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DOCUMENT

Source: TG-Cardio Topic Driver

Title: Att.2 - CfTGP (TG-Cardio) [same as Meeting H]

Purpose: Engagement

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Abstract: Calling on members of the health and artificial intelligence communities with a vested interest in application of AI in cardiovascular disease (CVD) risk prediction! Become engaged in a subtopic group dedicated to establishing a standardized benchmarking platform for application of AI in CVD risk prediction within the International Telecommunication Union (ITU)/World Health Organization (WHO) Focus Group on “Artificial Intelligence for Health” (FG-AI4H). This document is based on the version seen in meeting E, reproduced for meeting G for easier reference, and has been updated for meeting H. It does not include content relevant to the subtopic group on artificial intelligence in coronary computed tomography angiography (referenced below in the list TG-Cardio subtopics).

This version of the CfTGP is the same as seen in Meeting H (FGAI4H-H-006-A02), reproduced for easier reference as a Meeting N document.

SUBTOPIC CATEGORIES UNDER TG-CARDIO: Inclusive of the subtopic on CVD risk prediction, subtopics under TG-Cardio may address a range of applications of AI in CVD management which are broadly classified by [Yan et al \(2019\)](#) into the 4 subtopic categories listed below:

CLINICAL PREDICTIONS - Cardiovascular disease (CVD) Risk Prediction. (Subtopic for this “Call for Participants” in this document – Subtopic Driver(s) Muthambi et al.)

CARDIAC IMAGE ANALYSES – Coronary CT Image Processing/Image Recognition for Coronary CT angiography (CCTA) in coronary artery disease (CAD) diagnosis. (Subtopic TDD in separate document pending - Subtopic Driver(s) Guo et al.)

INTELLIGENT ROBOTS – Surgical Robot Technologies incl. AI-assisted Minimally Invasive Cardiac Surgery (Subtopic not yet proposed)

PRECISION MEDICINE – AI-assisted Individualized Medicine and healthcare customized for each patient. (Subtopic not yet proposed)

Call for Participation in TG-Cardio | Subtopic Group on Cardiovascular Disease (CVD) Risk Prediction

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

Participation in both the Focus and Topic/Subtopic Group is generally open and free of charge. Anyone who is from a member country of the ITU may participate. On 14 March 2019, ITU published an official "call for participation" document outlining the process for joining onto the Focus Group and each Topic/Subtopic Group by [following the steps in this onboarding document](#). For the topic group TG-Cardio, interested participants are expected to join subtopic groups of interest directly; for the TG-Cardio subtopic on CVD risk prediction, this updated document replaces the previous “call for participation” in TG-Cardio. Other subtopics within TG-Cardio will also issue corresponding calls for participation which will also be publicly accessible here.

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 thirteen topic groups. These are concerned with: AI and cardiovascular disease (CVD) risk prediction, child growth monitoring, dermatology, falls among the elderly, histopathology, neuro-cognitive diseases, ophthalmology (retinal imaging diagnostics), psychiatry, radiotherapy, snakebite and snake identification, symptom checkers, tuberculosis, and volumetric chest computed tomography.

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 About the AI for Health Topic Group, TG-Cardio & the TG-Cardio Subtopic Group on Cardiovascular Disease (CVD) Risk Prediction

2.1 **Topic Group TG-CARDIO:** The TG-Cardio topic group is a community of stakeholders from the health and AI communities with a shared interest in the topic of AI applications in CVD. The TG-Cardio topic group/community of stakeholders will be differentiated into 4 subtopic groups (corresponding with the identified 4 categories of subtopics) which will be represented in the **Topic Group Coordinating Forum** by the respective Subgroup Drivers. Subtopic Drivers will thus be the members of the Topic Group Coordinating Forum with responsibility to:

- Serve as Forum Co-Chairs of the TG-Cardio Topic Group Coordinating Forum
- When requested, assist the Convening Topic Driver of TG-Cardio (*Inaugural Chair* of the Topic Group Coordinating Forum), Dr. Benjamin Muthambi, in presiding over proceedings of the forum, liaising with subtopic groups, and representing the Topic Group in Focus Group proceedings;
- Collectively identify and develop consensus (or vote) on matters of shared interest across subtopics (incl. agreeing on common due dates for achievement of key milestones applicable cross subtopic group);

Current Members of the TG-Cardio | Topic Group Coordinating Forum are:

- TG-Cardio Topic Driver & Inaugural Chair: Dr. Benjamin Muthambi (IEPH, South Africa)
 - Subtopic Represented: CLINICAL PREDICTIONS - Cardiovascular disease (CVD) Risk Prediction.
- TG-Cardio Topic Co-Chair: Dr. Nathan Guo (ShinKun Technology, MIIT, China)
 - Subtopic Represented: CARDIAC IMAGE ANALYSES – Coronary CT Image Processing/Image Recognition for Coronary CT angiography (CCTA) in coronary artery disease (CAD) diagnosis

As outlined above, participation in the TG-Cardio | Topic Group Coordinating Forum is limited to Subtopic Drivers.

