Computer-assisted Auscultation as a screening tool for Cardiovascular Disease: A cross-sectional study

by

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DECLARATION

I, ………*Liesl Joanna Zühlke*………………………, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Date: 14 February 2011

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Part A: Protocol

Computer-assisted Auscultation as a screening tool for Cardiovascular Disease: A cross-sectional study

1. Synopsis:

Cardiac auscultation remains an important diagnostic tool that provides clinicians with a wealth of information regarding patients' cardiac health. In association with clinical features, auscultation gives the physician sufficient information to make diagnoses and guide referrals. However the qualitative nature of this practice, combined with inadequate training and of late, skills, may limit the ability of clinicians to detect and diagnose abnormalities using this method alone. The ability to make an accurate diagnosis in particular discerning an innocent murmur from one suspicious of pathology has been diminished as this skill is being lost. Computer-assisted auscultation is a tool with the potential to make a quantitative and objective assessment of cardiac auscultation. The purpose of this study is to determine whether the two computer-assisted auscultation methods currently available (Sensi® and Cardioscan® respectively) can accurately and with ease, identify patients who would qualify for referral for echocardiography for heart disease. We envisage that if deemed to be accurate, this tool could be incorporated into a tertiary cardiac clinic to aid diagnoses and patient management.

2. Research questions:

The proposed research therefore addresses the following research questions:

- How accurate is computer-assisted auscultation at identifying patients who would qualify for referral for echocardiography for heart disease?
- How does the Sensi® system under development in Cape Town compare with the FDA-approved Cardioscan® system?
- How feasible is the application of computer-assisted auscultation within a tertiary cardiac clinic?

3. Background and Rationale:

Ever since the invention of the stethoscope by Laennec in 1816, it has been an indispensable aid for the evaluation and management of patients in everyday practice. (1) In the hands of skilled practitioners, cardiac auscultation is an important diagnostic tool that provides clinicians with a wealth of information regarding the cardiac status of a patient. In association with other clinical features, auscultation gives the physician sufficient information to make diagnoses and guide referrals in the majority of situations. In addition, it connects the physician and the patient and constitutes an important part of the ritual of "laying-on of hands", creating a relationship between the physician and the patient. (2)

Prior to the development of the electrocardiogram (ECG) and more recent imaging modalities, the stethoscope was hailed as the most useful investigative tools in the cardiologist's armamentarium and cardiologists of the past were legendary in their mastery of the "art" of cardiopulmonary auscultation. (3)

However the qualitative nature of this practice may limit the ability of clinicians to detect and diagnose abnormalities using this method alone. In fact, there is decreasing confidence in clinical skills generally and ever-increasing reliance on laboratory and diagnostic investigation to solve clinical problems. This is particularly so in cardiology with an increased reliance on echocardiography as the 'new stethoscope'. (4) As early as the nineties, a mere 50 years after the invention of echocardiography, reports (5, 6) bemoaning the poor auscultatory skills of residents was published together with serious concerns regarding inadequate training and emphasis on the importance of this skill. (7) In a recent multi-centre study of physicians, trainees, students and faculty, it was reported that although the sensitivity for systolic murmurs was high (0.84), it carried a very low specificity (0.4) and when tested with diastolic murmurs, the sensitivity was in fact no better than chance (0.5) (8) In addition to this alarming trend, a conventional stethoscope has no ability to record sounds, offer a visual display or transmit sounds to multiple listeners, all critical to the effective teaching of auscultation. (5)There is thus an

urgent need to explore other methods which can be employed in both the practice and teaching of cardiac auscultation. We suggest that computer-assisted auscultation may provide this much-needed extension of an old friend. (9)

3.1. Innocent murmurs

Heart murmurs are common in the general public although many have no clinical relevance and are termed "innocent" murmurs. Innocent heart murmurs are sounds made by blood circulating through heart chambers and valves or blood vessels near the heart. Innocent heart murmurs are more common in children and are considered to be harmless. (10) Up to 80% of paediatric patients will have a murmur on examination although less than 1% will eventually have a congenital heart defect. (11) Praecordial murmurs are also common in young adults, occurring in between 29-52% of the general population. (12) Over-referral of patients with innocent murmurs for echocardiography is most likely due to the declining expertise in cardiac auscultation coupled with increasing reliance on echo-based diagnoses but has serious cost and personnel implications.

Echocardiography is considered to be the gold standard to determine pathological cardiac lesions. However the American Heart Association and the American College of Cardiology (AHA/ACC) defines Class 1 recommendations for echocardiography as those patients where "clinical features indicate at least a moderate probability that a murmur reflects structural heart disease." (13)The AHA/ACC guidelines strongly discourage indiscriminate use of echocardiography as a screening tool due to the not insignificant cost and the over-sensitive nature of the results. In current resource-restrained times, the appropriate use of technology, skills and personnel is an important factor to consider when managing referrals. High-end echo machines are exorbitantly expensive and even the decreasing price of portable machines is difficult to justify in developing countries.

In 2009, South Africa had twenty four practicing paediatric cardiologists, equally distributed between public and private sector units, with a further eight undergoing training. (14) This is woefully inadequate for the needs of the country's children and significantly less than the 88 paediatric cardiologists required for the population of South Africa. (15)   Although paediatric cardiologists can accurately diagnose an innocent murmur with a high degree of sensitivity and specificity (16), a referral to a paediatric cardiologist implies inappropriate use of skilled and scarce personnel. Travel to centres where cardiologists are based, with attendant costs and loss of income, is costly to patients and parents. The cost in terms of understanding and concern regarding the diagnosis of an innocent murmur is of course difficult to estimate as would be the cost of an inaccurate diagnosis of innocent murmur. (17)

3.2. Referrals for structural heart disease

Although the American Heart Association and the American College of Cardiology (AHA/ACC) only recommends that patients with suspected pathological murmurs be referred for an echo, (18) patients are still routinely referred to a specialist cardiac unit for echocardiography for the evaluation of a murmur. In a retrospective review of 3 460 adult referrals for echocardiogram with the coding "murmur" as the primary reason for the referral, less than 50% had significant valvular disease. (19) In another study, approximately two thirds of patients referred to a cardiac centre for initial evaluation of heart murmurs had no cardiac abnormalities.(20) In paediatrics, although heart murmurs are the most common reason for referral to cardiologists, 50-70% of these murmurs are benign. (21). The usefulness of a device to aid diagnostic accuracy of referring physicians in determining pathological murmurs cannot be over-emphasized.

3.3 Computer-assisted auscultation

In the pre-echocardiography era, the standard acoustic/mechanical stethoscope was used as a tool to differentiate not only innocent from pathological murmurs but to diagnose cardiac disease consistently and accurately. The advent of echocardiography has led to the use of portable machines which have proven to have superior sensitivity when compared to the mechanical stethoscope in screening for valvular heart disease in asymptomatic children. (22) The yield by portable echocardiography is 10 times greater than the mechanical stethoscope, leading to the recommendation to abandon the ordinary stethoscope. (4)However, the relatively high cost of high-quality portable echocardiography machines and the need for trained echocardiographers hamper the adoption of this screening modality on a large scale in poor developing countries where valvular heart disease remains endemic. It is therefore mandatory to explore other simple, sensitive, accessible, and affordable technologies, such as the newly developed electronic/digital stethoscope.

The electronic stethoscope may overcome the disadvantages of the mechanical stethoscope. The digital stethoscope provides better sound quality and visual display of the wave form of the sound. (9) Signals obtained electronically may be subjected to objective visual and numerical analysis, transmission to distant sites, and storage for medical and research purposes. The quantitative measurement of the intensity of the heart sounds and murmurs in the spectral display which is recorded simultaneously with the waveform of the sounds allows objective classification into normal and abnormal sounds. (23) Of particular importance in developing countries, is the cost, time and human resource saving associated with its use. The digital stethoscope is a fraction of the cost of a portable echocardiography machine, and can be used by nurses or other community health workers on all patients. Of the most value perhaps, is the possibility of providing

objective, reliable findings that are readily interpretable by practicing clinicians to facilitate appropriate referrals to tertiary services.

The Zargis ® Medical Corporation has FDA clearance for the first product with clinically validated indications for uses including the detection of heart murmurs. Sensitivity for detection of murmurs increased from 77% to 89% with the use of computer-assisted auscultation (CAA) while the referral sensitivity increased from 87% to 93%. (24)

The development of a South African hand-held electronic device that can record heart sounds using a digital stethoscope, analyze the recordings and aid examiners in distinguishing between innocent and pathological murmurs is now at an advanced stage. To date, the hand-held device has a screening sensitivity and specificity of 90% and 97% respectively compared to agreement with echocardiography. (25)

Computer-assisted auscultation provides increased objectivity to a traditionally subjective, increasingly difficult clinical skill. A diagnostic support tool that could increase sensitivity and specificity of the echocardiography referral decisions could potentially be highly cost-effective, facilitate a more efficient use of personnel and resources and may indeed be the promising technology required to improve the referral decisions of primary care physicians. (23)

4. Hypothesis

Primary: Computer-assisted auscultation is accurate at identifying patients who require referral for echocardiography for heart disease in a tertiary cardiac service for both adults and children.

Secondary: The Sensi® unit compares favourably to the FDA- approved Cardioscan® system both in terms of feasibility and accuaracy.

5. Objectives:

The aims of this study are:

1. To evaluate the sensitivity and specificity of computer-assisted auscultation when compared to echocardiography to identify patients who require referral for heart disease.

2. To evaluate the Sensi® system in comparison with the FDA-approved Cardioscan® system.

3. To describe the feasibility of performing computer-assisted auscultation within a tertiary cardiac clinic.

6. Significance and Implications:

Computer-assisted auscultation is a tool with the potential to make a quantitative and objective assessment of cardiac auscultation. Incorporating CAA into clinical practice could potentially allow for appropriate additional information in terms of structural heart disease and may well serve as a clinician's tool especially in resource-poor settings allowing for easier diagnosis.

We envisage that this will improve the quality of patient care and reduce the costs associated with inappropriate referral and the use of more expensive technologies. In addition it would add a further dimension to patient management in terms of the ability to store audio files in patients' records and providing a new platform for teaching and training.

7. Methods

7.1 Study design

In this cross-sectional study, eighty consecutive patients referred for assessment to either the Groote Schuur Hospital (GSH) cardiac clinic or the cardiologists at Red Cross War Memorial Children's Hospital (RCWMCH) will be recruited for the study. All patients will be enrolled by a qualified nursing sister and once consent has been given, enrolled in the study. Participants will undergo an examination using both of the computer-assisted auscultation methods with results recorded in audio files and noted in unique-numbers case record forms. Patients will thereafter undergo the standard examination as per standard of care which will include in each case, an echocardiogram and clinical examination. At the end of the examination session, the nurse will complete a case record form detailing the referral request, findings of physicians, the echocardiogram findings and the results of the audio files of the two auscultation methods. It is possible that in certain cases the physicians' examinations and echocardiogram will occur before the auscultation, as the auscultation will in no way influence the standard procedures occurring at each institution. The findings of referring physicians will not be entered into the computer at the time of auscultation, hence not influencing the outcome of the computer assessment. The results of the computer's findings will not be revealed to any treating physicians.

