

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Cluster randomised feasibility trial to improve the Control of Hypertension In Rural India (CHIRI): a study protocol
AUTHORS	Riddell, Michaela; Joshi, Rohina; Oldenburg, Brian; Chow, Clara; Thankappan, K; Mahal, Ajay; THOMAS, NIHAL; Srikanth, Velandai; Evans, Roger; Kalyanram, Kartik; Kartik, Kamakshi; Maulik, Pallab; Arabshahi, Simin; Varma, R; Gugilla, Rama; Suresh, Oduru; Mini, GK; D'Esposito, Fabrizio; Sathish, Thirunavukkarasu; Mohammed, Alim; Thrift, Amanda

VERSION 1 - REVIEW

REVIEWER	Raghupathy Anchala Public Health Foundation of India The Indian Institute of Public Health, Hyderabad India
REVIEW RETURNED	31-May-2016

GENERAL COMMENTS	<p>A well detailed protocol that aims to test out clearly defined hypothesis. The methods are apt to answer the research questions. The following minor revisions would be required:</p> <ol style="list-style-type: none">1. Since the three sites are mentioned in the methods section, it will be apt to present hypothesis only after explaining the three sites.2. Sampling frame from the Rishi valley is not very clear and is not presented as precisely as the other two sites.3. The paper doesn't mention what the 'control group' receives.4. Discussion is too short. Include limitations and key strengths of your study protocol.
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REVIEWER	Rajeev Gupta Eternal Heart Care Institute and Research Centre, Mount Sinai New York Affiliate, Jaipur, India
REVIEW RETURNED	02-Jul-2016

GENERAL COMMENTS	<p>General comments:</p> <ol style="list-style-type: none">1. This is an important area of research, especially in low and lower-middle income countries such as India. Hypertension is a major problem in rural as well as urban populations in the country, treatment and control rates are poor and there are limited studies that have focused on interventions to improve control.2. This is essentially a methods paper. However, the major lacuna is that the authors have not identified nor discussed any of the previous identical studies that have been performed in India or are being conducted.
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	<p>Specific comments:</p> <ol style="list-style-type: none"> 3. In abstract section, the introduction statement is long and redundant. 4. The background/objective should clearly report the objectives. 5. The methods component of the abstract should provide specific details of sampling. 6. Urban rural convergence of hypertension in India should be highlighted (Gupta. J Hum Hypertens 2016;30:79-82) in the "introduction" section. 7. In "introduction" section, the hypotheses should be before objectives. 8. The hypotheses section should be in the form of a paragraph and not as bullets. 9. The methods section does not report on standardization protocol for data collection, physical measurements and training of ASHA workers. Was there any previous studies performed to assess the efficacy of training of the health workers? If yes, please describe results. If no, this is a major study limitation. 10. BMI >23 for Asians is no longer the criteria for overweight in Asians and should be deleted. 11. The methodology of qualitative components is poorly written. Please describe the questions asked, preferably in a Table. This shall help in replication of the study at other sites in India. 12. The authors have not discussed the previous similar studies in India. There are a number of smaller studies and a couple of larger studies. These studies have been discussed in the PREPARE study methods paper (Fathima et al. Am Heart J 2013;166:4-12) and methods paper of DISHA study (Jeemon et al. BMC Public Health 2016;16:e264). DISHA study has almost exactly the same protocol as in the present study and should be discussed. Also discuss the similarities and differences of the present study from these two studies. 13. Please add limitations of the present study in the discussion section.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Raghupathy Anchala

Institution and Country: Public Health Foundation of India, The Indian Institute of Public Health, Hyderabad, India Competing Interests: None declared

A well detailed protocol that aims to test out clearly defined hypothesis.

The methods are apt to answer the research questions. The following minor revisions would be required:

1. Since the three sites are mentioned in the methods section, it will be apt to present hypothesis only after explaining the three sites.

We agree that it makes more sense to understand the setting before outlining the hypotheses.

Consequently, we have moved the details on the study setting so that they are presented immediately prior to the hypotheses (page 7).

2. Sampling frame from the Rishi valley is not very clear and is not presented as precisely as the other two sites.

We have added further detail to the description of the RV sampling (page 10):

Rishi Valley region: The study population comprised the six villages of the Kurabalakota Mandal in the Chittoor District, Southern AP. These villages comprised 221 hamlets or small habitations. Hamlets were stratified by population size (small, medium and large) and then 139 were randomly selected in accordance with the sampling strategy using computer-generated random numbers (generated at Monash University). This was to ensure sampling of approximately equal numbers of hamlets from each size stratification. Six hamlets were excluded due to migration of population. We also excluded the hamlet in which the Rishi Valley Rural Education Centre was located because the population was largely transient, comprising teachers and students who reside in the hamlet only during school time. A study centre was set up in a communal area of the hamlet convenient for all the residents. All residents aged at least 18 years were invited to participate in the cross-sectional survey. Research officers ensured that all residents were informed of the presence of the study team in the habitation by house-to-house notification and encouragement to attend.

