PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Technology-enabled examinations of cardiac rhythm, optic nerve, oral health, tympanic membrane, gait and coordination evaluated jointly with routine health screenings: An observational study at the 2015 Kumbh Mela in India
AUTHORS	Shah, Pratik; Yauney, Gregory; Gupta, Otkrist; Patalano, Vincent; Mohit, Mrinal; Merchant, Rikin; Subramanian, S V

VERSION 1 – REVIEW

REVIEWER	S.E. Wildevuur FSW, VU University Amsterdam (NL)
REVIEW RETURNED	08-Aug-2017

GENERAL COMMENTS	First of all, I would like to compliment the authors on te research conducted in a still virginal area. The market of technology enabling non-invasive diagnostic screening is growing but we still lack evidence on the significance and efficacy of such devices. The authors stated in the first paragraph that the significance and efficacy is unevaluated for primary screening of patients (l. 24). Ofcourse, this is an important research field. However, the study seems to compares apples and oranges. As the authors indicated the effectiveness of technology-enabled screening is limited (l. 79). The authors compare multiple types of TES, of which the significance and efficacy are not clear from these studies AND they compare it with traditional vital sign examination, using video's. From the study the main research topic seems to be comparing the two different approaches to find evidence of the significance and efficacy of TES vs conventional vital sign examination. What have been conducted as research is not so much the efficacy and the significance of TES but how TES is compared to conventional vital sign examination. To phrase (l 258) that "these subjects were either previously undiagnosed or unaware of health conditions" does not follow from the research question and the results. Other comments: - l.28 A novel remote web platform was developed. Why and how? - l. 105 The self reporting via a computerized questionnaire could be subject to misinformation. Why was this method used instead of having the person who performed the rest of the measurements (heart rate, blood pressure and so forth) ask these questions to the participants? - l. 134. Subjects unable to stay for the entire duration could exit the study at their own convenience. What happened to these results? Were these participants left out?

	- l. 137 There was an unequal amount of sexes (more male than female) but the gait analysis has an equal percent of both. Please explain. - l. 143 Suddenly swollen joints are measured. In the introduction Dental conditions, cardiac ECG arrhythmias [...] neurological fitness were mentioned. Please link self-reported medical history to the conditions that were within the scope of the study. Make clear which conditions are included with what type of symptoms and which one not. In l. 188 for example the authors refer to specific conditions thorugh diagnostic images and clinical findings. - l. 108 In line with the previous issue, It would have if the authors indicate in more detail what the different devices exactly measure. l. 116. The data analysis part was not clear to me. Did the physicians at a distance try to examine the vital signs? Please be more precise on this part. In general, please stick to the research question and the results that substantiate the answer to this question. Now, as indicated before, apples (TES) are compared with oranges (conventional vital sign measurement) cause not all circumstances are the same for the two different conditions. This is also the reasons that studies are conducted and published on how to set up the study design for eHealth solutions since it it not 'just' comparing one to the other. Please also read:

REVIEWER	Graciela Rojas University of Chile Chile
REVIEW RETURNED	16-Aug-2017

GENERAL COMMENTS	It is a very important manuscript that contributes to the development of health services in countries with limited access to the needed health services

REVIEWER	Enrique Castro Camus Mexico
REVIEW RETURNED	24-Oct-2017

GENERAL COMMENTS	The authots report a comparative study between conventional clinical vital sign diagnostics and "Technology Enabled Screening". The article is interesting and relevant to the journal, however, there are a few aspects that should be revised before publication. Firstly many numbers are reported without much rigor, such as percentages in the methods and results sections and give the impression of being "averages estimated by-eye", please report accurate numbers. Secondly, the TES tests, which is the central point of the article, are not defined in detail. What do they consist of? What are their operation principles (for instance an oximeter works by the IR transmission contrast)? How are the raw data acquired, processed and finally used for diagnostic purposes? These questions need a clear answer within the article.

