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Abstract: Calling on members of the medical and artificial intelligence/machine learning (AI/ML) communities with an interest in the applications of AI/ML for Human Reproduction and Fertility. We encourage engagement in the topic group dedicated to establishing an international standardised frameworks for development and benchmarking guidelines within the International Telecommunication Union (ITU) / World Health Organisation (WHO) Focus Group on “Artificial Intelligence for Health” (FG-AI4H).

This version of the CfTGP is the same as seen in Meeting M (FGAI4H-M-027-A02), reproduced for easier reference as a Meeting N document.

ITU/WHO Focus Group on artificial intelligence for health (FG-AI4H)

Call for Topic Group Participation: AI for Human Reproduction and Fertility (TG-Fertility)

The International Telecommunication Union (ITU)/World Health Organization (WHO) Focus Group on “Artificial Intelligence for Health” (FG-AI4H; <https://itu.int/go/fgai4h>) seeks engagement from members of the medical and artificial intelligence (AI) communities (including clinicians, technologists, entrepreneurs, potential benchmarking data providers, machine learning experts, software developers, researchers, regulators, policy-makers, companies/institutions, and field experts) with a vested interest in shaping the benchmarking process of AI for Human Reproduction and Fertility.

1 About FG-AI4H

Over the past decade, considerable resources have been allocated to exploring the use of AI for health, which has revealed an immense potential. Yet, due to the complexity of AI models, it is difficult to understand their strengths, weaknesses, and limitations. If the technology is poorly designed or the underlying training data are biased or incomplete, errors or problematic results can occur. AI technology can only be used with complete confidence if it has been quality controlled through a rigorous evaluation in a standardized way. Towards developing this standard assessment framework of AI for health, the ITU has established FG-AI4H in partnership with the WHO.

Thus far, FG-AI4H has established 24 topic groups. The topic groups are: use of AI in cardiovascular disease management, dermatology, diagnoses of bacterial infection and anti-microbial resistance, falls among the elderly, histopathology, malaria detection, maternal and child health, neurological disorders, ophthalmology, outbreak detection, psychiatry, radiology, snakebite and snake identification, symptom assessment, tuberculosis, volumetric chest computed tomography, dental diagnostics and digital dentistry, detection of falsified medicine, primary and secondary diabetes prediction, endoscopy, musculoskeletal medicine, point-of care diagnostics, sanitation for public health, and human reproduction and fertility.

Each topic group agrees upon representative benchmarking tasks in a pragmatic, best-practice approach, which can later be scaled and expanded to similar tasks. Every benchmarking task should address a health problem of relevance (e.g. impacting a large and diverse part of the global population or challenging to treat) and for which AI technology would provide a tangible improvement relative to the current practice (e.g. better care, results, and/or cost/time effectiveness).

For a rigorous and sound evaluation, undisclosed test data sets must be available (or have to be collected) for each task. All data must be of high quality and compliant with ethical and legal standards. In addition, the data must originate from a variety of sources so that it can be determined whether an AI algorithm can generalize across different conditions, locations, or settings (e.g. across different people, hospitals, and/or measurement devices). The format/properties of the data serving as input to the AI and of the output expected from the AI, as well as the benchmarking metrics are agreed upon and specified by the topic group.

Finally, the AI-to-be-evaluated will be benchmarked with the undisclosed test data on FG-AI4H computing infrastructure. Here, the AI will process single samples of the undisclosed test data set and predict output variables, which will be compared with the "ground truth." The results of the benchmarking will be provided to the AI developers and will appear on a (potentially anonymized) leaderboard.

2 Topic group: AI for Human Reproduction and Fertility (TG-Fertility)

A topic group is a community of stakeholders from the medical and AI communities with a shared interest in a topic. The objectives of the topic groups are manifold:

1. to provide a forum for open communication among various stakeholders,
2. to agree upon the benchmarking tasks of this topic and scoring metrics,
3. to facilitate the collection of high-quality labelled test data from different sources,
4. to clarify the input and output format of the test data,
5. to define and set-up the technical benchmarking infrastructure, and
6. to coordinate the benchmarking process in collaboration with the Focus Group management and working groups.

The primary output of a topic group is one document that describes all aspects of how to perform the benchmarking for this topic. The document will be developed in a cooperative way by suggesting changes as input documents for the next FG-AI4H meeting that will then be discussed and integrated into an official output document of this meeting. The process will continue over several meetings until the topic description document is ready for performing the first benchmarking.