7.2 Characteristics of the study population

Setting: Patients are referred to RCWMCH and GSH cardiac clinics as the 2 of the 3 major referral hospitals in the Western Cape. These patients are referred for both structural and functional concerns and referrals are from physicians as well as GPs or primary health care practitioners. These are the two largest referral centres in the Western Cape and will represent the patients referred for tertiary cardiac opinion.

7.3 Recruitment and enrollment

GSH: Patients referred for echocardiogram are referred directly to the echo clinic. These patients will be approached by our nursing sister and screened for possible participation. This will occur prior to or in some cases after the echocardiogram has been performed and will not influence the waiting time of the participants. The research nurse will ensure that patients do not miss their space in the queue. The entire process should take less than 15 minutes to complete.

RCWMCH: Patients referred to paediatric cardiology are referred in one of 2 ways: either directly to the senior registrar on call or to the cardiac clinic. On the days that the nursing sister is on site on clinic days, she will liaise with the sister running the clinic and identify all new referrals and approach them to participate in the study, again taking care not to lose any places in the queue. Patients will be examined in a separate cubicle and thereafter return to the queue for standard care. The names of patients referred directly to the senior registrar will be given to the study sister who will then approach the patient and his/her legal guardian for consent before enrolling a patient in the study. These patients are normally in-patients and will be seen by cardiologist when time allows- hence these patients will not be inconvenienced by the study. Auscultation in these patients can occur at the bedside providing environmental conditions are appropriate.

7.4 Inclusion and exclusion criteria:

80 consecutive patients from the two institutions will be recruited. Recruitment will occur on the days when the trained sister is on site only. All stable patients outside of the newborn period will be screened for possible inclusion. Patients over the age of 18 will approached to give consent; consent will be taken from the legal guardians of children under the age of 18 as well as assent from those over the age of 8 years. Patients speaking and understanding English and Afrikaans will be

approached for possible participation in the study. If an interpreter is available, patients speaking only Xhosa will also be approached.

Patients who have been operated upon or those who are unable to provide or those who refuse informed consent will be excluded from participation. Patient deemed too unstable will also be excluded from the study.

7.5 Research procedures and data collection methods

Patients will be enrolled and using designated case record forms (CRF) data will be captured regarding baseline demographic data, reason for referral, clinical, echo findings followed by the findings of the two systems.

Data collection method:

Patients will be examined in a quiet area in either the cardiac clinic or at the bedside. When using the Zargis® system, the patient is auscultated using a Bluetooth Littman® electronic stethoscope. The heart sounds and if present murmurs are transmitted to a receiving computer loaded with the Cardioscan ®software. The heart sounds are recorded at 4 positions for 20 seconds each. The software will analyse the recording for up to one minute and the display the findings as abnormal or normal. Computer-assisted auscultation findings will be stored on a password-controlled netbook in .zac files for the Zargis® system. These files will be downloaded to a portable hard-drive for storage and analysis.
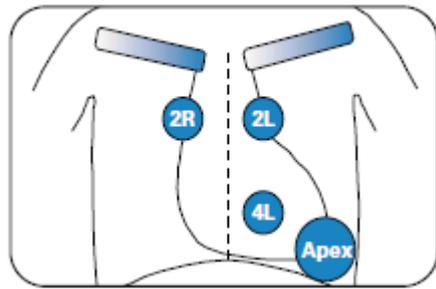
user interface.

Figure 1. Areas of Auscultation   Figure 2. Zargis ®user interface.
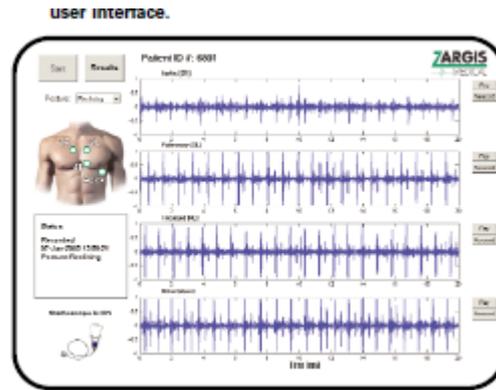
With the Sensi® system, 3 ECG electrodes will be placed upon the chest. Following this, recordings at the same four precordial positions will be made. Again the recordings will take 20-30 seconds per site and up to one minute to analyse. The results are displayed on the computer and converted into .pdf files while the audio files are saved as .wmv files.

As one can see from Fig 2 above, the records in the four positions will be displayed as would be any murmurs detected together with the analysis decision. The nursing sister conducting the study will undergo extensive training on the operation of both systems; equipment will be kept in a secure location and protected to ensure that neither the stethoscopes nor the laptop are damaged.

7.6 Data safety and monitoring

1.   Data: The research sister will keep all recordings in a data base on a computer provided by the principal investigator. All audio files can only be accessed via a password. The Bluetooth stethoscope itself can only be utilized if the matching computer and passwords are connected. The associated patient consent and clinical forms will also be kept by the research sister and then transferred and filed in a locked facility at Groote Schuur Hospital. Keys are kept by the sister and the principal investigator.

2.   The Principal investigator will collect the recordings and forms on a predefined time from the locked facility and enter it onto an additional data base. This will be done on regular intervals and will serve as a back-up and will also be kept in a locked facility.

3.   The sister will collect the echocardiogram reports from the cardiac clinic at Groote Schuur and Red Cross Children's Hospitals. If any doubts regarding diagnosis exist, she will confirm the diagnosis with the cardiologist on call without revealing the findings of the computer-assisted auscultation.

4.   The Principal investigator will evaluate all recordings and forms before approving it as suitable for use and included it in the final analysis.

5.   Finally a study monitor will review the entire process before commencing the study and again at the end of the study to ensure quality assurance and control. This monitor will be approached by the P.I. to perform this task.

7.7 Data analysis

Data will be entered into an Excel spreadsheet and analysed using STATA® version 11, Stata Corporation, 4905 Lakeway Drive, College Station, Texas 77845 USA. The original paper based questionnaire will be entered onto a database. All original questionnaires will also be stored for validation purposes. A sample size of 80 patients was calculated to achieve <10% confidence intervals around an estimated sensitivity of 90% for either computer-assisted stethoscope.

The variables as listed in Table 1 will be collected.

Table 1. Variables collected			
Variable Name	**Scale of Measurement**	**Variable Name**	**Scale of Measurement**
Age in months/years	Numerical Continuous	Echo category	Categorical nominal
GSH or RXH	Categorical Binary	0= Normal, no heart disease	
Ward vs. Outpatient referral	Categorical Binary	1= Acyanostic congenital	
Reason for referral	Text field	2+ Cysnotaic congentital	
CAA completed 0=Both completed 1=One only	Categorical Binary	3= Valvular heart disease 4=Cardiomyopathies 5= Other.	
Clinical Diagnosis	Categorical Nominal	S quality	Categorical Nominal
Findings on Cardioscan ® 1=Abnormal 2=Normal	Categorical Binary	0= Excellent 1= Some problems but protocol complete 2= Bad, protocol not completed	
Findings on Sensi® system 1=Abnormal 2=Normal	Categorical Binary	S confidence	Numerical continuous
		C quality	Categorical Nominal
Echocardiogram diagnosis	Categorical Nominal	0= Excellent 1= Problems but protocol completed	
Standard Auscultation	Categorical Nominal	2= Bad, protocol not completed	
Murmur class 0= normal Heart Sounds,, no murmur 1= 1/6 Ejection Systolic Murmur 2= 2/6 Ejection systolic murmur 3= 3/6 Haolsystolic murmur 4=2/6 midsystolic murmur 5=2/6 Diastolic murmur 6=2/6 Continous murmur	Categorical nominal	S _prot 0=Protocol not completed 1=Protocol completed	Categorical Binary
		C_prot 0=Protocol not completed 1=Protocol completed	Categorical Binary
		Echo_diagnosis 0=Normal 1=Abnormal	Categorical Binary
Zargis® recommendation 0=Normal 1=Abnormal	Categorical Binary	Cardioscan® recommendation 0=Normal 1=Abnormal	Categorical Binary
Agecategory 0=Children 1=Adults	Categorical Binary		

The findings of the computer analysis will be recorded as normal or abnormal. The echocardiography findings will be correlated with the findings of the computer assisted method and the sensitivity and specificity to detect heart disease requiring echo will be reported upon. The results will also be stratified in terms of the two hospitals and age categories. The findings in adults and children will be analysed using the Mantel-Haenszel Test for heterogeneity. Analyses will be performed on the subcategories of pathologies. The 2 methods will be compared and the feasibility in terms of conducting the study will be assessed.

8. Expected benefits to individual participants and potential societal benefits

There will be no immediate benefits to any of the patients involved in the study. Computer-assisted auscultation potentially could improve the diagnostic accuracy of standard auscultation; provide objective and repeatable findings and aid in the teaching and training of clinicians and students in standard auscultation. Potentially this could also be a cost-effective device that could be widely used by primary care physicians, community nurses or even health care workers and as such be an ideal tool for us in resource-poor settings. In addition many murmurs in childhood are termed innocent as they do not represent any pathology and in fact, should not be subject to unnecessary referrals.

9. Consent and assent

A screening log will be held of all potential participants. All participants that are eligible for inclusion will then be approached and given the opportunity to enter the study. Recruitment will only be done at the cardiac clinics and through cardiology registrars on call. Informed consent and assent will be taken by the research sister.

As auscultation is a common and widely accepted standard of care, we do not envisage any worries or concerns to be raised by patients or their carers. In the consent process

we will explain that the computer-generated findings will not be transmitted to the physicians and that the results of the computer findings will have no influence on current care but is focused on testing new technology and influencing future approaches. As the entire process takes less than 15 minutes (including consent process) we foresee that it will be acceptable to all patients.

10. Description of risks and benefits

As auscultation is a common and widely accepted standard of care, we do not envisage any additional risks for patients or their carers. Auscultation will be performed using a digital stethoscope that connects to a computer-programme using a Bluetooth device. The Sensi® system has 3 electrocardiogram (ECG) electrodes in addition to the device which is applied to the chest.

Both the Cardioscan® and Sensi® systems take 20 seconds per recording area (4 precordial positions) and then an additional minute to analyse.

