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Process evaluation of a randomised controlled trial of a pharmacological strategy to improve hypertension control: protocol for a qualitative study

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ABSTRACT

Introduction Globally, the prevalence of uncontrolled hypertension is high, particularly in low- and middle-income countries. There is a critical need for strategies to improve hypertension control. The early use of a fixed low-dose combination of three antihypertensive drugs (triple pill) has the potential to significantly improve hypertension control. The **TRI** ple Pill vs. **U** sual care **M** anagement for **P** atients with mild-to- moderate **H** ypertension (TRIUMPH) randomised controlled trial (RCT) is designed to test the effects of this strategy compared with usual care in patients with mild-to-moderate hypertension. This paper reports the protocol of a process evaluation of the TRIUMPH RCT. The objectives are to understand factors related to implementation of the intervention, mechanisms of effect, contextual factors that underpin the effectiveness of the triple pill strategy and the potential barriers and facilitators to implementing the strategy in clinical practice.

Methods and analysis Face-to-face semistructured in-depth interviews with a purposive sample of TRIUMPH RCT participants and healthcare professionals in Sri Lanka will be conducted. Healthcare professionals will include physicians and their staff who were involved in conducting the TRIUMPH RCT. Interviewees will be recruited sequentially until thematic saturation is achieved. Interviews will be audio recorded, transcribed verbatim and analysed in NVivo using framework analysis methods.

Ethics and dissemination The TRIUMPH RCT and process evaluation have received approval from the relevant Ethics Review Committee. All participants will be asked to provide written consent before participation. Findings from the study will be disseminated through publications and conference presentations.

Trial registration number ACTRN12612001120864 , SLCTR/2015/020 ; Pre-results.

Strengths and limitations of this study

- Multiple sampling strategies to recruit a large number of interviewees to cover diverse views.
- Use of rigorous methods of data collection and analysis following a standard protocol.
- First of its kind study to explore barriers to hypertension control in Sri Lanka.
- Inability to recruit participants who did not attend the end of study visit.

INTRODUCTION

High blood pressure (BP) is the number one preventable cause of early loss of life worldwide.[1] Consequently, there has been much attention on efforts to prevent and treat high BP to avert premature deaths. Interventions that have been tested to improve hypertension control range from population-wide approaches such as national policies to reduce salt intake[2] to radical and individual-based approaches such as renal denervation.[3] By far, pharmacological treatment has been the most widely tested and is one of the most effective individual medical approaches to BP control.

A myriad of drugs with distinct and complementary physiological effects are at the disposal of physicians for prescription. Yet one in three people treated for hypertension have uncontrolled BP (>140/90 mm Hg).[1] The current approach to the pharmacological treatment of hypertension commonly known as stepped care strategy involves initiation of monotherapy, with treatment intensification (dose uptitration or adding other drugs) at subsequent follow-up visits. While guidelines recognise that most patients need multiple drugs to achieve BP control,[4 5] most patients receive only monotherapy.[6]

There are many patient- and provider-related factors relating to this stepped care strategy that might contribute to inadequate BP control. For instance, the cost and inconvenience of multiple clinic visits and treatment modification,[7 8] and non-adherence to treatment, which is worsened by increasing number of drugs[9] are major determinants

to BP control. In addition, therapeutic inertia, the resistance of prescribers to intensify therapy in the face of uncontrolled hypertension, is a recognised problem[10 11] that is difficult to overcome. While fixed-dose combination (FDC) drugs are promising solutions to such issues,[12] their use in clinical practice is primarily reserved for patients already established on multiple treatments, or more rarely, in the early stages of treatment for patients with markedly elevated BP.[4 5]

The use of an FDC comprising three antihypertensive drugs in low doses (triple pill) as early or initial treatment has the potential to significantly improve hypertension control. The rationale is based on sound pharmacological principles: each drug will act on distinct and major physiological pathways of hypertension producing significant reduction in BP, and the use of low doses minimises adverse effects. Furthermore, its early use will achieve faster BP control and obviate the need for multiple clinic visits for treatment modification. However, the use of this strategy in clinical practice requires a shift in paradigm as it entails significant change in the prescribing behaviours of doctors, acceptance by the patients and regulatory approval. High quality evidence of its effectiveness and the reasons for its success or failure are needed.

