation, this a first trial of Simulation modelling use in IVF, would you like to see this developed further and adjusted for future use.

12 responses



Can you think of an example of a process/pathway in IVF that you would like to see modelled to run different scenarios

12 responses

Egg collection to TE Biopsy

.

No

embryo thaw

I can`t think of anything specific, because I guess it was covered in presentation.

More in depth to see what causes the egg freeze delays. Might help us convince recovery to give men a shorter window to produce before we convert to egg fz if we can prove the wait time to be frozen is not a lab based issue.

Thaws

Yes

PGT pathway from referral to FET

Paper set up, egg collections and thaws, modelled to see the difference between when consents/virology have to be completed before the start of stimulation, compared with the current situation. To see how much time and effort would be saved chasing them. Another idea could be looking at the pathway if all patients have ETs at D5 and feezing is done at D5 onwards rather than 2PN freeze (as other clinics do) to see how much better success rates would be and how much time would be saved.

Time to go through a vec list

Creating a way to manage ET/EC lists to run more smoothly

Do you have further comments or feedback 12 responses

Brilliant presentation.

.

Really good starting point, it would be good to see it in use clinically

Might work better for laboratory roles that do not involve so much admin/patient contact

None

Would love to have heard more about the different simulations that have been run and their impacts. Obviously a time constraint but the whole presentation was very interesting!

It was a great presentation Aida, and you really showcased all your hard work!

Congratulations!

It's something new I learned. Thank you

AI and simulation have to part of an efficient and forward thinking healthcare system

It would be great to try and quantify the time spent on processes not on Ri witness, such as phone calls to patients and lab/paper set up. Since these are the things that are most time consuming. Maybe even as a smaller project just looking at one of them and seeing how things could be streamlined.

No

No, I think it's a really interesting concept but obviously it's such a complex process that it's very hard to quantify to make the model as accurate as possible

Appendix 24*. GSTT embryology team stress survey 2020 – unpublished*

Stress Survey Report
5th March 2020

During the week of 2nd March, I conducted a stress survey, provided by the Federation of Clinical Scientists. I am not aware of any policy on workplace stress, nor any audit or risk assessment that has been carried out. In the last 6 months, 3 members of embryology staff have been signed off work with work-related anxiety/depression, all of whom were referred to Occupational Health.

I sent 8 surveys to all current, permanent members of staff in the Embryology team at Guy's ACU, with a response rate of

5/6 respondents said they felt stressed by their work, and that this level of stress was unacceptable. 4/6 felt this was causing them harm. One of these 6 is a new, junior member of staff.

Causes of stress
5/6 felt that the demands of the job (too much work, insufficient time, not enough rest breaks) contributed to the stress.
4/6 named lack of control, relationships at work, change, working environment and lack of learning opportunities as further contributors.

Individual comments include:
"I have previously been signed off for 2 weeks by my GP for work-related stress, and I currently have problems sleeping due to work-related anxiety"

"pressures at work have lead to problems like indigestion, feelings of deep anxiety, disturbed sleep and a fear to take a day off sick as I would feel like I am deserting my colleagues"

"We work in a very loud environment all day (79dB)"

"Our team of professional Clinical Scientists stand accused of not understanding the issues faced by other teams when we raise our concerns regarding patient safety and our own mental wellbeing"

"When the Speak up Guardian promised our team support (emotional or otherwise) at a meeting she had called, I was disappointed when it did not materialise, both for me and my colleagues. We pull together as a team, but this sustained level of pressure is breaking us"

"I feel set up to fail"

"We have unrealistic deadlines compared to staff numbers - when we ask about it we are made to feel uncomfortable"