The auscultation will take place in a standard clinic room within the cardiac clinic or at the bedside when appropriate. Any patients deemed in any way unstable or ill will be excluded from the study and referred for immediate medical attention if required.

11. Privacy and confidentiality

Privacy and confidentiality will be maintained at all times. All examinations and screening procedures will occur in private, all data will be recorded on case record forms, maintaining patient confidentiality, revealed only to the study team. The research sister is GCP-trained and NIH certified. Audio records will be stored on a netbook computer which will be password-protected.

12. Reimbursement for participation

As patients will not be inconvenienced nor be required to travel, we will not offer any compensation.

13. Emergency care and insurance for research-related injuries

Any critically ill patients or patients in the newborn period will be excluded. Children are often referred for structural heart disease and as the incidence of congenital heart lesions at birth is just under 1% (26), this is an important group to include in our study. Possible risks related to examination are felt to be minimal.. Patients are covered by the University of Cape Town no-fault insurance.

14. Significance

Computer-assisted auscultation potentially could improve the diagnostic accuracy of standard auscultation; provide objective and repeatable findings and aid in the teaching and training of clinicians and students in standard auscultation. Potentially this could also be a cost-effective device that could be widely used by primary care physicians, community nurses or even health care workers and as such be an ideal tool for us in resource-poor settings. In addition many murmurs in childhood are termed innocent as they do not represent any pathology and in fact, should not be subject to unnecessary referrals.

15. Conclusion

Although echocardiography is a sensitive tool for detecting structural heart disease, it is expensive and out of reach for many low-income countries. Diagnostic skills appear to

have decreased markedly of late and this has led to an over-reliance on echocardiography and hence increased referrals to tertiary centres for benign conditions such as innocent murmurs.

We believe that computer-assisted auscultation method is a feasible, effective and valuable new tool to assess patients in a tertiary cardiac setting for referral for echocardiography.

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17. Appendices

17.1 Consent Form (English)

Participant Information Leaflet and consent form: Adults

Computer-Assisted Auscultation

Title:	Is computer-assisted auscultation accurate at identifying heart disease requiring referral for echocardiography in a tertiary cardiac clinic?
FHS HEC No:	
Principal Investigator:	Dr Liesl Zühlke MBCHB DCH FCPaeds Cert Card(SA)
Address and Contacts:	Groote Schuur Hospital, Old Main Building 021 4047676
Contact number:	0214047676

This is a very important form. You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand.

- It is very important that you are fully satisfied and clearly understand what this research entails and you could be involved.

- Your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you or negatively in any way whatsoever.

- You are also free to withdraw from the study at any point, even if you do initially agree to let take part.

This study has been approved by *the Faculty of Health Sciences Human Ethics Committee no: 359/2010* and will be conducted according to the ethical guidelines and principles of the International Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research. This is an important form. Before you make a decision to take part in the study, it is important that you understand why the project is being conducted and what it will involve. If you have any questions feel free to ask your doctor. Your signature on this form means that you wish to take part in this study.

What is this research study all about?

The aim of this project is to determine whether a computer can tell which heart sounds and murmurs will need specialist attention. To achieve this, two special stethoscopes will be used to record your hearts sounds and this will be sent to a recorder/computer where the heart sound data will be analysed. This will only take a few minutes to do. You will still be seen by the doctor and have whatever tests he/she feels are necessary. The doctor will not see the results of the computer's opinion.

Why have I been invited to participate?

You have been chosen for this study since they have been referred to these heart clinic/heart specialists. Once you consent to participate, our research staff will collect some information about you and use the special stethoscopes to listen to your heart and record the heart sounds. No other tests will be performed for this study. You will then have your normal examination by the doctors. We will ensure that you do not lose your place in the queue.

Are there benefits to taking part in this study?

There are no direct benefits to you by participating in the study. By participating in the study you will be providing us with valuable information regarding a possible future test that can help doctors and patients. This may ultimately lead to improvements in care of patients like you in the future.

What are the risks in participating in the study?

There are no risks to you in participating in this study. All the equipment is approved, a qualified nursing sister will perform the test and everything will be done at this clinic/or at the bedside.

Do I incur any costs due to my participation in the study?

No, you will not incur any extra costs as a result of participating in the study. You will not be reimbursed for participating in the study.

Voluntary Participation

It is entirely your decision to participate in the study. If you want to discontinue from the study at any point of time you are free to leave without stating any reason. Your withdrawal will not affect your treatment at this hospital. Irrespective of your decision to participate in the study, you will still receive the standard treatment for your illness.

What about confidentiality?

The investigators will ensure that personal information obtained from you for the study will remain confidential throughout the study period. When the results are published in a medical journal, your name and other details will not be disclosed.

What will happen in the unlikely event of me getting injured in any way, as a direct result of taking part in this research study?

A full investigation, that includes your involvement, will be launched and you will be compensated if negligence was the cause of the injury.

Thank you for taking time to read this information sheet.

If you have any study related queries you can contact, **Dr. L.Zühlke**, Paediatric Cardiologist Department of Paediatric Cardiology, Red Cross Children's Hospital at **021- 4047676.**

If you wish to take part in this study, please sign and date the consent form given to you. You will be given a copy of the information sheet and your signed consent form.

Declaration by patient

By signing below, I *(name of patient)*..

agree to take part in a research study entitled: **Computer-Assisted Auscultation:**

 Is computer-assisted auscultation accurate at identifying heart disease requiring referral for echocardiography in a tertiary cardiac clinic?

I declare that:

- I have read or had read to me this information and consent form and that it is written in a language with which I am fluent and comfortable.

- I have had a chance to ask questions and all my questions have been adequately answered.

- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.

- I may choose to withdraw   from the study at any time and I will not be penalised or prejudiced in any way.

- I may be asked to leave the study before it has finished if the study doctor or Study nurse feels it is in my best interests.

Signed at *(place)*.. on *(date)*.......................................2011.

✕
_____
Printed name Signature Date

Declaration by investigator

I (*name*) .... declare that:

_ I explained the information in this document to
....

_ I encouraged him/her to ask questions and took adequate time to answer them.

_ I am satisfied that he/she adequately understand all aspects of the research, as discussed

above

_ I did/did not use a interpreter (*if a interpreter is used, then the interpreter must sign the*

declaration below).

Signed at (*place*)... on (*date*).. 2011.

X _____

Signature of investigator

• I assisted the investigator (*name*) .... to explain

the information in this document to (*name of participant*)

.... using the language of Afrikaans/Xhosa.

• We encouraged him/her to ask questions and took adequate time to answer them.

3. IF THE PARENT/GUARDIAN CANNOT READ THE FORM THEMSELVES, A WITNESS MUST SIGN HERE:

I was present while the informed consent document with benefits, risks and procedures were read to the parent/guardian and the participant. The parent/guardian has freely and voluntarily agreed to allow her/his daughter/son to take part in the research.

Signed at (*place*) .... on (*date*) .... 2011.

X _____

Signature of witness

17.2 Consent Form (Afrikaans)

<u>Deelnemer Informasieblad en toestemmingsvorm: Kinders</u>
<u>Vir gebruik deur ouers/wettige voog</u>

Rekenaar-Geassisteerde Gehoor van hartklanke:

Titel:	**Is rekenaar-geassisteerde gehoor van hartklanke akkuraat daarin, om hartprobleme wat verwysing vir eggokardiogram na 'n tersiêre hartkliniek vereis, te identifiseer?**
FHS HEC Nr:	
Hoof Ondersoeker:	Dr Liesl Zühlke MBCHB DCH FCPaeds Cert Card(SA)
Adres en Kontakbesonderhede:	Rooikruis Kinderhospitaal, Mowbray 021 6585366 Groote Schuur Hospitaal, Ou Hoofgebou 021 4047676
Kontaknommer:	0214047676

Hierdie is 'n baie belangrike vorm. U kind (of wyk, indien toepaslik), word gevra om deel te neem aan 'n navorsingsprojek. Die inligting wat hierdie vorm bevat, beskryf die inhoud van die projek. Ruim asseblief tyd in om dit te lees. Voel vry om enige vrae oor enige deel van hierdie projek wat u nie heeltemal verstaan nie aan die studie personeel of dokter te rig.

- Dit is baie belangrik dat u heeltemal tevrede is en duidelik verstaan wat hierdie navorsing behels en hoe u kind daarby betrokke kan wees.

- U kind se deelname is heeltemal vrywillig en u beskik oor die reg om deelname te weier. Indien u nee sou sê, sal dit nie u of u kind op enige wyse benadeel nie.

- U is ook vry om hom/haar ten enige stadium van die projek te onttrek, selfs al het u aanvanklik ingestem om hom/haar te laat deelneem.

Hierdie studie is goedgekeur deur *die Fakulteit van Gesondheidswetenskappe Menslike Etiese Kommittee nr:* en sal uitgevoer word volgens die etiese regulasies en beginsels van die Internasionale Verklaring van Helsinki, Suid-Afrikaanse Riglyne vir Goeie Kliniese Praktyk en die Mediese Navorsingsraad (MNR) Etiese Riglyne vir Navorsing.

Dit is 'n belangrike vorm. Voor u besluit om deel te neem, is dit belangrik dat u verstaan hoekom hierdie projek uitgevoer word en wat dit behels. Voel vry om enige vrae aan u dokter te rig. Jou handtekening op hierdie vorm sal beteken dat jy kies om deel te neem aan die studie.

Waaroor gaan hierdie navorsingstudie?

Die doel van hierdie projek is om te bepaal of 'n rekenaar kan aandui watter hartklanke en geruise die aandag van 'n spesialis nodig het. Om dit reg te kry, sal twee spesiale stetoskope gebruik word om u kind se hartklanke op te neem. Die opname sal na 'n opnemer/rekenaar gestuur word waarop die hartklank data geanaliseer gaan word. Dit sal slegs 'n paar minute neem om te doen. U sal steeds deur die dokter gesien word en alle toetse ondergaan wat hy/sy voel nodig is. Die dokter sal nie die uitslag van die rekenaar-opinie sien nie. **Hoekom is my kind gevra om deel te neem?**

Jou kind is gekies vir hierdie studie omdat hy/sy verwys is na hierdie hartkliniek/hart spesialis. Sodra u toestemming gee vir u kind om deel te neem, sal ons navorsing personeel sekere inligting oor u kind insamel en die spesiale stetoskope gebruik om na u kind se hart te luister en die hartklanke op te neem. Geen ander toetse sal vir hierdie studie uitgevoer word nie. Jy sal daarna jou normale ondersoek by die dokters ondergaan. Ons sal seker maak dat u nie u plek in die ry verloor nie.

Is daar enige voordeel daarin om deel te neem aan die studie?