3. The paper doesn't mention what the 'control group' receives.

We have now included a section describing the control condition participants at the bottom of page 18 and top of page 19 (and reproduced below):

Control group

At the time of the initial data collection, all participants with elevated BP (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg) in the control sampling units are informed that their BP is elevated and are advised to visit their local health provider for further investigation. Additionally, these participants are provided basic nutritional advice such as reducing dietary salt, reducing use of palm oil, increasing intake of fruits and vegetables, increasing physical activity, and reducing use of tobacco and alcohol. Participants who were previously aware of their hypertensive status are advised to revisit their doctor for review of their medication and to take their medication as told by their doctor. No further care or advice is provided during the intervention period.

At the end of the intervention period the participants with hypertension in the control sampling units are revisited for outcome measures, as outlined below. At this time these participants receive further advice and recommendations regarding their hypertension status. Furthermore, they are provided with pictorially-based educational material about hypertension and how to manage the disease.

4. Discussion is too short. Include limitations and key strengths of your study protocol.

We have expanded the discussion to include limitations and strengths (pages 24-25). We have also included discussion of the role of task shifting in NCD management in populations with limited access to health care and have briefly discussed similar studies currently underway in India (pages 23-24).

Strengths and limitations

A limitation to this study is that the training programme delivered to ASHAs has not been formally tested. This may limit the efficacy of the intervention. However, after seeking input from ASHAs involved in the pilot training, we were able to make important refinements to both the ASHA training booklet and the educational resources for participants. We also assessed the ASHAs skills in measuring anthropometry and BP, as well as their knowledge of hypertension and NCDs before and after the formal training period as well as at the end of the intervention. This will enable us to determine the competencies of the ASHAs.

There are also a number of strengths to this study. First, this is a large community based study in three economically and developmentally diverse rural populations in Southern India, with detailed data on demographics; lifestyle-related factors including physical activity, tobacco use, and alcohol consumption; dietary factors, including cooking practices and use of salt; stress; and overcrowding. Secondly, there is detailed knowledge about hypertension and its risk factors, awareness of

hypertensive status, and further details about use of medications, barriers to treatment including access, cost, adoption of lifestyle factors and compliance with medication use. Such a rich data set will enable detailed exploration of associations between hypertension and economic and epidemiological transition. Furthermore, the additional qualitative studies, including the medicines availability survey, in-depth interviews, and focus group discussions, will allow us to triangulate potential barriers to diagnosis, treatment and control of hypertension. Data are collected using validated and standardised tools which will allow comparisons with other studies in India and other LMICs.

Finally, the feasibility study of employing ASHAs in community-based activities to prevent and manage hypertension will add to the increasing body of evidence for utilising non-physician health workers in the detection and management of NCDs, particularly in LMICs.

Task shifting discussion:

Task shifting disease management and control from physicians to non-physician health workers is increasingly being explored as a possible solution for populations with limited access to health care. In a systematic review of task shifting for non-communicable disease management in low and middle income countries Joshi et al suggest that the use of non-physician health workers may be effective and additionally be cost effective.[45] There are mixed results for the effectiveness of community health workers (CHWs) in identification and management of cardiovascular disease in various settings in India.[46, 47] Further trials to assess the effectiveness of CHWs in the management of cardiovascular risk factors are currently underway.[48, 49] Neither of these trials are testing the exclusive use of ASHAs in specifically delivering hypertension self-management education and monitoring. However these trials, along with ours, will provide valuable evidence which may encourage the government to fund ASHAs to manage non-communicable diseases or to identify a new cadre of village health workers to work in the area of non-communicable disease. Because ASHAs are employed in most rural regions, the programme is more likely to be scalable across rural India. This information will also contribute to disease prevention at a global level as the lessons learned could be suitably adapted across other similar settings.

Reviewer: 2

Reviewer Name: Rajeev Gupta

Institution and Country: Eternal Heart Care Institute and Research Centre,

Mount Sinai New York Affiliate, Jaipur, India Competing Interests: None declared

General comments:

1. This is an important area of research, especially in low and lower-middle income countries such as India. Hypertension is a major problem in rural as well as urban populations in the country, treatment and control rates are poor and there are limited studies that have focused on interventions to improve control.