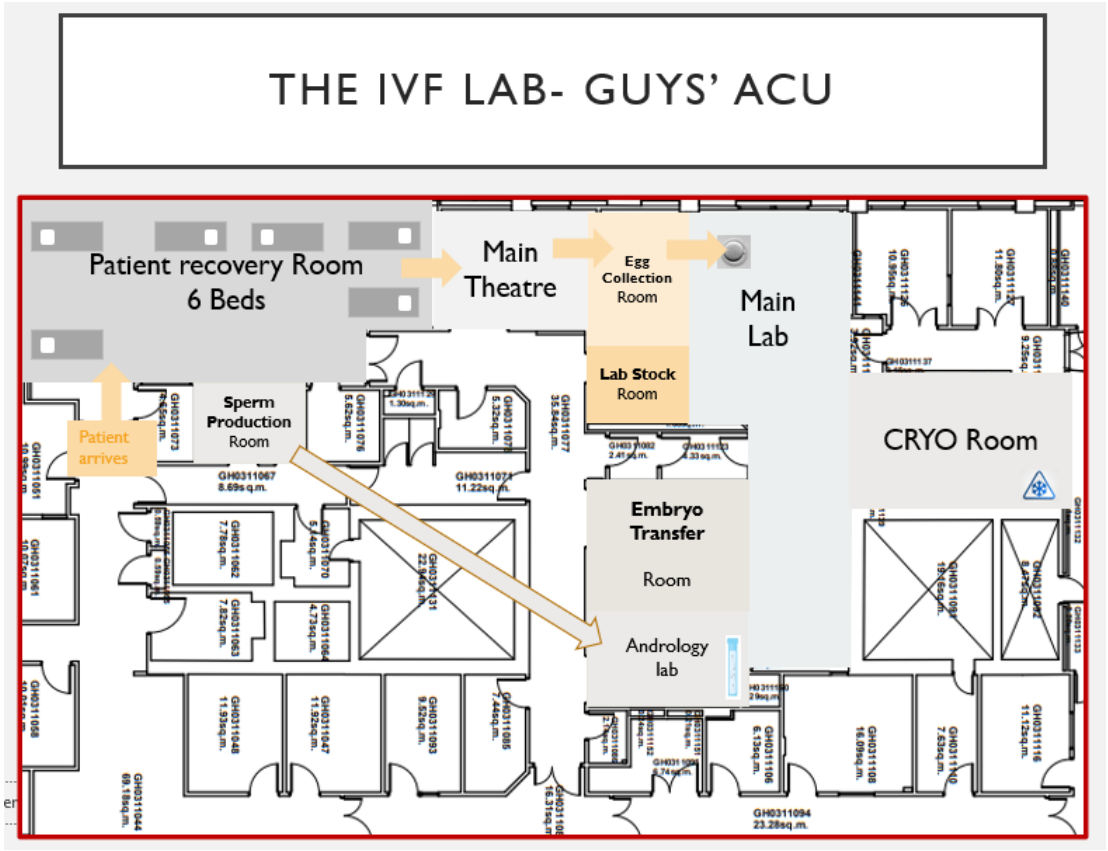
"this overload of work has escalated in the last 6-12 months to a level that feels completely out of control, the anxiety I now experience pervades through my work and home life"

Employers have a duty to assess the risk of stress-related ill health arising from work activities, and take action to control that risk. I would request that a risk assessment is undertaken urgently to determine how this situation can be resolved, and I would like to be involved/consulted in the risk assessment.