REVIEWER	Maulik Majmudar Massachusetts General Hospital, Boston, MA, USA
REVIEW RETURNED	31-Oct-2017

GENERAL COMMENTS	The authors should be commended for their effort to opportunistically "screen" hundreds of individuals for a set of medical conditions using smart/ connected devices without the need for expert users. They clearly demonstrate that novel technologies can be leveraged to routinely screen/ test individuals. I am bit confused, however, by the use of the term, "vital sign measurements." I think I understand what they mean, but in my opinion, the authors incorrectly use "vital sign measurements" in comparison to detailed screening via organ specific testing. Specifically, one does not expect any abnormality in vital signs when looking for abnormalities in oral health, ophthalmologic health, or gait/neurologic assessment. The authors would be better off using the term "routine health screening", which usually involves screening for obesity, hypertension, and diabetes, among others. In addition, I believe that the key point of this manuscript is the fact that "comprehensive health screening" of various organ systems can be carried in a convenient and cost-effective manner with the use of newer commercially-available technologies, and in doing so, they can identify a significant proportion of "apparently healthy" individuals with clear abnormalities that may have serious downstream health consequences. The authors should also expand on the "remote analysis" of data collected so that the readers can better understand the amount of time it takes to review the data and arrive at a diagnosis. Also, how was the analysis of remotely collected data validated? By definition, "screening" should be a relatively convenient, low-cost, and scalable approach. So, if the remote analysis of data obtained via technology-enabled screening was a timely process, it may make the entire screening process, impractical in regards to resource utilization. May be the authors would like the manuscript to focus on "routine health screening" versus "comprehensive health screening with the use of technology" and evaluate the number of abnormalities picked up with either approach and the differences in time/ effort/ resources required to do so.

VERSION 1 – AUTHOR RESPONSE

- Please revise your title to state the research question, study design, and setting (location). This is the preferred format for the journal.

Author response: The title has been revised to: Evaluation of technology-enabled examinations of cardiac rhythm, optic nerve, oral health, tympanic membrane, gait and coordination jointly with routine health screenings: An observational study.

- Please include an 'Article summary' section consisting of the heading: 'Strengths and limitations of this study', and containing up to five short bullet points, no longer than one sentence each, that relate specifically to the methods of the study reported. This should be placed after the abstract.

Author response: “Strengths and limitations of this study” section has been added after the abstract in lines 47-54 of the revised manuscript to now read:

- This is one of the first studies to investigate using technology-enabled screenings to augment routine health examinations
- A remote examination platform was developed to facilitate diagnoses of health conditions by multiple physicians
- The overall study size is large, but some organ-specific tests will benefit from larger studies.
- Sample sizes for each test were different with respect to number of subjects and gender distribution.
- The study is cross-sectional.

- Please remove all study findings from the introduction section.

Author response: We have removed all findings from the final paragraph of the introduction in the revised manuscript.

- Please ensure the manuscript is correctly formatted as per our guidelines for research articles: http://bmjopen.bmj.com/pages/authors/#research For example please remove the section titled "what this study adds".

Author response: A thorough re-examination of the revised manuscript was done to ensure adherence to the guidelines. We have revised the manuscript to conform to the guidelines, and made following structural changes: 1) The abstract in lines 22-42 of the revised manuscript is structured with the proper sections, with individual sections added for design, setting, participants, and results. 2) We removed three sections after the abstract that did not conform to the guidelines: “What is already known about this subject”, “What are the new findings”, and “Impact on clinical practice.”

Reviewer: 1
Reviewer Name: S.E. Wildevuur
Institution and Country: FSW, VU University Amsterdam (NL)
Please state any competing interests: None declared

Please leave your comments for the authors below

First of all, I would like to compliment the authors on te research conducted in a still virginal area. The market of technology enabling non-invasive diagnostic screening is growing but we still lack evidence on the significance and efficacy of such devices.