This topic group is dedicated to AI applications for Fertility.

2.1 Overview of the topic group

This topic group focuses on early identification, diagnosis, and treatment decision support of infertility related conditions with the applications of artificial intelligence (AI) and machine learning (ML) and other approaches.

Patient identification: Infertility is currently characterised by the failure to establish a clinical pregnancy after 12 months of regular, unprotected sexual intercourse or due to an impairment of a person's capacity to reproduce either as an individual or with his/her partner. [1]. Even though this definition can serve as guidance, the earliest infertility can be identified and treated, and live birth of a healthy baby achieved, the better. There are two main reasons driving the urgency in initiating treatment early as possible: (i) the psychological burden on patients going through infertility [2] and (ii) the facts that gamete quality decreases ageing [3,4].

The application of technologies that can assist in the early identification of patients that are still not aware of being at risk of need of fertility treatment in the short-midterm future is of extreme importance. The use of AI and ML could effectively support the identification of any infertility risk by analysing existing electronic health records (EHR) of patients that underwent fertility treatment (including data from wearables with the patients' consent) compared to healthy population.

Diagnosis: Infertility is a highly complex disorder of the reproductive system. There are 2 forms of male or female sterility: primary and secondary. The primary form affects germ cell structure or physiology, causing arrest of germ cell development and ultimately cell death. Primary female infertility includes premature ovarian failure (POF), polycystic ovary syndrome (PCOS), endometriosis, and leiomyoma. Primary male sterility disrupts spermatogenesis and is associated with abnormal semen (i.e., abnormal sperm count, morphology, or motility), but often the semen is normal (idiopathic infertility). Secondary infertility arises due to systemic or syndromic genetic defects, including developmental, endocrine, and metabolic defects [5] Therefore, the identification of a specific cause/disease can take months and sometimes years to be correctly identified and therefore treated efficiently. The use of AI could assist in identifying at higher efficiency the main conditions that can lead to reproductive challenges. This more efficient diagnosis could take place at the clinical practice by combining demographical, lifestyle and genetic data. In addition, the capturing of a

patient's signs and symptoms including pain, irregular menstrual cycles and others biological indicators could also be supported using chatbots and similar approaches to reduce time of diagnosis.

Treatment: The fertility treatment is complex as it combines several activities managed by several healthcare professionals, such as obstetrician-gynaecologists, nurses, andrologists and embryologists. There are today several types of treatments and techniques that vary in level of complexity and invasiveness depending on the patient diagnosis [6]. In addition, differently from other treatments, a part of the treatment of infertility happens extracorporeally while gametes and embryo are handled in in vitro conditions until the transfer back to the patient/receptor uterus.

Differently from other therapeutic areas, Human Reproduction treatments are relatively new, and this field has been witnessing intense progress over the past 40 years [7]. Consequently, there are several possible treatments, strategies and techniques when stimulating patients, selecting gametes and embryos as well as supporting early stage of pregnancy. The use of AI in fertility treatment can be applied to support clinicians in decision making processes during the selection of treatment regimens and protocols, the definition of medication starting dosage as well as the continuous adjustment during stimulation protocol and the decision of ideal time for triggering of ovulation. In the laboratory setting, AI can be used as support tool to define the techniques to be used for each patient and to select the best embryo for transfer back to patient.

2.2 Relevance of this group

Infertility is more than a quality-of-life issue, with considerable public health consequences including psychological distress, social stigmatization, economic strain, and marital discord. Globally, infertility affects 15% of couples at reproductive age [8]. In addition, infertility has also been associated with an increased risk of subsequent chronic health conditions such as cardiovascular disease [9].

The infertility stigma is no longer associated to females exclusively. It is estimated that out of ~50 million couples suffering from the condition, 1/3 is attributed to female factors, 1/3 attributed to male factors and 1/3 classified as unexplained or a combination of both partners. This makes fertility unique to other clinical conditions, as it does not only rely in one individual, but a couple and their biological interaction [10].