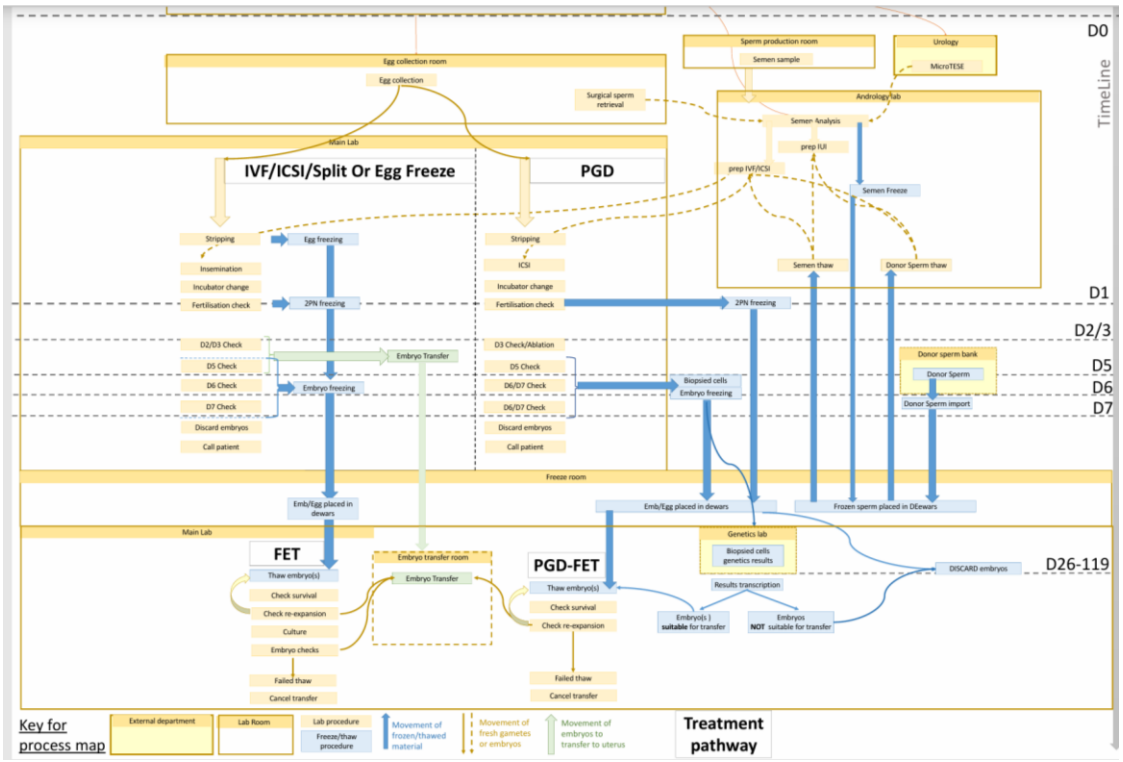
Tackling stress can improve staff commitment to work, performance and productivity, reduce intention to leave and staff turnover, improve attendance levels and improve the image and reputation of the Unit.

Eleanor Wharf
Clinical Embryologist

Appendix 25. *Floorplan of the different parts of GSTT-ACU IVF lab*



Appendix 26. *GSTT- ACU IVF lab pathways*



Appendix 27. *List of queues in the simulation model*

Continue to Next Day post ET
D1 post PGD fert check
Day 3 to Day 5 ICSI
Day 5 to Day 6 ICSI
Day 6 to Day 7 ICSI
Day1 to Day 2 ICSI
Dewars Embryos and Eggs
Dewars Sperm
EC Arrivals
FET Arrivals
PGD stripped to ICSI
Post PGD check D3
Post PGD check D5
Post PGD check D6
Post PGD D7
Queue 2 for Flow Stopper 2
Queue 2 for Queue for Fertilisaton check2
Queue 2 for Queue for Incubator Change 2
Queue 3 for Queue for Fertilisaton check2

Queue for Andrology Lab
Queue for Back to Recovery
Queue for Biopsied PGD
Queue for Contact Patient
Queue for D2 check and pre transfer ICSI
Queue for D3 Check ICSI
Queue for D3 Check Queries ICSI
Queue for D3 Check_Ablation PGD
Queue for D5 check ICSI
Queue for D5 check PGD
Queue for D6 Check ICSI
Queue for D6 Check PGD
Queue for D7 Check ICSI
Queue for D7 Check PGD
Queue for Discard embryos PGD

Queue for Discard embryos with witness ICSI
Queue for discard WCS
Queue for dummy Lab PGD
Queue for dummy Main Lab Egg Freezing
Queue for dummy Main Lab ICSI
Queue for dummy Main Lab IVF
Queue for dummy Room requirement
Queue for dummy Split Patients
Queue for dummy Split Rules
Queue for Egg Freezing
Queue for egg fz Prepare Dishes and Labels
Queue for Egg Fz Stripping
Queue for Embryo Freezing
Queue for Embryo Freezing And Continue
Queue for Embryo Transfer
Queue for Embryologist speaks to patient
Queue for Embryos taken out of dewars
Queue for Fertilisation check IVF