Author response: Thank you for your positive and constructive feedback. We hope this work will inform and engender future research in this area.

The authors stated in the first paragraph that the significance and efficacy is unevaluated for primary screening of patients (l. 24). Ofcourse, this is an important research field. However, the study seems to compares apples and oranges. As the authors indicated the effectiveness of technology-enabled screening is limited (l. 79). The authors compare multiple types of TES, of which the significance and efficacy are not clear from these studies AND they compare it with traditional vital sign examination, using video's. From the study the main research topic seems to be comparing the two different approaches to find evidence of the significance and efficacy of TES vs conventional vital sign examination. What have been conducted as research is not so much the efficacy and the significance of TES but how TES is compared to conventional vital sign examination. To phrase (l 258) that "these subjects were either previously undiagnosed or unaware of health conditions" does not follow from the research question and the results.

Author response: Thank you for this insight and presenting a complementary evaluation of this work. We agree with you that one of the objectives of the study was to find evidence of the significance and efficacy of multiple TES tests vs conventional vital sign examination and we discuss this in the original submission. The manuscript had attempted to convey that past studies did not sufficiently investigate the combined usage of multiple TES devices to augment primary care examinations vs. effectiveness of each individual test. The TES tests used in the study have been validated to be efficacious for certain subsets of conditions by previous reports cited in the introduction of the original submission and appear in lines 64-76 of the revised manuscript. The original statement has also been clarified by rephrasing line 79 (now in lines 74-76 of the revised manuscript) to: "The majority of previous studies using newer TES approaches have been performed in silos concentrating on individual devices or specific anatomical sites, often precluding more comprehensive assessment of patient health." Line 258 has also been rephrased (now in lines 268-270 of the revised manuscript) to clarify the relationship between TES and routine health screenings and now reads: "TES thus facilitates more thorough and non-invasive primary care screenings and may expedite early interventions for conditions not identified by routine health screenings."

This study could be interpreted as two parts: one about the prevalence of conditions identified in individual TES tests and another about the value proposition of using multiple TES tests in conjunction with routine health screenings, resulting, as the reviewer points out, in further validation of the devices used for technology-enabled screening. The objective of presenting routine health screenings alongside TES tests was to recreate the state of primary healthcare and so to be able to determine if multiple TES tests can be used to diagnose conditions that would remain undiagnosed by routine health screenings alone. We agree with the reviewer that it is difficult to directly compare those conditions measured by TES tests and routine health screenings. To this end, we have removed, rephrased, and clarified such comparisons in the following sections:

- The 'objectives' section of the abstract has been rephrased in lines 22-24 of the revised manuscript to: "Technology-enabled non-invasive diagnostic screening (TES) using smartphones and other point-of-care medical devices was evaluated in conjunction with conventional routine health screenings for the primary care screening of patients."
- The analysis of the 111 subjects who completed all screenings has been rephrased to clarify that TES augments rather than replaces routine health screenings in lines 239-257 in the revised manuscript
- The discussion in the revised manuscript no longer compares the results of TES and routine health screenings by rephrasing lines 268-270 in the revised manuscript to:

"TES thus facilitates more thorough and non-invasive primary care screenings and may expedite early interventions for conditions not identified by routine health screenings."

Other comments:

- l.28 A novel remote web platform was developed. Why and how?

Author response: A remote annotation platform was developed for the purpose of clinically evaluating TES results by a panel of physicians. Remote annotations were chosen in order to maximize physicians' time in the field for screening additional subjects. Subsequently, the remote examination platform was utilized to share de-identified data to protect patient privacy with physicians who provided clinical evaluations for each test. Multiple physicians were able to use the remote platform to provide diagnoses for each TES test leading to comprehensive analyses whereas in the field only one physician would have been able to make a diagnosis. Supplementary Figure 2 shows remote interfaces shared with remote physician annotators. We have rephrased lines 112-114 in the revised manuscript to motivate the remote web platform and refer readers to an revised discussion in the supplementary methods section: "Expert physicians conducted diagnostic feature annotation of de-identified images and videos collected by TES via a web-based examination portal in order to