Daar is geen direkte voordele verbonde aan u of u kind se deelname aan die studie nie. Deur deel te neem aan die studie sal u ons van waardevolle inligting voorsien aangaande 'n moontlike toekomstige toets wat dokters en pasiënte kan help. Dit mag uiteindelik lei tot verbeteringe in die toekomstige sorg van pasiënte, soos uself.

Wat is die risiko's daaraan verbonde om aan die studie deel te neem?

Deelname hou geen risiko's vir u of u kind in nie. Al die toerusting is goedgekeur, 'n gekwalifiseerde suster sal die toets uitvoer en alles sal gedoen word by hierdie kliniek/ langs die bed.

Sal my deelname aan die studie my enigeiets kos?

Nee, u sal nie enige ekstra uitgawes hê as 'n resultaat van u deelname aan die studie nie. U sal nie finansiële vergoeding ontvang vir deelname aan die studie nie.

Vrywillige Deelname

Dit is heeltemal u eie besluit om deel te neem aan die studie. Indien u op enige stadium van die studie wil onttrek, is u vry om so te doen, sonder om enige rede te gee. Jou onttrekking van die studie sal nie u behandeling by hierdie Hospitaal affekteer nie. U sal steeds standard behandeling vir u kondisie ontvang, ongeag u besluit om deel te neem aan die studie of nie.

Wat van konfidensialiteit?

Die ondersoekers sal u verseker dat alle persoonlike inligting wat van u verkry is, konfidensieël gehou sal word, regdeur die duur van die studie. Wanneer die resultate

gepubliseer word in 'n mediese joernaal, sal u naam en ander besonderhede nie bekend gemaak word nie.

Wat sal gebeur ingeval die onwaarskynlike gebeur en u kind beseer word as 'n direkte resultaat van deelname aan die navorsingstudie?

'n Volledige ondersoek, wat u betrokkenheid insluit sal volg, en u sal vergoed word indien enige nalatigheid die oorsaak was van die besering.

Dankie vir die tyd wat u afgestaan het om die inligtingsblad te lees.

Indien u enige studie-verwante vrae het, kan u **Dr. L.Zühlke**, Pediatriese Kardioloog by die Departement van Pediatriese Kardiologie, Rooikruis Kinderhospitaal kontak by **021- 4047676.**

Indien u kies om deel te neem aan die studie, kan u asseblief die toestemmingsvorm wat aan u gegee word teken, asook die datum aandui. U sal 'n afskrif van die inligtingsblad en die getekende toestemmingsvorm gegee ontvang.

Verklaring deur ouer/wettige voog

Deur hieronder te teken, stem ek *(naam van ouer/wettige voog)…………………………………………..*

in om my kind (name van kind) .... wat

…………………….jaar oud is, te laat deel neem aan die navorsingstudie getitel: **Rekenaar-geassisteerde Gehoor van hartklanke: Is rekenaar-geassisteerde gehoor van hartklanke akkuraat daarin, om hartprobleme wat verwysing vir eggokardiogram na 'n tersiêre hartkliniek vereis, te identifiseer?**

Ek verklaar dat:

- Ek hierdie inligting en toestemmingsvorm gelees het, of dat dit aan my gelees is en dat dit geskryf is in 'n taal waarin ek vlot is en waarmee ek gemaklik voel.

- Indien my kind ouer as 7 jaar is, hy/sy moet instem om deel te neem aan die studie en dat sy/haar INSTEMMING EN BEGRIP aangedui moet word op die vorm.

- Ek het die geleentheid gehad het om vrae te vra en al my vrae is voldoende beantwoord.

- Ek verstaan dat my deelname aan die studie **vrywillig** is en dat daar nie druk op my geplaas is om my kind te laat deelneem nie.

- Ek mag kies om my kind op enige stadium te onttrek en dat my kind op geen wyse gepenaliseer of bevooroordeel sal word nie.

- My kind gevra mag word om die studie te verlaat voor dit klaar is, indien die studie dokter of navorser voel dit in my kind se beswil is.

Geteken te *(plek)*.. op *(datum)*.......................................2010.

X
_____
Signature of parent/legal guardian

Verklaring deur ondersoeker

Ek (*name*) .... verklaar dat:

⎯ Ek die informasie in die dokument aan .... verduidelik het

⎯ Ek hom/haar aangemoedig het om vrae te vra en dat ek genoeg tyd ingeruim het om dit te beantwoord.

⎯ Ek tevrede is dat hy/sy all die aspekte van die navorsing voldoende verstaan, soos bo bespreek

⎯ Ek het 'n tolk geberuik / nie (*indien 'n tolk gebruik is, moet die tolk die verklaring hieronder teken*).

Geteken te (*plek*).. op (*datum*)... 2010.

X
_____
Signature of investigator

Verklaring van tolk

Ek (*name*) ....verklaar dat:

• Ek die ondersoeker (*name*) .... geassisteer het deur die informasie in hierdie dokument aan (*name van die ouer/wettige voog*)

....te verduidelik in die taal van Afrikaans/Xhosa.

• Ons het hom/haar aangemoedig om vrae te vra en het genoeg tyd geneem om dit te beantwoord.

• Ek het die feite aan my voorgelê korrek vertolk.

• Ek is tevrede dat die ouer/wettige voog die inhoud van hierdie ingeligte-toestemming dokument volkome verstaan en dat sy/haar vrae bevredigend beantwoord is.

Geteken te (*plek*) .... op (*datum*) .... 2010.

X _____

Signature of interpreter

3. INDIEN DIE OUER/VOOG NIE HIERDIE VORM SELF KAN LEES NIE, MOET 'N GETUIE HIER TEKEN:

Ek was teenwoordig terwyl die ingeligte-toestemming dokument insluitend voordele, risiko's en prosedures aan die ouer/voog en die deelnemer gelees is. Die ouer/voog het vrylik en vrywilliglik ingestem om sy/haar dogter/seun te laat deelneem aan die navorsing.

Geteken te (*plek*) .... op (*datum*) .... 2010.

X _____

Signature of witness

Vorm van Instemming en Begrip vir Kinders 8 jaar en ouer

Ons is dokters en susters van Rooikruis Kinderhospitaal, Groote Schuur Hospitaal en Tygerberg

Hospitaal en ons is besig om 'n studie te doen oor die harte van kinders. Ons wil graag sien of 'n rekenaar kan sien watter hartklanke spesiale dokters nodig het om meer toetse te doen. Ons kyk na kinders wat na hierdie kliniek gestuur is. Ons wil graag vra of ons na jou hart kan luister met hierdie spesiale stetoskope. Dit sal nie seer wees nie en is baie vinnig.

Indien jy ja sê om deel te neem aan die studie, sal jy dokters help om te weet hoe om ander kinders beter te behandel in die toekoms. Jy mag sê dat jy nie in die studie wil wees nie. Niemand sal vir jou kwaad wees as jy nee sê nie.

Voor jy besluit, kan jy vir ons vrae vra. As jy in die studie wil wees, moet jy jou name op hierdie papier skryf. Dit beteken dat jy gelukkig voel om deel te wees van die studie.

Kinder Deelnemer:

X
Printed name Signature Date

Studie dokter of navorsing suster:

X
Printed name Signature Date

Getuie:

X
Printed name Signature Date

17.3 Case Record Form

Computer-assisted auscultation

d	d	m	m	2	0	y	y

Pt sticker

Hosp eg RXH, GSH

Echo clinic	
Ward, if yes, which?	
Opd ref	

Informed consent: yes..

Informed assent: yes..

Age in Months:

Age in years:

Reason for referral to clinic/cardiologist:…………………………………………………………..

Findings

Zargis Cardioscan:

Completed Protocol:

Yes

NO

Conclusion: normal ☐   abnormal ☐

Attached .zac file ☐

Diacoustic Sensi :

Completed Protocol:

Yes

No

Confidence level: ☐☐☐ %

Conclusion: normal ☐   ☐ abnormal

Attached .avi file ☐

<u>Clinical Diagnosis:</u>

Clinical Diagnosis:

Reported by:

Position: eg MO/Reg/GP/Cardiologist

Source   doc   [   ]   attached:

<u>Echocardiographic Diagnosis:</u>

Echo Diagnosis:

Reported by:

Position: eg tech/Reg/GP/Cardiologist

Source   doc   [   ]   attached:

Part B: Structured Literature Review

1. Introduction

For decades, cardiac auscultation has been an important diagnostic modality, providing skilled clinicians with important information regarding patients' cardiac health. In association with other clinical features, auscultation gives the physician sufficient information to make diagnoses and guide referrals. In addition, it is simple, cheap and accessible. However, this practice remains qualitative and highly subjective. The ability to discern an innocent murmur from one suspicious of pathology is rapidly diminishing. The time has come to reconsider the way we use auscultation and bring it into the current technological era. The development of digital stethoscopes and the additional analysis software elevates the simple stethoscope into a tool with the potential to make cardiac auscultation a quantitative and objective assessment.

2. Background

Ever since the invention of the stethoscope by Laennec in 1816, it has been an indispensable aid for the evaluation and management of patients in everyday practice. (1) In the hands of skilled practitioners, cardiac auscultation is an important diagnostic tool, allowing clinicians to diagnose cardiac disease consistently and accurately. In addition, it connects the physician and the patient and constitutes an important part of the ritual of 'laying-on of hands', creating a relationship between the physician and the patient. (2) Prior to the development of the electrocardiogram (ECG) and more recent imaging modalities, the stethoscope was hailed as the most useful investigative tools in the cardiologist's armamentarium, and cardiologists of the past were legendary in their mastery of the 'art' of cardiopulmonary auscultation. (3, 4)

However, of late, there is decreasing confidence in clinical skills generally and ever-increasing reliance on laboratory and diagnostic investigation to solve clinical problems. This is particularly so in cardiology with an increased reliance on echocardiography as the 'new stethoscope'. (5) In as early as the nineties, a mere 50 years after the

invention of echocardiography, reports bemoaning the poor auscultatory skills of residents were published (6, 7) together with serious concerns regarding inadequate training and emphasis on the importance of this skill. (8) In a multi-centre study of physicians, trainees and faculty, it was reported that although the sensitivity for systolic murmurs was high (0.84), it carried a very low specificity (0.35), and when tested with diastolic murmurs, the sensitivity was in fact no better than chance (0.49). (9)

In addition to this alarming trend, a conventional stethoscope has no ability to record sounds, offer a visual display or transmit sounds to multiple listeners, all critical to the effective teaching of auscultation. (6) There is thus an urgent need to explore other methods which can be employed in both the practice and teaching of cardiac auscultation. (10)