Queue for Fertilisation check on screen ICSI
Queue for Fertilisation check PGD
Queue for Flow Stopper 2
Queue for Freezing Semen
Queue for ICSI PGD
Queue for Incubator Change ICSI
Queue for Incubator Change PGD
Queue for Insemination ICSI
Queue for Insemination IVF
Queue for Moving Eggs and Embryos to Dewars
Queue for No Freezing Semen
Queue for paperwork available
Queue for Pre Transfer ICSI
Queue for Queue for Incubator Change 2
Queue for Queue for Insemination
Queue for Semen Assessment
Queue for Sperm Production
Queue for stripping ICSI
Queue for stripping PGD

Queue for Thaw
Queue for Thaw Check re_expansion
Queue for Thaw Check Survival
Queue for Theatre
SA Arrivals
Stripped to ICSI
To PGD Freezing

Appendix 28. *List of activities in the simulation model*

D7 Check PGD Data entry ICSI Discard embryos PGD Discard embryos with witness ICSI Discarded Embryos and Sperm dummy 1 day delay ICSI dummy 1 or 2 day delay PGD dummy Batch dummy EC Arrivals dummy FET Arrivals dummy Flow Stopper (plus 1 day) ICSI dummy Flow Stopper PGD dummy ICSI_IVF dummy Lab PGD dummy Main Lab Egg Freezing dummy Main Lab ICSI dummy Main Lab IVF dummy Next Step	

***Appendix 29**. List of End points in the simulation model*

Discarded Embryos
End 10
End 11
End 13
End 9
End of biopsy PGD
Failed Thaw
Failure to Fertilise ICSI
Failure to Fertilise IVF
No Eggs Collected
No fertilisation PGD
Semen Discard
Transfer Completed

Appendix 30. *List of timing distributions*

Activity Name	Distribution Type	P1	P2	P3	P4	Offset
dummy Split Patients	Fixed	0	0	0	0	
Sperm Production	Triangular	15	30	40	0	
dummy Main Lab IVF	Fixed	0	0	0	0	
Theatre	Gamma	3.9	4.69	0	0	5.67
Back to Recovery	Average	5	1.25	0	0	
Embryologist speaks to patient	Triangular	3	5	12	0	
paperwork available	Fixed	0	0	0	0	
Andrology lab pre sample prep 1	Triangular	0	8	68	0	
Insemination IVF	Triangular	0.4	3.8	6.4	0	
dummy Lab PGD	Fixed	0	0	0	0	
stripping PGD	Triangular	5.2	10.4	28.6	0	
ICSI PGD	Erlang	21	2	0	0	5
Incubator Change PGD	Average	1	0.25	0	0	
Fertilisation check PGD	Triangular	1	10	53	0	
D3 Check_Ablation PGD	Average	10	2.5	0	0	
D5 check PGD	Triangular	2	5.4	13	0	
D6 Check PGD	Triangular	12	15.6	23	0	
D7 Check PGD	Triangular	2	5.6	13	0	
Discard embryos PGD	Average	10	2.5	0	0	
dummy Flow Stopper PGD	Fixed	0	0	0	0	
dummy 1 or 2 day delay PGD	Fixed	420	0	0	0	

Thaw	Triangular	4	17.9	29	0	
Check Survival	Average	2	0.5	0	0	
dummy Room requirement	Fixed	0	0	0	0	
dummy Main Lab ICSI	Fixed	0	0	0	0	
stripping ICSI	Triangular	5.2	10.4	28.6	0	
Insemination ICSI	Triangular	0.4	3.8	6.4	0	
Incubator Change ICSI	Average	1	0.25	0	0	
Fertilisation check on screen ICSI	Average	30	7.5	0	0	
D2 check and pre transfer ICSI	Average	10	2.5	0	0	
D5 check ICSI	Triangular	2	5.4	13	0	
D6 Check ICSI	Triangular	2	5.6	13	0	
D7 Check ICSI	Triangular	2	5.6	13	0	
Discard embryos with witness ICSI	Average	1	0.25	0	0	
dummy Flow Stopper (plus 1 day) ICSI	Fixed	0	0	0	0	
dummy 1 day delay ICSI	Fixed	420	0	0	0	
Embryo Freezing	Triangular	12	12	92.9	0	
Biopsied PGD	Weibull	1.53	35	0	0	0.199
Lab prep 1	Triangular	11	38	50	0	
Post Prep 1	Triangular	5	52	207	0	
Andrology lab pre sample prep 2	Triangular	0	8	68	0	
Lab prep 2	Triangular	11	38	50	0	
Post Prep 2	Triangular	5	52	207	0	