maximize time in the field for screening additional subjects (Supplementary Methods)." The technical description of the platform has also been expanded in lines 92-95 in the supplementary appendix of the revised manuscript to: "Videos captured by TES devices were categorized by patient ID and TES examination and displayed directly to expert physicians via a web-based examination portal conducted diagnostic feature annotation of de-identified images and videos. This password-protected secure interface was developed using web technologies (HTML, JavaScript, node.js) for this purpose and displayed an image or video for one patient at a time for a given examination." The code of the remote annotation tool will be available upon request to the authors.

- l. 105 The self reporting via a computerized questionnaire could be subject to misinformation. Why was this method used instead of having the person who performed the rest of the measurements (heart rate, blood pressure and so forth) ask these questions to the participants?

Author response: A physician administered the questionnaire and subjects provided verbal answers that were entered into the computerized form to ensure uniformity and prevent misinformation. We agree that receiving past medical records from a healthcare provider would have been preferable, but since this was a large field study we did not have access to those records. This has been clarified in lines 97-101 in the revised manuscript to: "A designated physician administered a medical questionnaire, where subjects provided verbal answers and the physician was responsible for entering their answers into a computerized interface. The detailed questionnaire included geographic and demographic questions as well as questions about past medical history and current illnesses but did not capture data from past healthcare records."

A specific physician administered each measurement—TES tests and those included as routine health screenings— for the duration of the study to maintain uniformity. The physician assigned to administer the questionnaire did so for all subjects. We have added this clarification to the methods section in lines 101-102 in the revised manuscript: "Height, weight, systolic and diastolic blood pressure, resting heart rate, and temperature were also each measured, separately by a different physician." We have rephrased all mentions of "self-reported medical history" to "medical questionnaire" throughout the revised manuscript to clarify how the questionnaires were administered.

- l. 134. Subjects unable to stay for the entire duration could exit the study at their own convenience. What happened to these results? Were these participants left out?

Author response: Subjects were allowed to exit the study at their own convenience. Two types of analyses were performed:
1) Analyses of results from specific tests include data from all subjects who completed that test.
2) The data from 111 subjects who completed all TES tests and routine health screenings were analyzed together. Whereas, data from subjects who were unable to complete all TES tests and routine health screening were not considered in this more comprehensive analysis.
We have rephrased the data analyses of exiting subjects and subjects who completed all tests in lines 94-95 in the revised manuscript: "Subjects could exit the study at their convenience, and the study design allowed for different numbers of subjects for each test (Table 1)." A sentence stating that data from all subjects was analyzed has been added in lines 122-123 in the revised manuscript: "Analyses of results from specific tests include data from all subjects who completed that test." Lines 135-136 in the revised manuscript have been rephrased to no longer reference subjects exiting since it has been addressed in the methods section. Lines 241-242 in the revised manuscript have been rephrased to: "Subjects who exited the study before completing all routine health screenings and TES tests were not considered in these analyses." We have also rephrased lines 325-327 in the revised manuscript to read: "Due to some subjects leaving the study early, the numbers of patients examined by each TES

test and routine health screening were not identical, restricting more comprehensive analyses to the 111 subjects who completed all tests."

- l. 137 There was an unequal amount of sexes (more male than female) but the gait analysis has an equal percent of both. Please explain.

Author response: Subjects exited the study at their convenience; the subjects who stayed long enough to complete the gait analysis happened by chance to be equal numbers of males and females. We clarify the sex distribution for the gait analysis in lines 138-141 in the revised manuscript as: "The gender breakdown for nearly all tests was approximately 60% males and 40% females, though gait analysis had an equal percent of both because the subjects who stayed long enough to complete that screening happened by chance to be split equally among males and females."