2.2 Subtopic Group TG-CARDIO | CVD Risk Prediction:

The TG-Cardio subtopic group on CVD risk prediction is a community of stakeholders from the health and AI communities with a shared interest in AI applications in *CVD risk prediction*.

The **TG-Cardio Subtopic Driver Team** consists of Dr Benjamin Muthambi (IEPH), the topic driver and convener of the CVD Risk Prediction subtopic, in collaboration with co-conveners Dr Nao Sipula, and Mr Jason Paul (WatifHealth).

Call for Peer-Reviewer & Technical Advisory Participants - TG-Cardio's CVD Risk Prediction Subtopic Stakeholder Community/Consultative Forum:

This updated "*Call for Participants*" seeks Peer-Reviewer & Technical Advisory Participants for the above-referenced subtopic group in constituent subgroups corresponding with roles/tasks listed below under Forum Objectives, Roles and Tasks.

This forum is open to all participants and stakeholders in TG-Cardio with an interest in the proceedings of the subtopic CVD risk prediction. A number of potential participants have already submitted expressions of interest in participation in TG-Cardio, including experts in Cardiovascular Disease risk prediction and related AI/Machine Learning, etc. Notices of invitation of comments/input according to a time-phased schedule of online asynchronous/synchronous

events/meetings, and information on how to access a collaboration forum portal will be sent to TG-Cardio participants via email (and subsequently, the TG-Cardio | CVD risk prediction subtopic list to be setup) after the FG-AI4H meeting in New Delhi on 12-13 November 2019.

Stakeholder Community/Consultative Forum Objectives & Participant Subgroup Roles/Tasks:

Forum Objectives: The initial objectives of the Subtopic's Stakeholder Community/Consultative Forum include:

- Providing a forum for open communication among various stakeholders
- Providing peer-review and advisory support to the benchmarking process set out in the TG-Cardio TDD in collaboration with the Subtopic Driver Team (Subtopic Group Convenor & Secretariat referenced above), Focus Group FG-AI4H management, and working groups.

Participant Subgroup Roles/Tasks: More specifically, participants are expected to select/join and actively participate in at least one (1) technical advisory/consultative subgroup which corresponds with each of the roles/tasks listed below pertaining to peer-review and refinement of sections of the subtopic's TDD, namely:

- To provide a forum for open communication among various stakeholders
- To provide peer-review and advisory support to the benchmarking process set out in the TG-Cardio TDD in collaboration with the Subtopic Driver Team (Topic Group Convenor & Secretariat referenced above), Focus Group management, and working groups
- To establish and actively participate in technical advisory/consultative subgroups responsible for peer-review and refinement of:
 - The objectives section of the CVD risk prediction subtopic TDD and IRB protocol for this subtopic's project incl. replication studies;
 - The literature review, background and rationale section of the TDD and IRB protocol for this subtopic's project incl. replication studies;
 - Sub-sections of the Methods section of the TDD and IRB protocol for this subtopic's project: Epidemiology/Evaluation Study Design, Undisclosed Data Management incl. Procurement and Preparation Procedures; Statistical Methods, Metrics, & Programming Tools; and Benchmarking Procedures and Infrastructure:
 - Agree on benchmarking tasks of this topic and scoring metrics
 - Facilitate the collection of high-quality labelled test data from different sources,
 - Clarify the input and output format of the test data
 - Define and set-up the technical benchmarking infrastructure
 - R Programming: Data Management, Predictive Analytics, Statistical Analyses, Shiny Web App
 - Ethics section of this subtopic's TDD and IRB protocol for the project (Pre-IRB) for this subtopic & quality assurance of each replication project's proceedings
 - Project management planning & infrastructure, reproducible reporting tools & writing templates in R Markdown
 - Requirements for undisclosed data contributions for use in replication studies for ITU/WHO external benchmarking
 - Final version of TDD document

TG-Cardio Stakeholder Community Forum is accepting expressions of interest in each of the above-referenced specific roles/tasks. More specific details on how to get involved are outlined under the section “How to Get Involved” (Section #5).

3 Introductory Subject Information: AI for Health Topic Group: Cardiovascular Disease (CVD) Risk Prediction

This section (Section 3) introduces the subject matter of the topic including objectives and intended benchmarking task, relevance and data availability, followed by the next section (Section 5) on how to get involved.

3.1 Project Objectives/Problem to be addressed: Diabetics have higher CVD risk, hence improved CVD risk prediction is critical for better diabetes management and reducing mortality. The proposed project aims to:

a) To assess: i) CVD risk prediction accuracy of various machine learning (ML) methods benchmarked against CVD risk based on actually observed occurrence of first CVD event (truth) documented in diverse cohorts/populations data, and ii) replicability/reproducibility of ML

prediction of CVD risk using 'external data' from diverse populations meeting prescribed criteria but 'not previously accessed' (undisclosed) data to the ML algorithms under evaluation;

b) Compare CVD risk prediction accuracy of ML algorithms referenced above in section 3.1. (a) to:

i) several routine clinical-use CVD risk scoring tools/calculators, and ii) traditional multivariate statistical methods (in collaboration with other co-investigators who recently undertook similar risk prediction accuracy studies);

c) Determine which methods, if any, consistently show better predictive accuracy across diverse populations. Using the above-referenced methods, benchmarking, anticipated findings and peer-review thereof, the project expects to establish an evidence-based standards-setting blueprint.