Andrology lab pre sample prep 3	Triangular	0	8	68	0	
Lab prep 3	Triangular	11	38	50	0	
Post Prep 3	Triangular	5	52	207	0	
Split Rules	Fixed	0	0	0	0	
ICSI_IVF	Fixed	0	0	0	0	
Split	Fixed	0	0	0	0	
Frozen Sperm	Fixed	0	0	0	0	
dummy Main Lab Egg Freezing	Fixed	0	0	0	0	
Stripping	Triangular	5.2	10.4	28.6	0	
Moving Eggs and Embryos to Dewars	Average	10	2.5	0	0	
Embryo Transfer	Average	20	2.5	0	0	
D3 Check Queries ICSI	Average	10	2.5	0	0	
D3 Check ICSI	Average	10	2.5	0	0	
Embryo Freezing And Continue	Triangular	12	12	92.9	0	
Semen Assessment	Triangular	10	10	30	0	
Freezing Semen	Average	30	7.5	0	0	
No Freezing Semen	Triangular	2	5	10	0	
dummy Batch	Fixed	0	0	0	0	
Freezing for PGD	Beta	1.04	1.35	7	80.6	
dummy Next Step	Fixed	0	0	0	0	
Prepare Dishes and Labels	Average	5	1.25	0	0	
Egg Freezing	Pearson V	4.39	105	0	0	-2.87

Contact Patient	Average	2	0.5	0	0	
Embryos taken out of dewars	Average	3	0.75	0	0	
Check re_expansion	Average	1	0.25	0	0	
dummy Split Sample and Patient SA	Fixed	0	0	0	0	
dummy Path	Fixed	0	0	0	0	
Fertilisation check IVF	Exponential	9.1	2.5	0	0	
Contact patient ICSI	Average	10	2.5	0	0	
Data entry ICSI	Average	5	1.25	0	0	
Pre Transfer ICSI	Triangular	0.6	1.9	5.2	0	
Sperm Production 2	Triangular	15	30	40	0	
Discarded Embryos and Sperm	Fixed	0	0	0	0	
dummy Andrology Lab	Fixed	0	0	0	0	

Appendix 31. *Patient arrival spreadsheet for egg collection- Simul8 model*

EC	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	WC
week 1	0	0	0	0	0	0	0	03/01/2022
week 2	6	0	11	0	9	0	0	10/01/2022
week 3	14	0	2	0	13	0	0	17/01/2022
week 4	12	0	13	0	15	0	0	24/01/2022
week 5	10	0	14	0	14	0	0	31/01/2022
week 6	11	8	10	0	10	0	0	07/02/2022
week 7	14	7	8	4	7	0	0	14/02/2022
week 8	6	8	7	5	14	0	0	21/02/2022
week 9	11	1	10	6	10	0	0	28/02/2022
week 10	5	7	9	2	8	0	0	07/03/2022
week 11	16	11	8	7	11	0	0	14/03/2022
week 12	8	7	7	3	10	0	0	21/03/2022
week 13	7	1	8	4	5	0	0	28/03/2022
week 14	12	7	7	5	9	0	0	04/04/2022
week 15	11	5	7	4	8	0	0	11/04/2022
week 16	10	8	7	4	10	0	0	18/04/2022
week 17	11	5	8	6	9	0	0	25/04/2022
week 18	6	11	8	2	13	0	0	02/05/2022
week 19	7	7	6	1	5	0	0	09/05/2022
week 20	10	5	6	2	6	0	0	16/05/2022
week 21	9	4	9	1	11	0	0	23/05/2022
week 22	8	4	5	5	11	0	0	30/05/2022
week 23	9	6	7	4	13	0	0	06/06/2022