3. The Needs

3.1 Innocent murmurs

The ability to differentiate between an innocent and a pathological murmur is a fundamental skill for primary health care physicians. Innocent heart murmurs, made by blood circulating through heart chambers and valves or blood vessels near the heart, are more common in children and are considered to be harmless. (11) Up to 80% of paediatric patients will have a murmur on examination, although less than 1% will eventually have a congenital heart defect. (12) Precordial murmurs are also common in young adults, occurring in between 29-52% of the general population. (13) Differentiating between an innocent and a pathological murmur requires considerable skill and confidence as well as intimate knowledge of the manoeuvres required to confirm the innocent nature of the murmur, coupled with the appropriate physical examination. (14) However, due to frequently limited auscultation experience and decreasing confidence in clinical skills, this skill is being lost. (15) In fact, in a study by Gaskin, the innocent murmur was the most frequently misdiagnosed lesion when testing auscultatory skills in paediatric residents. (16) Over-referral of patients with innocent murmurs for echocardiography also has serious cost and personnel

implications. The cost in terms of understanding and concern regarding the diagnosis of an innocent murmur is difficult to estimate, as would be the cost of an inaccurate diagnosis of an innocent murmur. (17) The diagnosis of an innocent murmur by a paediatric cardiologist has been shown to result in parental acceptance of the absence of disease and therefore led to children being treated normally. (18) This may be due to the weight given to a sub-specialist opinion, as opposed to that of a general physician or paediatrician. However, this fundamental differentiation between an innocent and a pathologic murmur should be within the skill set of any generalist. (19)

3.2 Class I recommendations for echo

Echocardiography is considered to be the gold standard to determine pathological cardiac lesions. Yet, the guidelines by the American Heart Association and the American College of Cardiology (AHA/ACC) strongly discourage indiscriminate use of echocardiography as a screening tool due to the cost and the over-sensitive nature of the results. The AHA/ACC defines Class 1 recommendations for echocardiography as those patients where 'clinical features indicate at least a moderate probability that a murmur reflects structural heart disease'. (20)A study evaluating the ACC/AHA echocardiographic guidelines demonstrated a 100% negative predictive value for innocent murmurs detected by experienced cardiology staff. In this study, an approach following the guidelines on the use of echocardiography would have prevented 58% of echocardiograms, at a not insignificant cost. (21) In addition, Class II a recommendations are defined as conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness and efficacy of echocardiography. Finally, Class III recommendations speak to conditions for which there is evidence and/or general agreement that echocardiography is not useful and may in some cases be harmful. In current resource-restrained times and low- or middle-income countries, the appropriate use of technology, skills and personnel is an important factor to consider when managing referrals. High-end echo machines are exorbitantly expensive,

and even the decreasing price of portable machines is difficult to justify in developing countries.

3.3 The lack of sufficiently qualified practitioners

In 2009, South Africa had only 24 practicing paediatric cardiologists (22), significantly less than the 88 paediatric cardiologists required for the children of South Africa. (23) This is woefully inadequate for the needs of the country's 18.7 million children. Although paediatric cardiologists can accurately diagnose an innocent murmur with a high degree of sensitivity and specificity (24), a referral to a paediatric cardiologist for an innocent murmur implies inappropriate use of skilled and scarce personnel as well as the attendant costs related to travel and loss of income. A dearth of practicing physicians is a problem shared by many low- and middle-income countries with access to sub-specialists or even specialists confined to larger centres and capital cities only. (25)

3.4 The range of auditory sounds

Standard auscultation, though cheap and accessible, is highly subjective, relies heavily on the skill and experience of the operator, and is subject to inherent human acoustic abilities. In addition, different stethoscopes also have different abilities, and electronic or digital stethoscopes have the added benefits of being able to increase the sound and amplify certain elements. The range at which we hear heart sounds and murmurs is within the range of frequencies detectable by the human ear. The human ear is capable of hearing frequencies within the range of 20-20,000 Hz during childhood and 50-12,000 Hz in adulthood. (26) The human ear performs best in the range 1-2 kHz while below 30Hz or above 18 Hz, the sensitivity falls effectively to zero. It is thus not surprising that some physicians encounter problems when identifying some murmurs or added sounds. Firstly, the cardiac threshold lies close to the threshold of hearing, so

that low-frequency murmurs such as the diastolic murmur of mitral stenosis in the range 20-70Hz are often missed by physicians.
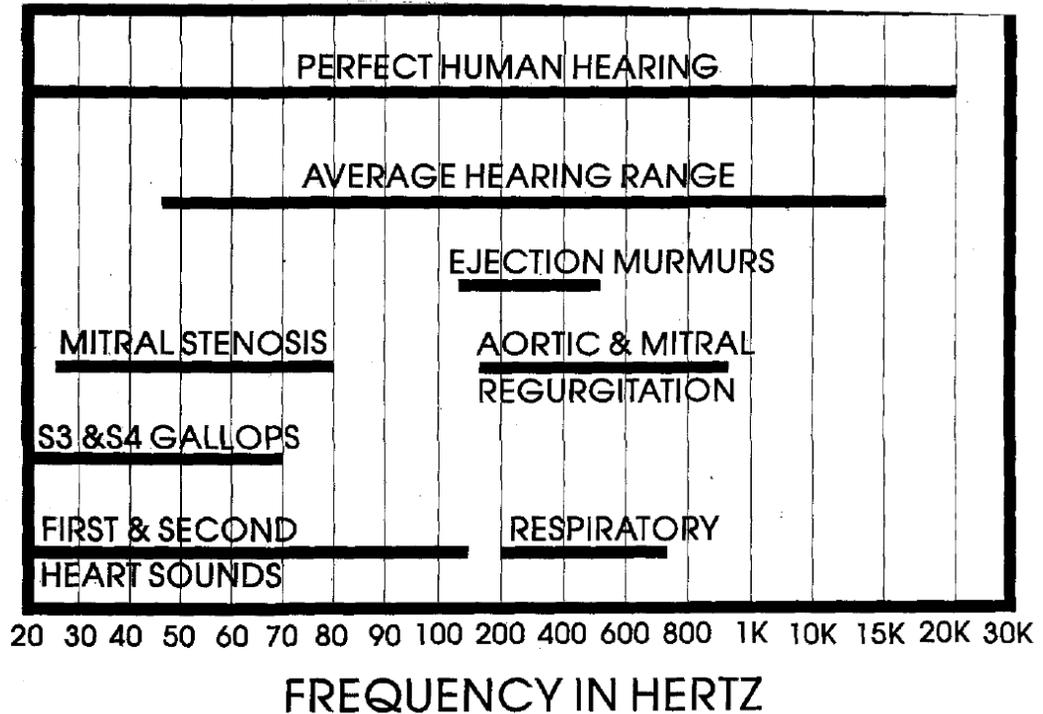

Fig.1 Relative Frequency ranges (Taken from Selig M. Am Heart Journal. 1993) (27)

Secondly, the ear has great difficulty in detecting certain sounds in the presence of other loud sounds or high ambient noise. Hospital wards are notorious for having high levels of ambient noise and monitors with loud alarms. Thirdly, the auscultator needs intensive training to achieve the ability to actively listen, selectively discern and lock on pertinent information while blocking out extraneous noise such as breath sounds. Fourthly, the human ear also has great difficulty in discriminating time intervals. The smallest interval that can be confidently discriminated is 20 msec. It is hardly surprising, therefore, that the awareness of the splitting of the second sound, occurring within 30 msec, may be a difficult new skill to acquire. Finally, some colleagues (elderly physicians or younger colleagues who may have listened to loud music for prolonged periods) may simply not possess the acoustic ability to hear high-frequency sounds such as the soft diastolic murmur of aortic regurgitation. (27) Although the stethoscope is a simple

instrument, skilled use is anything but simple. Proficiency requires good hearing, the ability to concentrate and discriminate, a quiet environment and a sense of auditory pattern recognition. It is clear, therefore, that standard auscultation is highly subjective, clearly dependent on many variables, lacks sufficient sensitivity and is limited by inherent human acoustic abilities.

3.5 The waning art of auscultation

The lack of ability of today's physicians to competently and confidently diagnose a pathological murmur and reliably discern this from an innocent murmur has been blamed on many things, from the increasing reliance on technology to the lack of experienced teachers, coupled with decreased bedside teaching. Despite the fact that directors of medical school programs considered auscultation an important clinical skill worthy of additional training, only 27.1% of internal medicine and 37.1% of cardiology programs offered any structured teaching of auscultation. (6)Of more concern in this study, was the findings that the accuracy levels, when tested on 12 pre-recorded cardiac events, was only 0% to 56.2% for cardiology fellows (median 21.9%) and 2% to 36.8% for medical residents (median 19.3%). Of even more concern was the finding that residents improved little with time and training and were never better than third-year medical students. A multi-centre study, testing medical students, trainees, physicians and teaching faculty, more comprehensively, demonstrated low specificity for systolic murmurs (0.35) and low sensitivity for diastolic murmurs (0.49). (9) Paediatric residents fared somewhat better when tested on patients with a variety of cardiac diagnoses. (28) Although the overall accuracy rate was only 30%, there was an improvement with experience, and the ability to identify an innocent murmur was 84% in the more experienced residents. These studies have led to wide-spread concerns regarding the waning art of auscultation and the need for more directed teaching of cardiopulmonary auscultation. Several models have been proposed, from using heart sounds simulator laboratories and repetition to the creation of an auscultation's school. (29, 30) The inherent shortcomings of the standard stethoscope viz. the

inability to play back or store heart sounds and transmit sounds to multiple listeners is a major barrier to effective teaching and training in auscultation. (7) The ability of a digital stethoscope to record sounds, replay them at different speeds, provide a visual display, and develop a database of heart sounds for ongoing teaching creates a unique and invaluable platform for teaching auscultation.

3.6 Referrals for structural heart disease

Although AHA/ACC only recommend that patients with suspected pathological murmurs be referred for an echo, (31) patients are still routinely referred to a specialist cardiac unit for echocardiography for the evaluation of a murmur. In a retrospective review of 3 460 adult referrals for an echocardiogram with the coding 'murmur' as the primary reason for the referral, less than 50% had significant valvular disease. (32) Despite a higher percentage of female referrals (61.8% vs. 38.2% males), the percentage of abnormal valves in females was even lower than in males (45.6% vs. 53.5%).

In another study, approximately two thirds of patients referred to a cardiac centre for initial evaluation of heart murmurs had no cardiac abnormalities. (33) In paediatrics, although heart murmurs are the most common reason for referral to cardiologists, 50% to 70% of these murmurs are benign. (34) The usefulness of a device to aid diagnostic accuracy of referring physicians in determining pathological murmurs cannot be over-emphasized.