3.2 Relevance/Background, significance and rationale:

Cardiovascular disease (CVD) is the global leading cause of morbidity and mortality (WHO, 2014). CVD accounts for > 2/3 of mortality among type 2 diabetes patients (ADA, 2019). Widely used clinical CVD risk scoring tools/calculators incorporate several factors with well-established etiological associations with CVD such as age, sex, BMI, systolic blood pressure, smoking, A1C, lipid levels, age at diagnosis &/or onset of diabetes, diabetes duration, and antihypertensive and lipid-reducing drugs, but do not necessarily include a comparable set of predictors. In addition, these methods often fail to identify many people who would benefit from preventive treatment, while others receive unnecessary interventions. For example, approx. ~50% of myocardial infarctions (MIs) and strokes occur among persons predicted to be at risk of CVD by routinely-used risk calculators (Ridker et al, 2008). Highlighting the need for standardization, prior systematic CVD risk prediction accuracy studies often used: disparate study populations; either traditional multivariate statistical methods or disparate ML algorithms; incomparable sets of predictors often not considering the broader range of potential predictor data made possible by mining electronic health records, big data aggregation, or accounting for complex interactions that ML can handle more easily; and also used different measures of predictive accuracy. This study hypothesizes that ML algorithms can improve CVD predictive accuracy over CVD risk scoring tools/calculators used

in the standard of practice across diverse populations. If demonstrated, ML-assisted DSS should be considered as the underlying approach for standard of practice in CVD risk prediction.

3.3 Data availability:

Public Data: Anonymized data already acquired for preliminary work for this project are publicly accessible academic training-use data extracted from the NIH-funded Framingham Heart Study which were in turn sourced from the BioLINCC data repository under NIH data sharing terms.

Undisclosed Data: 'External data' meeting prescribed criteria but 'not previously accessed' (undisclosed data) to train the ML algorithms under evaluation, will be sourced for replication studies from various repositories identified as suitable potential data sources including multiple researcher-use data obtainable under well-established NIH-funded research data sharing terms applicable to the NHLBI/National Heart, Lung, and Blood Institute's Open BioLINCC Biologic Specimen and Data Repository, i.e. NIH/NHLBI BioLINCC; UK NHS/CPRD data repository; and a diverse range of other data sources with suitable data identified in the literature, and other data sources still to be identified through a planned call for data-contributing project participants (per above-referenced AI for cardiovascular disease risk prediction topic group's Project Phase-Specific Technical Contributor Subgroups/Forums. The identified potential sources of 'not previously accessed/undisclosed data' contain clinical and other patient data used in routine clinical care by CVD risk scoring tools/calculators, and in research using traditional multivariate statistical methods or ML algorithms.

4 Details about activities of the CVD risk prediction subtopic group:

General information on the subtopic is on this publicly accessible [landing page of the TG-Cardio subtopic on CVD risk prediction](#). Proceedings and more specific collaboration documents on this subtopic group including the initial technical proposal for the CVD risk prediction subtopic ([C-017-R1](#)), drafting of the topic description document (TDD) for the CVD risk prediction subtopic, discussions, and other information is posted at the [TG-Cardio CVD risk prediction subtopic group's collaboration site](#), which can be accessed with a free ITU account (see "Getting involved" below).

5 Getting involved: To join this subtopic group, please follow the steps below:

- 1) **Self-introduction step:** Send an e-mail to the focus group secretariat (tsbfgai4h@itu.int) and the topic driver (brm5@caa.columbia.edu). Please use a descriptive e-mail subject (e.g. "Participation topic group AI for cardiovascular disease risk prediction"), briefly introduce yourself and your organization, concisely describe your relevant experience and expertise, and explain your interest in the topic group;
 - 2) **Onboarding steps to access collaboration site:** To enable access and facilitate subsequent assignment to the appropriate role/task subgroup of the subtopic, parties interested in joining onto the Focus Group and each Topic/Subtopic Group are encouraged to [follow steps in this onboarding document](#) to gain access to the ITU/FG-AI4H collaboration site;
 - a. Participation in FG-AI4H and topic/subtopic groups is free of charge and open to all. To attend the workshops and meetings, please visit the Focus Group website for information (<https://www.itu.int/go/fgai4h>), incl. where you can find the whitepaper, other information, and the access point to the collaboration site.
 - b. Join the e-Mail Lists of Focus Group FG-AI4H & Topic Group TG-Cardio's Subtopic on Group Mailing Lists to receive regular updates of ongoing proceedings;
 - 3) **Navigate collaboration site to subtopic TDD section(s) relevant to your technical strengths and interests:** Identify and participate in discussions, peer-review and refinement of relevant section(s) of subtopic TDD;
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