- l. 143 Suddenly swollen joints are measured. In the introduction Dental conditions, cardiac ECG arrhythmias [...] neurological fitness were mentioned. Please link self-reported medical history to the conditions that were within the scope of the study. Make clear which conditions are included with what type of symptoms and which one not. In l. 188 for example the authors refer to specific conditions thorugh diagnostic images and clinical findings.

Author response: The medical history questionnaire asked many different questions, one of which was about swollen joints, to identify novel cross-correlations between seemingly unlinked medical history conditions and other screenings. Dental conditions, ECG arrhythmia, and neurological fitness were each tested by the TES tests as mentioned in line 188, which now have been rephrased in lines 195-197 in the revised manuscript to: "Fig 2 shows representative diagnostic images and associated diagnoses captured using TES." Lines 147-148 have been added in the revised manuscript to clarify origin of swollen joints and related conditions: "Medical histories of dental issues, swollen joints, hearing difficulties, and leg cramps were each reported by 26.1%, 25.3%, 21.9%, 18.6% of the population, respectively." We have revised the discussion of the medical history in the Results section in lines 163-164 in the revised manuscript to direct readers to the full list of medical history questions in the supplement: "Supplementary Tables 2, 3, and 4 each show the full list of questions asked by the medical questionnaire."

Conditions were identified from the routine health screenings using clinically accepted ranges for those measurements. These ranges and associated references are provided in lines 85-91 in the supplementary appendix of the revised manuscript: [Obes Res. 1998;6 Suppl 2:51S-209S, Circulation. 2005;111(5):697-716, Med Devices (Auckl). 2014;7:231-9]. Additional citations that refer readers to this more detailed discussion have been included at the beginning of the Results section in lines 128-130 of the revised manuscript: "Accepted clinical ranges add reference for each condition identified by routine health screenings through consultation with physicians and were applied automatically to the routine health screening data without requiring physicians to annotate the data on a per-patient basis (Supplementary Methods)."

The specific clinical conditions identified by the doctors have been added to the end of that discussion in in lines 107-109 of the supplementary appendix of the revised manuscript: "Conditions outside the normal range identified by physicians for each TES test are as follows. Oral imaging: caries, missing teeth, periodontal disease; tympanic membrane imaging: perforated eardrum, effusion; optic nerve head photography: width of optic rim 0.01-0.1; coordination analyses: abnormal finger-nose test."

Each TES test had a single remote annotation interface that all physicians were shown. A description of the interfaces and resulting diagnoses has been added in lines 95-103 of the supplementary appendix of the revised manuscript.

- l. 108 In line with the previous issue, It would have if the authors indicate in more detail what the different devices exactly measure.

Author response: Lines 40-79 in the supplementary appendix of the revised manuscript now describe the devices and the mechanisms by which they operate for each of the TES tests. We now direct readers to this discussion by rephrasing lines 110-111 in the revised manuscript: “The supplementary appendix details specific procedures for each device and the principles by which each operates.” The conditions annotated in TES tests were added to lines 106-109 of the supplementary appendix of the revised manuscript as described above.

l. 116. The data analysis part was not clear to me. Did the physicians at a distance try to examine the vital signs? Please be more precise on this part.

Author response: Lines 112-124 in the revised manuscript and lines 92-102 in the supplementary appendix of the revised manuscript now describe the web annotation interface. Supplementary Figure 2 presents the interfaces used by physicians for remote examination. The aforementioned revisions have been made to describe how physicians remotely annotated only the TES videos. We have revised lines 128-130 in the revised manuscript to more precisely describe that the doctors did not remotely examine vital signs: “Accepted clinical ranges for each condition identified by routine health screenings through consultation with physicians and were applied automatically to the routine health screening data without requiring physicians to annotate the data on a per-patient basis (Supplementary Methods).”