Thank you.

2. This is essentially a methods paper. However, the major lacuna is that the authors have not identified nor discussed any of the previous identical studies that have been performed in India or are being conducted.

We have now included further discussion to highlight other studies both in India and globally on page 23 last paragraph (and over onto page 24). This is also copied below:

Task shifting disease management and control from physicians to non-physician health workers is increasingly being explored as a possible solution for populations with limited access to health care. In a systematic review of task shifting for non-communicable disease management in low and middle

income countries Joshi et al suggest that the use of non-physician health workers may be effective and additionally be cost effective.[45] There are mixed results for the effectiveness of community health workers (CHWs) in identification and management of cardiovascular disease in various settings in India.[46, 47] Further trials to assess the effectiveness of CHWs in the management of cardiovascular risk factors are currently underway.[48, 49] Neither of these trials are testing the exclusive use of ASHAs in specifically delivering hypertension self-management education and monitoring. However these trials, along with ours, will provide valuable evidence which may encourage the government to fund ASHAs to manage non-communicable diseases or to identify a new cadre of village health workers to work in the area of non-communicable disease.

Specific comments:

3. In abstract section, the introduction statement is long and redundant.

The introduction to the abstract has now been shortened (page 3), and now reads:

“Hypertension is emerging in rural populations of India. Barriers to diagnosis and treatment of hypertension may differ regionally according to economic development.”

4. The background/objective should clearly report the objectives.

The following has been clarified and outlined in the background section of the abstract (page 3):

“Our main objectives are to estimate the prevalence, awareness, treatment and control of hypertension in three diverse regions of rural India; identify barriers to diagnosis and treatment in each setting and evaluate the feasibility of a community based intervention to improve control of hypertension.”

5. The methods component of the abstract should provide specific details of sampling.

The following has now been added to the methods section of the abstract (page 3):

Wards/villages/hamlets of a larger Mandal are identified as the primary sampling unit (PSU). PSUs are then randomly selected for inclusion in the cross-sectional survey, with further randomisation to intervention or control.

6. Urban rural convergence of hypertension in India should be highlighted (Gupta. J Hum Hypertens 2016;30:79-82) in the "introduction" section.

Thank you. This is an important consideration. Urban rural convergence of prevalence has now been added to the introduction section, paragraph 1, as follows:

With the rapid urbanisation of India, lifestyle changes, known to be associated with increased risk of hypertension, become more common. These lifestyle changes may be driving the convergence of the prevalence of hypertension between urban and rural India.[4] Such convergence is observed in the pooled estimates, using random effect analysis, for South India where there were no detectable differences in the prevalence of hypertension between rural and urban populations (urban: 31.5% (95%CI, 23.6, 39.5) vs rural: 28.3% (95%CI, 21.4, 35.1), $p = 0.62$).[3]

7. In "introduction" section, the hypotheses should be before objectives.

The hypotheses are based on the objectives, and so we have placed the objectives first.

8. The hypotheses section should be in the form of a paragraph and not as bullets.

There are many hypotheses, as there are many parts to this protocol. We believe it would be simpler for readers to understand the hypotheses if kept in the numbered format.

9. The methods section does not report on standardization protocol for data collection, physical measurements and training of ASHA workers.

We have added further information to the text to clarify and expand the description of the methods and strategies used to ensure standardised data collection and ASHA training on page 11 (last paragraph):

To ensure standardisation, data collectors are trained in collection of anthropometric and blood pressure measurements in accordance with the WHO STEPS protocol.[26]. This training, conducted by the project manager for at least 5 days, is to ensure consistency of data collection between sites. Training is provided in a similar manner to ensure that questionnaire administration is also consistent across all sites. A study-specific training manual containing step-by-step procedures for all data collection (anthropometric and survey administration) is provided to each data collector. Data collection at each site is further monitored by site supervisors. Follow-up training by the project manager and/or site supervisor is also undertaken at each site approximately one month after commencement of data collection to ensure that data collection methods are implemented according to the protocol.

Further details of the training of the ASHA worker appear on page 16 (and are copied below):

For the intervention, ASHAs in each location are trained to deliver the self-management sessions of the intervention and to collect data regarding the implementation of the intervention. Training of ASHAs is standardised and undertaken by the site supervisors at each site in accordance with the study specific ASHA training manual to ensure consistency of training between sites. Training of ASHAs was first piloted at the Rishi Valley site using four volunteer ASHAs not involved in the implementation of the intervention. Pilot training was conducted by the Project Manager and included each site supervisor utilising “train the trainer” principles.[38] Materials and resources for training ASHAs, as well as standardised resources and education material for delivering the intervention were initially developed in English. ASHAs involved in the pilot training provided important feedback that enabled us to refine the educational resources for ASHAs and participants. Once these resources were finalised, they were translated/back translated into site specific language (Telugu and Malayalam).