3.7 Portable echocardiography versus auscultation

Recently, portable echo machines have been proven to have superior sensitivity when compared to the mechanical stethoscope in screening for valvular heart disease in asymptomatic children. (35) The yield by portable echocardiography is 10 times greater than the mechanical stethoscope, leading to the recommendation to abandon the ordinary stethoscope. (5) However, the relatively high cost of high-quality portable

echocardiography machines and the need for trained echocardiographers hamper the adoption of this screening modality on a large scale in poor developing countries where valvular heart disease remains endemic. It is therefore mandatory to explore other simple, sensitive, accessible, and affordable technologies.

3.8 Digital stethoscopes: development and properties

The pursuit of a quantitative and objective stethoscope has plagued investigators for decades, and electronic stethoscopes have been available commercially for some time. (36) Early criticisms related to ease of use, distortion of sound, even creating artefactual sounds, and cumbersome designs. However, over the past decade rapid advances have been made not only in the electronic stethoscopes themselves, but also in the spectral and velocity analyses and automated diagnosis algorithms. (10) The addition of auscultation analysis software has now created vast new opportunities. Computer-assisted Auscultation (CAA) is now able to conduct a spectral and temporal analysis of heart sounds, graphically display energy profiles relating to systolic and diastolic murmurs and formulate a conclusion, relating findings probabilistically to ACC/AHA Class I referral guidelines (37), while providing better sound quality and visual display of the sounds' wave form. (10) The quantitative measurement of the intensity of the heart sounds and murmurs in the spectral display, which is recorded simultaneously with the waveform of the sounds, allows objective classification into normal and abnormal sounds. (38) Signals obtained electronically may be subjected to objective visual and numerical analysis, transmission to distant sites, and storage for medical and research purposes. Although a similar model for pulmonary auscultation does not exist commercially, several instruments are in development (39), and studies are underway to develop appropriate clinical applications. (40)

Of particular importance in developing countries is the cost, time and human resource saving associated with the use of a digital stethoscope. The digital stethoscope and associated software are a fraction of the cost of a echocardiography machine, as well as of the cost associated with travel by the patient to a tertiary centre for evaluation by a

cardiologist, and they can be used by nurses or other community health workers on all patients.

Zargis ® Medical Corporation has Food and Drug Administration (FDA) clearance for the first product with clinically validated indications for uses including the detection of heart murmurs as a physicians' aid. Sensitivity for detection of murmurs increased from 77 % to 89 % with the use of Computer-Assisted Auscultation (CAA), while the referral sensitivity increased from 87 % to 93 %. (41) A South African company recently published findings of a decision support system aimed at the paediatric population. A specificity of 94% and a sensitivity of 91% was achieved using novel signal processing techniques and an ensemble of neural networks as classifier. (42)(43)

3.9 Clinical opportunities

Clinical applications of computer-assisted auscultation have thus far been exceedingly promising in terms of diagnostic decision support, inexpensive screening, and referral decision support. Primary care physicians were able to increase the sensitivity of murmurs detected with the use of CAA from 77% to 89 %, while referral sensitivity increased from 87 % to 93 %, and specificity increased from 64 % to 79 %. (41) The need for a cost-effective screening method to detect athletes at risk of sudden cardiac death due to Hypertrophic Cardiomyopathy (HCM) led to a pilot study examining the level of agreement between auscultatory findings by a cardiologist and the results of CAA. (44) This study was able to identify apical systolic murmurs that are louder in standing than in reclining positions: a cardinal sign of HCM.

Acoustic cardiography is a related technique that records simultaneous digital ECG and heart sounds data, using dual-purpose ECG and heart sounds sensors rather than a digital stethoscope, while providing a computerised interpretation of the findings. An exploratory study determined that the use of this technology improved detection of coronary artery disease with stress testing. (45) The same investigating team was also

able to demonstrate that acoustic cardiography provides similar results, but with improved reproducibility and ease of use to echocardiography in the optimisation of cardiac resynchronization therapy. (46)

3.10 Opportunities for future research

The potential clinical utility of the digital stethoscope and associated software is tremendous, and its use in detecting cardiac disease is very exciting. Heart failure currently affects over 5 million people in the United States. The presence of S3 and S4 heart sounds is an early abnormality in affected patients, yet notoriously difficult to hear and frequently missed. However, these sounds may be detected by CAA. (47) In fact, acoustic cardiography has been demonstrated (48) to outperform B-Natiuretic Peptide (BNP) alone at detecting reduced left ventricular ejection fraction. The most common cause of acquired heart disease in the world, Rheumatic Heart Disease (RHD), has long been neglected due to its waning incidence in the developed world. (49) A landmark study in Mozambique and Cambodia, however, demonstrated the under-appreciation of affected patients by using portable echocardiography. (35) Wider application of this screening protocol using CAA may well be the simpler and more cost-effective way to screen for RHD in resource-poor settings. Preliminary work in this area is currently underway. (50)

4. Challenges and further development

Despite the remarkable potential of CAA, it has yet to be adopted into mainstream clinical practise by practitioners. Becket Mahnke (51) eloquently outlines some of the underlying reasons and identifies some key points. Firstly, it is vital that successful CAA systems have a clearly defined intended use, either screening or diagnostic. In addition, ease of use by minimally trained personnel in a primary care setting is of particular importance. Data must be analysed in real-time and be able to be stored in a format which can be integrated into clinical records. From a technical standpoint, standardized data sets would be of great benefit and need to be highly sensitive and specific. Finally,

a single-site CAA approach does not approximate the clinical routine of auscultation in different sites, use of diaphragm, bell and adjunct manoeuvres to comprehensively examine the heart and lungs.

This may well be achieved by use of a new recording device (Signal®, Zargis Medical, New Jersey) which allows for simultaneous acquisition of 6 auscultatory sites along with a single channel ECG and a plethysmography waveform. Work is currently underway to use this system for signal analysis. Close collaboration between engineers, clinicians and industry partners will be required to produce a CAA system which can truly become an important cardiac screening and diagnostic tool.

5. Conclusion

Heart disease is a major cause of morbidity and mortality throughout all age groups worldwide. For decades, the stethoscope and standard auscultation has been the first screening, diagnostic and prognostic tool utilised by health care providers. However, the inherent limitations of the standard stethoscope, coupled with decreasing clinical competence in its use, has resulted in ever-declining reliance in auscultatory findings, increasing referrals, and use of more expensive technologies when not clinically indicated. Computer-assisted Auscultation (CAA) provides improved objectivity to a traditionally subjective, increasingly difficult clinical skill. A diagnostic support tool that could increase sensitivity and specificity of the echocardiography referral decisions could potentially be highly cost-effective, facilitate a more efficient use of personnel and resources, and may indeed be the promising technology required to improve the referral decisions of primary care physicians.

Incorporating CAA into clinical practice could potentially allow for appropriate additional information in terms of structural heart disease and may well serve as a clinician's tool, allowing for easier diagnosis especially in resource-poor settings. In addition, it would add a further dimension to patient management in terms of the

ability to store audio files in patients' records, and in providing a new platform for teaching and training. The greatest value, perhaps, is the possibility of providing objective, reliable findings that are readily interpretable by practicing primary care clinicians to facilitate appropriate referrals to tertiary services.

[Word count: 3334]

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Part C: Journal manuscript

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Please see Authors instructions in appendices.

Title Page:

Screening for Cardiac Disease using Computer-Assisted Auscultation: A cross-sectional study

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Abstract:

Background: Cardiac auscultation is inherently qualitative, highly subjective and requires considerable skill and experience. Computer-assisted auscultation (CAA) is an objective referral-decision support tool that aims to minimise inappropriate referrals. This study evaluated the sensitivity and specificity of 2 computer-assisted auscultation systems in detecting echo-confirmed cardiac abnormalities.

Methods: There were 79 consecutive patients referred for assessment to a tertiary cardiac clinic recruited into the study. Participants underwent an examination using computer-assisted auscultation (CAA) methods in addition to the standard clinical examination and echocardiogram.

Results: The prevalence of echocardiography-confirmed structural heart disease was 53% (n= 42). The CAA systems were able to complete the recordings in virtually all the cases. The overall sensitivity of Cardioscan® to identify cardiac abnormalities in children was 92% [71-99%] and 60% [41-77%] in adults while the specificity was 47% [21-73%] and 67% [30-93%] in children and adults respectively. The sensitivity of the Sensi® system in identifying cardiac abnormalities in children was 79% [45-93%] and 84% [61-97%] in adults while the specificity was 57% [29-82%] and 67% [30-93%] in children and adults respectively. In subgroup analysis, the sensitivity for detecting acyanotic heart disease was 100% using both Cardioscan® and Sensi®.

Conclusion: Computer-assisted auscultation demonstrates suboptimal sensitivity and specificity in detecting cardiac abnormalities in children and adults. As both systems

demonstrate 100% sensitivity in detecting acyanotic heart disease, and theoretically carries significant potential in resource-limited settings, further development of current technologies to improve sensitivity and specificity for clinical applications is still warranted.

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Computer-assisted Auscultation

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Introduction

Cardiac auscultation is inherently qualitative, highly subjective and requires considerable skill and experience. The decline in teaching of auscultation and poor accuracy at diagnosing heart sounds and murmurs has resulted in a reduced ability to discern an innocent murmur from one suggestive of pathology. The current recommendation is that only patients with suspected pathological murmurs be referred for an echocardiogram. In resource-limited settings, a simple screening tool to identify the need for referral for further evaluation is urgently needed. A referral decision support tool that could increase sensitivity and specificity of echocardiography referral decisions could be the promising technology required to improve the referral decisions of primary care physicians, thereby minimising inappropriate referrals.