In general, please stick to the research question and the results that substantiate the answer to this question. Now, as indicated before, apples (TES) are compared with oranges (conventional vital sign measurement) cause not all circumstances are the same for the two different conditions. This is also the reasons that studies are conducted and published on how to set up the study design for eHealth solutions since it it not 'just' comparing one to the other. Please also read:

Author response: Thank you for your detailed feedback, it has helped in clarification of this work. The study the reviewer indicates unfortunately was not included in the response to authors. We have, however, undertaken meticulous and thorough revisions in accordance with what the reviewer has suggested. As discussed above, direct comparisons between TES and routine health screenings have been removed in the revised manuscript. We hope the revised manuscript suitably addresses your suggestions and questions.

Reviewer: 2
Reviewer Name: Graciela Rojas
Institution and Country: University of Chile, Chile
Please state any competing interests: I declare that I do not have any competing interest

Please leave your comments for the authors below
It is a very important manuscript that contributes to the development of health services in countries with limited access to the needed health services

Author response: The authors appreciate your positive response to our manuscript. Research in this area is especially important for expanding healthcare access in low- and middle-income countries, and we hope that this work will contribute to solutions for these pressing issues.

Reviewer: 3
Reviewer Name: Enrique Castro Camus
Institution and Country: Mexico

Please state any competing interests: None declared

Please leave your comments for the authors below

The authots report a comparative study between conventional clinical vital sign diagnostics and "Technology Enabled Screening". The article is interesting and relevant to the journal, however, there are a few aspects that should be revised before publication.

Firstly many numbers are reported without much rigor, such as percentages in the methods and results sections and give the impression of being "averages estimated by-eye", please report accurate numbers.

Author response: Thank you very much for the positive feedback. All percentages were calculated and reported rounded to the nearest percent. We now report all percentages to the nearest tenth of a percent throughout the text of the revised manuscript and where applicable in Table 1 and Supplementary Tables 2, 6, 7, 9, 11, 13. Lines 111-125 in the supplementary appendix of the revised manuscript describe the statistical methods we performed to determine correlations between conditions.

Secondly, the TES tests, which is the central point of the article, are not defined in detail. What do they consist of? What are their operation principles (for instance an oximeter works by the IR transmission contrast)? How are the raw data acquired, processed and finally used for diagnostic purposes? These questions need a clear answer within the article.

Author response: The principles by which the TES devices operate have now been described more comprehensively, and lines 40-79 in the supplementary appendix of the revised manuscript have been revised to include references to the devices and the mechanisms by which they operate for each of the TES tests. These references are listed below for easy access:

Pulse oximetry: Med Devices 743 (Auckl). 2014;7:231-9.
ECG: Smartphone ECG for evaluation 703 of STEMI: results of the ST LEUIS Pilot Study. J Electrocardiol. 2015;48(2):249-59
Tympanic membrane imaging: Am J Emerg Med. 2015;33(8):1089-92.
Oral imaging: Clin Oral Investig. 2016;20(1):151-9
Optic nerve head photography: J Ophthalmol. 2015;2015:823139
Microsoft Kinect: Annual 709 International Conference of the IEEE Engineering in Medicine and Biology Society (Embc). 2012:1960-7.

We have added additional description of the data acquisition, processing, and diagnosis in lines 92-95 in the supplementary appendix of the revised manuscript: “Videos captured by TES devices were categorized by patient id and TES examination and displayed directly to expert physicians via a web-based examination portal conducted diagnostic feature annotation of de-identified images and videos. This password-protected secure interface was developed using web technologies (HTML, JavaScript, node.js) for this purpose and displayed an image or video for one patient at a time for a given examination.” We also direct readers to the supplementary description in lines 110-111 in the revised manuscript: “The supplementary appendix details specific procedures for each device and the principles by which each operates.” The remote annotation process is described on lines 95-103 in the supplementary appendix of the revised manuscript. The specific conditions identified by the doctors have been added to the end of that discussion on lines 106-109 in the supplementary appendix of the revised manuscript: “Conditions outside the normal range identified by physicians for each TES test are as follows. Oral imaging: caries, missing teeth, periodontal disease; tympanic

membrane imaging: perforated eardrum, effusion; optic nerve head photography: width of optic rim 0.01-0.1; coordination analyses: abnormal finger-nose test."