Was there any previous studies performed to assess the efficacy of training of the health workers? If yes, please describe results. If no, this is a major study limitation.

We piloted the intervention training, as outlined above, but did not assess the efficacy of training the health workers prior to the intervention. This has been added to a section on “study strengths and limitations” at the end of the discussion (page 24) and copied below:

Strengths and limitations

A limitation to this study is that the training programme delivered to ASHAs has not been formally tested. This may limit the efficacy of the intervention. However, after seeking input from ASHAs involved in the pilot training, we were able to make important refinements to both the ASHA training booklet and the educational resources for participants. We also assessed the ASHAs skills in measuring anthropometry and BP, as well as their knowledge of hypertension and NCDs before and after the formal training period as well as at the end of the intervention. This will enable us to determine the competencies of the ASHAs.

There are also a number of strengths to this study. First, this is a large community based study in

three economically and developmentally diverse rural populations in Southern India, with detailed data on demographics; lifestyle-related factors including physical activity, tobacco use, and alcohol consumption; dietary factors, including cooking practices and use of salt; stress; and overcrowding. Secondly, there is detailed knowledge about hypertension and its risk factors, awareness of hypertensive status, and further details about use of medications, barriers to treatment including access, cost, adoption of lifestyle factors and compliance with medication use. Such a rich data set will enable detailed exploration of associations between hypertension and economic and epidemiological transition. Furthermore, the additional qualitative studies, including the medicines availability survey, in-depth interviews, and focus group discussions, will allow us to triangulate potential barriers to diagnosis, treatment and control of hypertension. Data are collected using validated and standardised tools which will allow comparisons with other studies in India and other LMICs.

Finally, the feasibility study of employing ASHAs in community-based activities to prevent and manage hypertension will add to the increasing body of evidence for utilising non-physician health workers in the detection and management of NCDs, particularly in LMICs.

10. BMI >23 for Asians is no longer the criteria for overweight in Asians and should be deleted.

There is still debate about differing cut-offs for different populations. We have deleted the BMI>23 comment and reference and replaced as detailed below (page 12):

A body mass index (BMI) ≥ 25 to 29.99 kg/m² is defined as overweight and BMI ≥ 30 kg/m² as obese according to the revised BMI classification.[27]

11. The methodology of qualitative components is poorly written. Please describe the questions asked, preferably in a Table. This shall help in replication of the study at other sites in India.

As requested, we have now included the questions used for the FGD and IDI as supplementary tables, and referred to them in the text:

Supplementary Table 2: Focus Group Question Guide for Participants with Hypertension

Question Number Guide question

- 1 Where do you usually go if you are ill with any disease?
 - 1a Why do you go where you go?
- 2 Where do you usually go for chronic diseases, especially cardiovascular diseases?
 - 2a Why do you go where you go?
- 3 What do you mean by high blood pressure?
- 4 Who gets high blood pressure (and cardiovascular diseases)?
- 5 What do you think causes high blood pressure?
- 6 How do people know if they have high blood pressure?
- 7 How blood pressure is usually diagnosed
 - 7a How was blood pressure diagnosed in you?
- 8 Could you tell me about the care you receive for your high blood pressure?
 - 8a Where do you usually go to receive care for your high blood pressure?
 - 8b Could you tell me your experiences of receiving care for your high blood pressure (time to go to hospital, time spent at hospital, your interactions with doctors and other health care workers)?
 - 8c Could you explain about the instructions that you receive from doctors and other health care workers?
- 9 What do you mean by control of high blood pressure?
 - 9a Could you tell me how blood pressure can be controlled?
 - 9b What do you think are the reasons for not being able to control high blood pressure?

- 10 Could you tell me what prevents you from seeking care for your blood pressure?
- 11 Could you explain about costs involved in getting care for your high blood pressure?
- 12 Could you explain where do you get your blood pressure medications?
- 12a What would you do if you don't get the same medications as prescribed by your doctor or other health care worker?
- 13 Could you explain about how you take your blood pressure medications?
- 14 Why do you think you are not able to take medications regularly?
- 15 Is there anything else you want to tell about high blood pressure treatment and control?
- 16 Could you tell me something about ASHAs in your village?
- 17 What could ASHAs do to control your high blood pressure?
- 18 If any program is done through your primary health centre to control your high blood pressure, what do you want it to be like?
- 19 Is there anything else you want to tell me?