Appendix 32*. GSTT-ACU embryology team annual leave spreadsheet*

Annual Leave

Jan

Name	Su 1	Mo 2	Tu 3	We 4	Th 5	Fr 6	Sa 7	Su 8	Mo 9	Tu 10	We 11	Th 12	Fr 13	Sa 14	Su 15	Mo 16	Tu 17	We 18	Th 19	Fr 20	Sa 21	Su 22	Mo 23	Tu 24	We 25	Th 26	Fr 27	Sa 28	Su 29	Mo 30	Tu 31
Ab		BH														DIL	DIL									A/L			A/L		
Cd		PT	A/L	A/L	A/L	PT			PT				PT			PT				PT			PT				PT			PT	
Af		BH	Stud		A/L	A/L				A/L	DIL	DIL	DIL				DIL	Stud								Stud			Stud		
Xg		BH				A/L													DIL	DIL											
Pa		BH	A/L	A/L	A/L	A/L																									
NB		BH														DIL			DIL	A/L			A/L								
JB		BH									Stud	Stud	Stud																		
PB		BH	A/L		A/L																					DIL	DIL				
NL		PT	A/L	PT	PT				PT		PT	PT	A/L			PT	A/L	PT	PT				PT	Sick	PT	PT				PT	
AS		BH																													
JX		BH																						DIL	DIL						
ZB		BH									A/L									A/L											
BF		BH	A/L	A/L	A/L	A/L			A/L																					DIL	DIL
BK		BH																													
EI		BH		PT		PT					PT		PT					PT		PT					PT		PT			DIL	DIL
TW		BH							A/L	A/L	A/L	A/L	A/L			A/L	A/L	A/L	A/L	A/L			A/L	A/L	A/L	A/L	A/L				
EX		BH															A/L														
KE		BH																													
LL		BH	A/L																												
MM		BH																													
NN		BH	Stud			PT			A/L	Stud	Stud	Stud	PT				Stud			PT			Stud	Stud	Stud	Stud	PT				
PP		BH				Stud							Stud							Stud							Stud				
XX																															
LL		BH	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L	M/L
Number on AL/DL		0	6	3	5	4			2	2	3	2	3			3	5	1	3	4			2	2	2	2	3			3	2
Total Number																															

April | May | June | July | August | Sept | Oct | Nov | Dec | Jan | Feb | March | AnnualLeav

Appendix 33. Embryologists staffing schedule spreadsheet in Simul8

Emb	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
week 1	0	5	5	4	3	2	2
week 2	7	9	8	9	8	3	3
week 3	10	11	12	12	10	3	3
week 4	9	11	10	11	10	3	3
week 5	11	12	12	10	8	3	3
week 6	9	10	10	8	9	3	3
week 7	9	10	8	7	7	3	3
week 8	7	9	9	8	7	3	3
week 9	7	8	7	7	7	3	3
week 10	9	10	9	12	9	3	3
week 11	8	8	8	8	7	3	3
week 12	9	8	8	8	7	3	3
week 13	7	8	8	9	7	3	3
week 14	7	10	10	8	8	3	3
week 15	8	9	8	9	10	3	3
week 16	10	9	9	9	9	3	3
week 17	10	11	10	10	10	3	3
week 18	13	11	11	9	9	3	3
week 19	9	9	9	9	8	3	3
week 20	11	10	9	11	10	3	3
week 21	14	14	12	11	9	3	3
week 22	11	12	10	11	11	3	3
week 23	10	12	9	8	8	3	3
week 24	8	12	9	9	8	3	3
week 25	12	13	10	10	9	3	3
week 26	11	13	11	11	10	3	3
week 27	10	11	9	11	10	3	3
week 28	12	11	9	10	9	3	3
week 29	11	12	9	12	10	3	3
week 30	11	12	12	11	10	3	3
week 31	10	10	12	12	10	3	3
week 32	12	11	12	11	10	3	3
week 33	11	9	9	10	8	3	3
week 34	12	11	12	11	9	3	3
week 35	14	12	12	10	10	3	3
week 36	11	11	11	12	11	3	3
week 37	11	12	9	10	9	3	3
week 38	9	12	10	12	10	3	3