Reviewer: 4
Reviewer Name: Maulik Majmudar
Institution and Country: Massachusetts General Hospital, Boston, MA, USA
Please state any competing interests: None

Please leave your comments for the authors below

The authors should be commended for their effort to opportunistically "screen" hundreds of individuals for a set of medical conditions using smart/ connected devices without the need for expert users. They clearly demonstrate that novel technologies can be leveraged to routinely screen/ test individuals.

Author response: Thank you for your positive and constructive feedback.

I am bit confused, however, by the use of the term, "vital sign measurements." I think I understand what they mean, but in my opinion, the authors incorrectly use "vital sign measurements" in comparison to detailed screening via organ specific testing. Specifically, one does not expect any abnormality in vital signs when looking for abnormalities in oral health, ophthalmologic health, or gait/neurologic assessment. The authors would be better off using the term "routine health screening", which usually involves screening for obesity, hypertension, and diabetes, among others. In addition, I believe that the key point of this manuscript is the fact that "comprehensive health screening" of various organ systems can be carried in a convenient and cost-effective manner with the use of newer commercially-available technologies, and in doing so, they can identify a significant proportion of "apparently healthy" individuals with clear abnormalities that may have serious downstream health consequences.

Author response: Thank you for this recommendation. We have changed all uses of "vital sign measurements" to "routine health screening" to more accurately describe the non-organ-specific screenings throughout the paper. We emphasize your assessment of the paper's key point in the discussion in lines 259-270 in the revised manuscript.

The authors should also expand on the "remote analysis" of data collected so that the readers can better understand the amount of time it takes to review the data and arrive at a diagnosis. Also, how was the analysis of remotely collected data validated? By definition, "screening" should be a relatively convenient, low-cost, and scalable approach. So, if the remote analysis of data obtained via technology-enabled screening was a timely process, it may make the entire screening process, impractical in regards to resource utilization.

May be the authors would like the manuscript to focus on "routine health screening" versus "comprehensive health screening with the use of technology" and evaluate the number of abnormalities picked up with either approach and the differences in time/ effort/ resources required to do so.

Author response: We have included the amount of time physicians spent on each video in lines 121-122 of the revised manuscript to read: "On average, each physician spent tens of seconds to approximately a minute annotating each per video." Diagnoses obtained through TES examinations were validated by asking multiple doctors for remote diagnoses and requiring a majority diagnosis. Lines 118-121 of the revised manuscript state: "A panel of at least three physicians for each type of

examination was assembled who remotely and independently annotated the data facilitated by the web interface. The majority ratings for each subject were then calculated for all TES tests. For subjects with no majority rating, the lesser of the tied ratings was chosen to not overstate the prevalence of diagnosed illnesses." We chose remote annotations in order to maximize physicians' time with subjects for screenings. We have rephrased lines 112-114 in the revised manuscript to explain the rationale for the remote web platform and to refer readers to an expanded discussion in the supplementary methods section: "Expert physicians conducted diagnostic feature annotation of de-identified images and videos collected by TES via a web-based examination portal in order to maximize time in the field for screening additional subjects (Supplementary Methods)." The authors appreciate the point made by the reviewer that screening should not be resource intensive. One of the objectives of this study was to evaluate contribution of TES to augment routine health screenings. A supplementary examination of the timeliness and scalability of TES is important but outside the scope of this study. The authors appreciate the point that comprehensive TES can be used in conjunction with routine health screenings and thank the reviewer. The extent to which TES and routine health screenings identify different subjects as abnormal has been included in the results subsection titled "TES synergistically identifies unique subset of abnormal individuals in conjunction with routine health screenings" in lines 239-257 of the revised manuscript.