Background

In the hands of skilled practitioners, cardiac auscultation is an indispensible diagnostic aid allowing clinicians to diagnose cardiac disease consistently and accurately. (1) Cardiac auscultation serves two important purposes, namely firstly as a screening tool (disease yes/no, requires referral yes/no) and secondly as a cardiac diagnostic tool (disease type and severity). Both these functions can be performed with a high degree of accuracy by cardiologists but less so by primary care health providers. (2) The

importance of the first function, i.e. as a screening tool to differentiate through auscultation whether a patient has cardiac disease and requires referral, should not be over-estimated in the primary health care setting. However, the task of primary care physicians of screening for cardiac disease is made more difficult by the fact that the probability of cardiac disease is low (<1 %). Yet, heart murmurs are very common in the general public, particularly in children, even though most have no clinical relevance. (3) Up to 80% of paediatric patients will have a murmur on examination although less than 1% will eventually have a congenital heart defect.(4) Precordial murmurs are also common in young adults, occurring in between 29-52% of the general population. (5)

Echocardiography is considered to be the gold standard to determine pathological cardiac lesions. However the American Heart Association and the American College of Cardiology defines Class 1 recommendations for echocardiography as those patients where "clinical features indicate at least a moderate probability that a murmur reflects structural heart disease." (6) The American Heart Association and the American College of Cardiology guidelines strongly discourage indiscriminate use of echocardiography as a screening tool due to the significant cost and the over-sensitive nature of the results. Despite this, patients are still routinely referred to a specialist cardiac unit for echocardiography for the evaluation of a murmur. In one retrospective review of 3 460 adult referrals for echocardiogram with the coding "murmur" as the primary reason for the referral in a University Medical Centre in California, less than 50% had significant valvular disease. (7)

The ability to accurately screen for cardiac disease is extremely important in sub-Saharan Africa and other resource-poor settings. The developing world is currently facing a "double burden of disease' the significant infectious disease agenda and the emerging agenda of non-communicable diseases in particular cardiovascular diseases. (8, 9) Cardiovascular disease can be diagnosed in its initial stages facilitating early initiation of therapy while congenital cardiac lesions can be detected early enough to avoid irreversible physiological consequences. In 2009 South Africa had 24 practicing paediatric cardiologists, equally distributed between public and private sector units. (10) This is woefully inadequate for the needs of the country's 18.7 million children and significantly less than the 88 paediatric cardiologists required for the population of South Africa. (11) Although paediatric cardiologists can accurately diagnose an innocent murmur with a high degree of sensitivity and specificity (12), a referral to a paediatric cardiologist for an innocent murmur implies inappropriate use of skilled and scarce personnel as well as a not insignificant social and economic cost. In South Africa and other settings, an accurate cardiac screening tool to identify patients requiring referral for echocardiography has tremendous potential to improve the quality of health care services and reduce costly and unnecessary referrals. Such a tool would need to be highly specific and likelihood ratios should be used in conjunction with pre-test probabilities to provide post-test probabilities of disease.

The goal of this study was to evaluate the sensitivity and in particular, the specificity of 2 computer-assisted auscultation systems in identifying patients who require referral

for suspected cardiac disease when compared to echocardiography. Attention was also paid to the differences between adults and children and comparing the results of the 2 systems.

Computer-assisted auscultation

Over the past decade rapid advances have been made in extending digital auscultation by using spectral and velocity analyses and automated diagnosis algorithms. (13) Computer-assisted auscultation (CAA) is now able to conduct a spectral and temporal analysis of heart sounds, graphically display energy profiles relating to systolic and diastolic murmurs and formulate a conclusion relating findings to the American Heart Association and the American College of Cardiology class I referral guidelines while providing better sound quality and visual display of the sounds' wave form. (13, 14) The quantitative measurement of the intensity of the heart sounds and murmurs in the spectral display, which is recorded simultaneously with the waveform of the sounds, allows objective classification into normal and abnormal sounds. (15) It has been demonstrated that artificial neural networks used in the pattern recognition and classification tasks associated with automated heart sounds analysis is able to achieve sensitivities and specificities of 100% when heart sound samples from selected patients were processed and then fed into a custom artificial neural network using a spectral resolution of 1 Hz and a spectrum of 0-210 Hz. (16)

Zargis ® Medical Corporation was the first product with clinically validated indications for use by physicians including the detection of heart murmurs. Sensitivity for detection of murmurs increased from 77% to 89% with the use of the Cardioscan® software while the referral sensitivity increased from 87% to 93%. Primary care physicians were able to decrease their average false positive referral rate from 37% to 21% (p<0.001) while reducing their false negative rates from 13% to 7%. (17) A South African company recently published findings of their decision support system aimed at the paediatric population. A specificity of 94% and a sensitivity of 91% were achieved using novel signal processing techniques and an ensemble of neural networks as classifier. (18) (19) A referral decision support tool such as CAA could potentially be highly cost-effective and facilitate a more efficient use of personnel and resources especially in low and middle-income countries.

Methods

We conducted a cross-sectional screening study among patients referred to Groote Schuur or Red Cross War Memorial Children's Hospital. These are 2 of the 3 major referral hospitals in the Western Cape. These referrals are from physicians, paediatricians or primary health care practitioners. Seventy-nine consecutive patients referred either assessment of possible heart disease, follow-up of known heart disease or cardiac evaluation in the setting of other diseases were recruited for the study between the period 1 October 2010 and 31 January 2011.

The University of Cape Town Human Research Ethics Committee reviewed and approved the protocol (HREC Ref No 359/10).

Consented participants underwent the standard examination including in each case, an echocardiogram and clinical examination followed by an examination using both of the computer-assisted auscultation methods. Neither the physician nor the echocardiographer was aware of the findings of the digital recordings. Echocardiograms were deemed normal if no diagnosis other than physiological pulmonary and tricuspid regurgitation was made. All studies with structural heart disease were deemed abnormal. All echocardiograms were performed by trained echocardiographers.

With the Cardioscan® system, the patient was auscultated using a Littman® Bluetooth electronic stethoscope. The heart sounds were recorded at the 4 standard positions for 20 seconds each. The Cardioscan ®software analysed the recording for up to one minute and then displayed the findings as abnormal or normal. Prior to auscultation using the Sensi® system, 3 ECG electrodes were placed upon the chest. Following this, recordings were made at the same four precordial positions using the Welch-Allen stethoscope®. All recordings were performed in the supine position and in a quiet environment. Prior to commencing the study, extensive training was undertaken and all procedures were conducted according to manufacturers' operating instructions.

Quality assurance was maintained throughout and equipment was checked at several intervals throughout the study.

Data were analysed using STATA® version 11, Texas, USA. The sample size of 79 patients was calculated to achieve <10% confidence intervals around an estimated sensitivity of 90% for either computer-assisted stethoscope. In the analysis, we calculated the sensitivity and specificity of the different CAA systems to detect abnormalities on echocardiogram and likelihood ratios for discrimination between benign and pathologic cases. Results were stratified by participant age (children versus adults) and pathological categories. The Mantel-Haenszel Test for heterogeneity was performed to examine the performance of the tests varied by age strata. All statistical tests were 2-sided at alpha=0.05. Repeat analyses were performed after excluding participants where the recordings were deemed reasonable (i.e. recordings completed with minor difficulties) as well after excluding any participants with heart rates over 120/min. The McNemars Test of significance was used to assess the difference between the calculated sensitivities and specificities of the systems.

Results

In total, consecutive 79 participants were recruited, 40 children and 39 adults (Table 1). The median age among children was 3 years (IQR, 1-7 years) and 46 years (IQR, 32 to 62 years) in adults. Slightly more than half of participants were female. Participants were drawn from both ward and outpatients referrals. The echocardiography-

confirmed prevalence of structural heart disease was 52% (n= 41, median age 9 years,IQR, 2-41 years) There were 24 participants without heart disease (30% of the total) and 14 (18%) patients diagnosed with a cardiac abnormality other than structural cardiac disease. These included cardiomyopathies (n=5), left ventricular dysfunction (n=5), pericardial effusion (n=1) and pulmonary hypertension (n=3).

Overall, the Cardioscan® system was able to complete the computer assisted auscultation recordings in 98% of participants (95% of children and 100% of adults) while the Sensi® system completed the recordings in 95% of participants (93% of children and 97% of adults). The quality of the Cardioscan® recordings was deemed excellent in 73 cases (92%), in 4 (5%) cases problems were encountered although the procedure was completed while in 2 (3%) recordings, the recording procedures could not be completed. The Sensi® recordings were incomplete in 4 cases (5%), there were recoding difficulties with 7 participants (9%) and the quality deemed excellent in 68 cases (86%).

The sensitivity of the Cardioscan® system in identifying heart disease on echocardiography in children was 92% [73-99%] (Table 3). The specificity was 47% [21-73%] with a positive likelihood ratio test of 1.8 and a negative likelihood ratio test of 0.6. In adults the sensitivity was 60% [41%-77%], the specificity was 67% [30%-93%], the positive likelihood ratio was 2 and the negative likelihood ratio was 0.2. The Sensi® system, however, had a positive likelihood ratio of 1.8 in children and 2.5 in adults, a

negative likelihood ratio of 0.4 in children and 0.2 in adults respectively. The sensitivities for children were 78% [56-93%] and for adults were 84% [60-97%]. The percentage correctly classified was 75% and 61% by Cardioscan® and 70% and 58% by Sensi® in children and adults respectively. The overall likelihood ratios for the test performance were significantly better in children compared to adults for both Cardioscan® [p=0.006] and Sensi® [p=0.02].There was no significant difference demonstrated when comparing sensitivities and specificities achieved by both systems in adults, however Cardioscan® did demonstrate significantly improved sensitivity in children than in adults.[McNemar's chi-square p<0.001]

Table 4 shows the performance characteristics of the 2 systems having excluded recordings with any problems and children with heart rates over 120 during recording. Although sensitivities increase marginally using both systems, there is a decrease in specificity demonstrated by Cardioscan®. In the analysis, the overall likelihood ratios for the test performance remains significantly better in children compared to adults for both Cardioscan® [p=0.006] and Sensi® [p=0.02] (Table 4)

A sub-analysis reviewed the findings in terms of the classification of cardiac disease (Table 5), prior to excluding poor quality recordings. The specificity to detect normal cases was low using both Cardioscan® and Sensi®. Cardioscan® was 54% [33-74%] and Sensi® was 61% [39-80]. However the sensitivity to detect acyanotic heart disease was 100% using both systems. The sensitivity to detect abnormalities in patients with

cyanotic heart lesions was 100% using the Sensi® system and only 75% using the Cardioscan® software. Sensitivities to detect abnormalities in cases with valvular disease or cardiomyopathies were below 75% using both systems.

Discussion

Computer-assisted auscultation is potentially a tool to screen for cardiovascular disease in particular at the primary health care level. This study sought to evaluate 2 available systems to detect cardiac disease in patients presenting for assessment at a cardiac clinic. Despite many theoretical advantages, neither system was able to demonstrate sufficiently high sensitivities or specificities in screening for cardiac disease in this population.

This is the first study evaluating the use of CAA to distinguish normal from pathologic cases in a cardiac clinic in a developing country setting. Although 2 previous studies of CAA were performed in South Africa, both of these related to development of an autonomous auscultation system and artificial neural networks. (19, 20) This study also represents the real-world situation in busy referral centres and reflects the pathology referred to cardiac clinics on a daily basis.

These data suggested a suboptimal sensitivity and specificity and likelihood ratio test results did not appear to warrant its use as a screening tool. This is particularly shown

in the sub- analysis of the cases with no demonstrated heart disease where both systems demonstrated a specificity of below 60% and consequently high percentage of false positives.

CAA has yet to make an impact of routine cardiovascular assessment. To be clinically acceptable, a high sensitivity and specificity must be achieved both when used as a referral decision tool and when quantifying the severity of lesions. The complexity of the signal processing involved as well as the inherent differences across populations and pathophysiological mechanisms of cardiovascular disease has delayed the introduction of CAA into clinical care.