Large amounts of data are generated as part of ART treatments. This is due to the biological complexity and variability of root causes that can lead to infertility. Moreover, the stepwise and complex nature of the laboratory procedures and add-on techniques that aim to improve treatment outcomes contribute to the data generation. The selection of the right treatment, gamete and embryo selection as well as times of procedures are within the areas that could benefit the most from AI applications that could support the clinical decision-making process.

There have been few developments in the last few years that are particularly relevant for this area, but most of them still in early stage of development:

- The development of tools that support the selection of blastocyst with highest potential of implantation and live birth
- The development of support software that assists the clinician during ovarian stimulation in the decision of dosage adjustment and ovulation triggering
- The development of wearables that track biomarkers such as core basal temperature to predict ovulation and diagnosis of high incidence infertility related conditions

More details about the activities of the topic group can be found in the documents [FGAI4H-L-034](#) and [FGAI4H-L-034-A01](#) presented at the meeting L of the focus group. These can be accessed with a free ITU account (cf. "Get involved").

Current members of the topic group on AI for Human Reproduction and Fertility are:

- Alison Campbell (CARE Fertility Group, alison.campbell@carefertility.com)
- Dan Nayot (The Fertility Partners, dan.nayot@thefertilitypartners.com)
- Eleonora Lippolis (Merck KGaA, eleonora.lippolis@merckgroup.com)
- Gerard Letterie (Seattle Fertility, gerard.letterie@seattlefertility.com)
- Stefan Wagner (European School of Management & Technology, stefan.wagner@esmt.org)
- Susanna Brandi (Merck KGaA, susanna.brandi@merckgroup.com)
- Tex VerMiylea (Ovation Fertility, mvermilyea@ovationfertility.com)
- Wenjing Zheng (Merck KGaA, wenjing.zheng@merckgroup.com)

Alison Campbell [...]

Dan Nayot [...]

Eleonora Lippolis is Senior Data Scientist at Merck KGaA. Eleonora holds a Master's degree in Bioengineering from the University of Pavia and a degree in Science and Technologies from the Italian Institute of Advanced Studies of Pavia. She worked as research assistant at the Institute of Human Genetics in Erlangen, Germany. She joined Merck four years ago and since has successfully led several data science healthcare projects.

Gerard Letterie [...]

Stefan Wagner is an Associate Professor of Strategy and Innovation (with tenure) and Director of PhD studies at ESMT Berlin. Also, he is a Senior Fellow at the Berlin Centre for Consumer Policies (BCCP) and serves on the boards of the European Policy for Intellectual Property Association EPIP and the Doctoral Program of the Berlin School of Economics. He has received prestigious prizes and scholarships including a Fulbright Scholarship and a stipend from the German Academic Scholarship Foundation (Studienstiftung des Dt. Volkes). His research interests cover the intersection of firm strategy, technological innovation, industrial organization and law. He applies state of the art methods from econometrics and machine learning to large-scale data sets to derive insights that are based on solid empirical evidence. Engaging with students and the public on important innovation policy issues is a key aspect of his work. Beyond the classroom, he has worked with numerous clients on questions of innovation as well as data analytics.

Susanna Brandi is Head of Portfolio Expansion at Merck KGaA. Susanna is a biomedical scientist with a Master's in Human Reproduction at Università Degli Studi di Napoli Federico Secondo. Susanna worked as an embryologist at the Geneva IVF Group in Sydney, Australia. She migrated to product development within the company focusing on automation and standardization of techniques and process within the IVF Laboratory. Susanna has been working with Merck for four years co-leading the assessment of AI and digital health associated products.

Tex VerMiylea [...]

Wenjing Zheng [...]

The topic group would benefit from further expertise of the medical and AI communities and from additional data. Calling for participants with interest in the use of clinical data for the development of algorithms. Knowledge in reproductive medicine and data science are preferred.

3 Get involved

To join this topic group, please send an e-mail to the focus group secretariat (tsbfgai4h@itu.int) and the topic drivers (susanna.brandi@merckgroup.com, leonora.lippolis@merckgroup.com). Please use a descriptive e-mail subject (e.g. "Participation topic group AI for Fertility"), briefly introduce yourself and your organization, concisely describe your relevant experience and expertise, and explain your interest in the topic group.

Participation in FG-AI4H is free of charge and open to all. To attend the workshops and meetings, please visit the Focus Group website (<https://itu.int/go/fgai4h>), where you can also find the whitepaper, get access to the documentation, and sign up to the mailing list.

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