Appendix 34. *Results from 110 Trial base runs*

Results

Transfer Completed	Number Completed	1659.55	1664.43	1669.31
Failed Thaw	Number Completed	14.02	14.75	15.47
Embryo Freezing	Number Completed Jobs	327.28	334.30	341.32
Practitioners	Utilization %	44.07	44.58	45.09
Embryologists	Utilization %	58.71	59.23	59.76
gblD5Biopsy	Value	261.54	267.22	272.90
gblD6Biopsy	Value	181.72	185.72	189.72
gblD7Biopsy	Value	44.09	45.59	47.10
gblEggCollectionProcedure	Value	1586.05	1615.86	1645.68
gblFreshTransfersCompleted	Value	761.29	776.24	791.18
gblTransferD2	Value	105.76	108.57	111.39
gblTransferD3	Value	224.39	229.36	234.34
gblTransferD5	Value	654.65	667.66	680.67
gblTransfersCompleted	Value	1659.55	1664.43	1669.31
Freezing Semen	Number Completed Jobs	411.14	414.22	417.29
No Freezing Semen	Number Completed Jobs	728.68	731.75	734.83
Egg Freezing	Number Completed Jobs	141.55	144.86	148.17
Embryo Transfer	Number Completed Jobs	2198.63	2213.49	2228.35
Embryo Viewer	Utilization %	14.76	15.05	15.33
No Eggs Collected	Number Completed	14.31	15.09	15.88
gblFrozenTransfersCompleted	Value	1436.53	1437.25	1437.98

Appendix 35. *List of queues in Simul8 Results section*

Queue Name	Queues relevant to Analysis
Queue for dummy Split Patients	
Queue for dummy Room requirement	
Queue for Andrology Lab	
Queue for Back to Recovery	
Queue for Embryologist speaks to patient	
Queue for dummy Main Lab IVF	
Queue for Insemination IVF	
Queue for Queue for Insemination	
Queue for dummy Lab PGD	
Queue for stripping PGD	
Queue for ICSI PGD	
Queue for Incubator Change PGD	
Queue for Fertilisation check PGD	
Queue for D3 Check_Ablation PGD	
Queue for D5 check PGD	
Queue for D6 Check PGD	
Queue for D7 Check PGD	
Queue for Discard embryos PGD	
Queue for Flow Stopper 2	
PGD stripped to ICSI	
Queue for Queue for Incubator Change 2	

Queue 2 for Queue for Fertilisaton check2	
D1 post PGD fert check	
Post PGD check D3	
Post PGD check D5	
Post PGD check D6	
Post PGD D7	
Dewars Embryos and Eggs	
Dewars Sperm	
Queue for Embryo Transfer	
Queue for dummy Main Lab ICSI	
Queue for stripping ICSI	
Queue for Insemination ICSI	
Queue for Incubator Change ICSI	
Queue for Fertilisation check on screen ICSI	
Queue for D2 check and pre transfer ICSI	
Queue for D5 check ICSI	
Queue for D6 Check ICSI	
Queue for D7 Check ICSI	
Queue for Discard embryos with witness ICSI	
Queue 2 for Flow Stopper 2	
Stripped to ICSI	
Queue 2 for Queue for Incubator Change 2	

Queue 3 for Queue for Fertilisaton check2	
Day1 to Day 2 ICSI	
Day 5 to Day 6 ICSI	
Day 6 to Day 7 ICSI	
Queue for Embryo Freezing	
Queue for Biopsied PGD	
Queue for Thaw Check Survival	
Queue for Thaw Check re_expansion	
Queue for Sperm Production	
Queue for dummy Main Lab Egg Freezing	
Queue for Egg Fz Stripping	
Queue for egg fz Prepare Dishes and Labels	
Queue for Moving Eggs and Embryos to Dewars	
Queue for Semen Assessment	
Day 3 to Day 5 ICSI	
Queue for D3 Check Queries ICSI	
Queue for D3 Check ICSI	
Continue to Next Day post ET	
Queue for Embryo Freezing And Continue	
Queue for Freezing Semen	
Queue for No Freezing Semen	
To PGD Freezing	

Queue for Egg Freezing	
Queue for Contact Patient	
Queue for Embryos taken out of dewars	
Queue for Thaw	
Queue for paperwork available	
Queue for dummy Split Rules	
Queue for Fertilisation check IVF	
FET Arrivals	
EC Arrivals	
SA Arrivals	
Queue for discard WCS	
Queue for Theatre	
Queue for Pre Transfer ICSI	