Both systems have previously demonstrated excellent sensitivities and specificities in preliminary evaluations (9, 21, 22), and there are several possible reasons for the relatively poor performance demonstrated here. This study represents a lower median age. It is also important to be aware of the physiological differences in children, in that even innocent murmurs are able to be conducted easily through the chest wall using very sensitive stethoscopes such as these electronic stethoscopes. In addition the Zargis software was designed not to be accurate in patients with a heart rate above 120 per minute.

The 2 systems have a different auscultation order and reversing the order of auscultation may result in errors, however stringent attention to the manufacturers

operating procedures together with repeated quality control was upheld throughout the study. The quality of recordings was deemed adequate if the auscultation sequence could be completed, this was not however verified with additional testing. Finally the Cardioscan® system made use of a Bluetooth® dongle which was left in the computer while simultaneously connecting to the Sensi ®system using another USB port. It is however unlikely that this could have affected the results of the Sensi system.

It has been suggested that the incorporation of other sensor modalities can provide important additional data which can also be utilised for further corroboration of conflicting results. (23) In our study, we auscultated at 4 sites and with the Sensi® system had the additional ECG electrodes to ensure correct partitioning of heart sounds, however still demonstrated poor accuracy. In addition, although this was only applicable to 1 of our adult cases, CAA in the cardiovascular examination of the morbidly obese has been shown not to be of assistance.(24)

Currently, algorithms for computer analysis have no uniformity or standardization resulting in a variety of end points and uses. Some algorithms have specifically designed to detect pathologic systolic murmurs only, (22), despite the fact that most diastolic murmurs are associated with pathology. In addition algorithms do not take into account the fact that important cardiac diseases for which screening would be of use, such as cardiac failure, may not have any murmurs but instead present with additional heart sounds as the hallmark feature on auscultation. In our study, several

cases presented without a murmur or only a grade 1 or 2 systolic murmur yet was diagnosed on echocardiogram with cardiac disease. To date, only experimental models exist to detect third heart sounds.(25)

This study had several strengths. It is the first study attempting to determine the role of 2 CAA systems in evaluating the presence of disease in patients presenting to a cardiac clinic for assessment or evaluation for cardiac disease. Cases with a wide range of cardiac pathologies and age ranges (minimum 2 months, maximum 79 years) were enrolled in order to approximate the typical patient population referred to these cardiac clinics. Although there was an expectedly high prevalence of disease, 30% of patients referred were found to have no cardiac lesions. We used clinical cases purposely as opposed to pre-recorded or digitized sound recordings. The patient population reflects the referral patterns from primary or secondary health facilities and thus achieves generalisability to settings with limited cardiology at primary care level. We were also able to enrol a large enough sample to power the study to determine the appropriate performance characteristics.

This study was designed to look at the function of CAA systems in referral decision support and therefore the comparative gold standard was the echocardiogram. It may have been of added worth to correlate the findings with standard auscultation to determine the presence of additional heart sounds or clicks. However detailed findings of clinical auscultation were not available on all patients and were not performed by a

single physician. Although we attempted to obtain a wide range of pathologies and ages, the mean age of the entire sample was 9 years which may be more representative of the paediatric population. This study was neither powered for numbers of adults and children, nor for all pathologic strata. Thus as the sample was not stratified according to pathologies, some pathologies such as the cardiomyopathies are under-represented.

Screening for heart disease using auscultation is a vital part of general paediatrics and family medicine and fulfils an important role in preoperative assessment and pre-screening for participation in athletics (26) (27). The essence of screening is detecting abnormalities requiring further cardiac evaluation. A referral decision support tool would facilitate this decision and provide much needed support for primary care staff away from more equipped centres. The ever-increasing need for skilled health care workers especially in low and middle income countries has led to the formation of a lesser trained cadres of assistant medical officers, community health workers and task shifting. (28) The use of technological advances to aid in this process can be invaluable and research in this area has demonstrated the potential benefits of technological aids. For example, the use of a referral support algorithm on hand-held PDA's (personal digital assistants) for community health care workers provided safe and effective community-based care to HIV-infected cases in Western Kenya and demonstrate the role of technology to expand the capacity of health care institutions in resource-constrained environments.(29) A simple, cost-effective and user-friendly tool to screen

for cardiac disease and support referral decisions especially from resource-poor settings is urgently needed.

In conclusion, CAA has the potential to extend the role of auscultation and improve the quantitative nature of a difficult skill. Currently there are neither standardized digital stethoscopes nor algorithms commercially available. We evaluated 2 systems currently available and were not able to demonstrate a sufficiently high sensitivity or specificity to justify their introduction into routine clinical medicine. That said, the promise that CAA could make a valuable contribution to clinical medicine in particular in the area of aiding with referral decision support for primary care practitioners suggests that further refinements and testing is warranted and should be encouraged and supported by clinicians.

[3232 excluding abstract]

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Appendices:

Tables

Table 1. Patient Characteristics

	Children	Adults	Total
No.	40	39	79
Age in years, med (IQR)	3(1-7)	46(32-62)	9(3-46)
Sex(M:F)	1: 1.1	1:1.4	1:1.3
Outpatient referrals	33	20	53
Ward referrals	7	19	26

Cardiac Diagnoses as determined by echocardiography

	Children		Adults		Total	
	n	%	n	%	n	%
Normal	15	38	9	23	24	29
Acyanotic congenital heart lesions e.g. ASD, VSD, PDA	16	40	2	5	18	24
Cyanotic congenital heart lesions e.g. TOF, UVH	4	10	0		4	5
Vavular Heart disease e.g. MS, AS, MVP	1	3	18	46	19	24
Cardiomyopthies e.g. DCM, HCM	3	8	2	5	5	6
Other: Hypertension	0	0	3	8	3	4
Left ventricular Failure	0	0	2	5	2	3
Pulkmonary Hypertension	1	3	2	5	3	4
Pericardial Effussion	0	0	1	3	1	1
Total:					79	100

Auscultatory findings

Children	ACC/AHA murmur referral class	No of patients (%)	
		n	%
Normal heart sounds, no murmur	NA	6	15
Grade 1/6, systolic ejection murmur	III	6	15
Grade 2/6, systolic ejection murmur	III	4	10
Grade 3/6, midsystolic murmur	I	12	31
Grade 2/6, halosystolic murmur	I	10	26
Grade 2/6, diastolic murmur	I	0	0
Grade 2/6, continuous murmur	I	1	3
Total:		39	100

Adults	ACC/AHA murmur referral class	No of patients (%)	
		n	%
Normal heart sounds, no murmur	NA	15	47
Grade 1/6, systolic ejection murmur	III	0	0
Grade 2/6, systolic ejection murmur	III	1	3
Grade 3/6, midsystolic murmur	I	4	13
Grade 2/6, halosystolic murmur	I	7	22
Grade 2/6, diastolic murmur	I	5	16
Grade 2/6, continuous murmur	I	0	0
Total:		32	100

Table 2: Completed Computer-Asssisted Auscultation Protocols				
		Children		Adults
Sensi® protocols				
Completed		37		38
Not completed		3		1
		40		39
Zargis® protocols				
Completed		38		39
Not completed		2		0
		40		39
Sensi ® confidence	mean(±SD)	90(±5)		87(±7)
Sensi ®Quality	Excellent	35(88%)	Excellent	37(95%)
	Reasonable	3(8%)	Reasonable	1(2.5%)
	Bad	2(4%)	Bad	1(2.5%)
Zargis ®Quality	Excellent	731(78%)	Excellent	38(97%)
	reasonable	6(15%)	reasonable	1(3%)
	Bad	2(7%)	Bad	0

	Children n=39	Adults n=39	Both n=78	Children n=37	Adults n=38	Both n=75
Sensitivity	92%[73-99%]	60%[41-77%]	74%[60-85%]	78%[56-93%]	55%[69-97%]	65%[51-78%]
Specificity	47%[21-73%]	67%[30-93%]	54%[33-74%]	57%[30-93%]	67%[30-93%]	61%[39-80%]
PPV	73%[54-88%]	86%[64-97%]	78%[65-89%]	75%[53-90%]	84%[60-97%]	79%[64-90%]
NPV	70%[40-97%]	33%[46-59%]	43%[29-68%]	62%[32-86%]	32%[13-57%]	44%[39-80%]
LR+	1.7	1.6	1.5	2.7	2.7	2.6
LR-	0.3	0.7	0.6	0.3	0.5	0.4
LR test	5.7	2.3	2.5	9	5.4	6.5
% Correct	72%	56%	64%	88%	63%	64%
OR	6[1-43]	2[0.4-16]	3[0.8-8]	9[2-55]	5[0.7-54]	6[1.7-21]
p values(M-H test for heterogeneity)			p=0.02			p=0.006

Table 4 . Performance Characteristics of Both Systems excluding poor quality recordings						
Cardioscan®			**Sensi ®**			
	Children n=27	**Adults n=36**	**Both n=64**	**Children n=28**	**Adults n=36**	**Both n=64**
Sensitivity	94%[73-99%]	55%[41-77%]	70%[55-83%]	82%[56-96%]	59%[39-78%]	68%[52-81%]
Specificity	56%[23-83%]	67%[30-93%]	60%[36-81%]	55%[30-82%]	67%[30-93%]	60%[36-81%]
LR+	2.1	1.7	1.7	1.8	1.8	1.7
LR-	0.1	0.7	0.5	0.3	0.6	0.5
LR test	21	2.4	3.2	6	3	3.4
OR	19[2-936]	3[0.4-18]	4[1-13]	6[0.8-46]	3[0.4-21]	3[0.9-11]
p values(M-H test for heterog€			p=0.006			p=0.02

	Sensitivity	Table 5: Specific Cardiac Pathologies: Adults and Children		
		Cardioscan®	Sensi ®	
		Specificity	Sensitivity	Specificity
Normal n=24		54%[33-74%]		61%[39-80%]
Acyanotic Congenital Heart Lesions n=17	100%		100%	
Cyanotic Congenital Heart Lesions n=4	75%		100%	
Valvular Lesions n=19	74%		72%	
Cardiomyopathies n=5	60%		40%	
Other n=9	33%		38%	

Part D: Annexes

1. Acknowledgements

This study was submitted in partial fulfilment of the requirements for the degree MPH [Clinical Research Methods], Faculty of Health Sciences, University of Cape Town.

2. Ethics Approval

UNIVERSITY OF CAPE TOWN

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16 August 2010

HREC REF: 359/2010

Dr L Zühlke
c/o Prof L Myer
Department of Paediatrics
Division of Cardiology

Dear Dr Zühlke

PROJECT TITLE: COMPUTER-ASSISTED AUSCULTATION: A VALIDATION STUDY.

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Approval is granted for one year till the 30th August 2011.

Please submit an annual progress report if the research continues beyond the approval period. Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

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