Supplementary Table 3: Interview guide for in-depth interview with doctors from Primary Health Centres (PHCs)

Question Number Guide question

- 1 Could you describe how you usually manage patients with hypertension?
- 2 Could you tell me in whom do you regularly check blood pressure?
- 2a What is the approximate percentage?
- 2b What are the reasons for not checking blood pressure?
- 3 Could you tell me about any guidelines that you follow for the diagnosis and management of hypertension?
- 3a If yes, what guidelines do you follow?
- 3b If no, what are the reasons?
- 4 What do you think about absolute risk approach for management of patients with cardiovascular disease?
- 4a Do you use absolute risk approach?
- 4b If not, could you tell me the reasons?
- 5 How do you think the health care system in which you are working now is equipped for the diagnosis and management of hypertension?
- 5a If yes, what are the reasons for inadequate diagnosis and treatment of hypertension?
- 5b If not, what can be done to improve it?
- 6 Do you feel you are sufficiently equipped to diagnose and manage individuals with hypertension?
- 7 Do you think you need anything more, such as training, to deal with individuals with high blood pressure?
- 8 Could you tell me how you manage hypertensive patients with complications?
- 9 Do you have any comments or suggestions for improving the diagnosis and management of individuals with hypertension?
- 10 Do you have any other thing to say?

Supplementary Table 4: Interview guide for in-depth interview with staff nurse or ANM/ASHA

Question Number Guide question

- 1 Could you describe me your typical "working" day and what is usually involves?
- 2 Could you tell me how you are involved in the management of chronic conditions?
- 3 Could you tell me about your involvement in identification and management of individuals with high blood pressure?
- 4 Could you tell me about any training that you have received for checking blood pressure and

identification and management of individuals with high blood pressure?

5 How do you think the health care system in which you are working now is equipped for the identification and management of individuals with high blood pressure?

5a If yes, then what do you think are the reasons for inadequate diagnosis and control of high blood pressure?

5b If not, what do you think can be done to improve it?

6 Do you feel you are sufficiently equipped to manage individuals with high blood pressure?

7 Do you think you need anything more, such as training, to deal with individuals with high blood pressure?

8 How is your relationship with other healthcare providers in your PHC and sub-centre?

9 Could you tell me how do you feel about completing all the tasks given to you in a working day?

10 What do you think about having another health care worker to work with you?

11 Could you tell me about your salary?

12 Do you have any other comments or suggestions about how we can improve the identification and management of individuals with high blood pressure?

13 Do you have any other thing to say?

12. The authors have not discussed the previous similar studies in India. There are a number of smaller studies and a couple of larger studies. These studies have been discussed in the PREPARE study methods paper (Fathima et al. *Am Heart J* 2013;166:4-12) and methods paper of DISHA study (Jeemon et al. *BMC Public Health* 2016;16:e264). DISHA study has almost exactly the same protocol as in the present study and should be discussed. Also discuss the similarities and differences of the present study from these two studies.

The following section has been added to the discussion which describes other activities globally and in India which have explored other studies using non physician health workers to provide NCD management (bottom of page 23 and top of page 24):

Task shifting disease management and control from physicians to non-physician health workers is increasingly being explored as a possible solution for populations with limited access to health care. In a systematic review of task shifting for non-communicable disease management in low and middle income countries Joshi et al suggest that the use of non-physician health workers may be effective and additionally be cost effective.[45] There are mixed results for the effectiveness of community health workers (CHWs) in identification and management of cardiovascular disease in various settings in India.[46, 47] Further trials to assess the effectiveness of CHWs in the management of cardiovascular risk factors are currently underway.[48, 49] Neither of these trials are testing the exclusive use of ASHAs in specifically delivering hypertension self-management education and monitoring. However these trials, along with ours, will provide valuable evidence which may encourage the government to fund ASHAs to manage non-communicable diseases or to identify a new cadre of village health workers to work in the area of non-communicable disease. Because ASHAs are employed in most rural regions, the programme is more likely to be scalable across rural India. This information will also contribute to disease prevention at a global level as the lessons learned could be suitably adapted across other similar settings.

13. Please add limitations of the present study in the discussion section.

We have added a section on study strengths and limitations (see response to point 9 above). This is on pages 24 and 25 in the manuscript.

VERSION 2 – REVIEW

REVIEWER	Rajeev Gupta Eternal Heart Care Centre and Research Institute, Mount Sinai New York Affiliate, Jaipur 302017 India
REVIEW RETURNED	07-Aug-2016

GENERAL COMMENTS	The revised article is much better than the original submission. All the comments have been adequately answered. The article is now acceptable for publication.
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