The TRIUMPH trial is a parallel-group, open-label, randomised controlled trial (RCT) designed to test the effectiveness of early use of triple pill compared with usual care for the management of hypertension.[13 14] In brief, patients from multiple outpatient clinics in Sri Lanka, with mild-to-moderate hypertension, either naïve to BP lowering drugs or receiving monotherapy were to be randomised to treatment with triple pill or continued usual care, for a period of 6 months. The primary outcome of the TRIUMPH RCT is improvement in the proportion of people with BP control. Secondary outcomes include reduction in BP, improvement in adherence and improvement in quality of life. The TRIUMPH RCT has recruited 700 participants.

While an RCT assesses the effects of intervention on predefined outcomes, a process evaluation helps to understand aspects of delivery and receipt of intervention, why and how the intervention worked, influence of the settings in which the intervention was delivered and potential barriers and facilitators to implementing the intervention into clinical practice.[15] Additionally, a process evaluation can help formulate hypotheses leading to further analyses of data from the RCT.

This paper presents the protocol for the process evaluation of a pragmatic RCT of a strategy of initial or early use triple pill compared with usual care for the management of hypertension among adults in Sri Lanka.

METHODS AND ANALYSIS

A logic model summarising the public health problem, evidence, resources, activities and anticipated outcomes of TRIUMPH study is depicted in figure 1. This logic model helps in understanding various components of the planned intervention, the resources in place, and sensitises us to potential interaction between these to produce the change. It also helps us to consider unintended influences on the trial results.[15]

Study design and sample

The process evaluation will employ qualitative methods of data collection and analysis and will involve semi-structured in-depth interviews with trial participants and healthcare professionals. Interviewees will be recruited, initially, following a mixed purposive sampling strategy, including maximum variation, extreme or deviant case[16] and subsequently by theoretical sampling to help explore themes that arise during initial analysis.[17] Maximum variation sampling will consider trial participants age, gender, treatment group, history of diabetes and cardiovascular diseases (CVD), income and lifestyle. Healthcare professionals will include physicians and their staff who participated in the TRIUMPH study. Interviews will be recruited sequentially until thematic saturation is achieved. From our previous experience,[18 19] we anticipate achieving thematic saturation with 20–25 trial participant interviews (approximately 10–12 each treatment group) and 10–15 health professional interviews.

The study team will include researchers with diverse background: AS (pharmacist, quantitative and qualitative researcher), TL (pharmacist, health economics and qualitative researcher), RW (physician, quantitative researcher), PG (social sciences researcher), SJ (health economist, quantitative and qualitative researcher) and AP (cardiologist, quantitative researcher), with some being part of the core team of TRIUMPH RCT and others completely independent.

Data collection

Data collection will be done by means of semistructured in-depth interviews with individual participants and healthcare providers. This method has primacy over other qualitative methods in the context of this study as they allow in-depth inquiry of the phenomenon, ensures confidentiality of the participants and enables prespecified topics to be explored while permitting the exploration of other ideas and thoughts that may spontaneously arise in the conversation.[20]

Interviews with trial participants will begin after the first participant enrolled in TRIUMPH RCT has completed their 6-month follow-up (end of study) visit. Healthcare professional interviews will be conducted following the end of follow-up of all trial participants in the TRIUMPH RCT. Consenting trial participant and healthcare professionals will be invited to an interview at the trial site or other place of their choice. Staff at TRIUMPH RCT sites will be notified of the identity of the trial participants nearer her/his end of study site visit. On the day of end of study visit, selected participants will be asked to confirm their willingness to be interviewed. The interviewer will discuss the objectives of the interview, and inform the interviewee of the potential

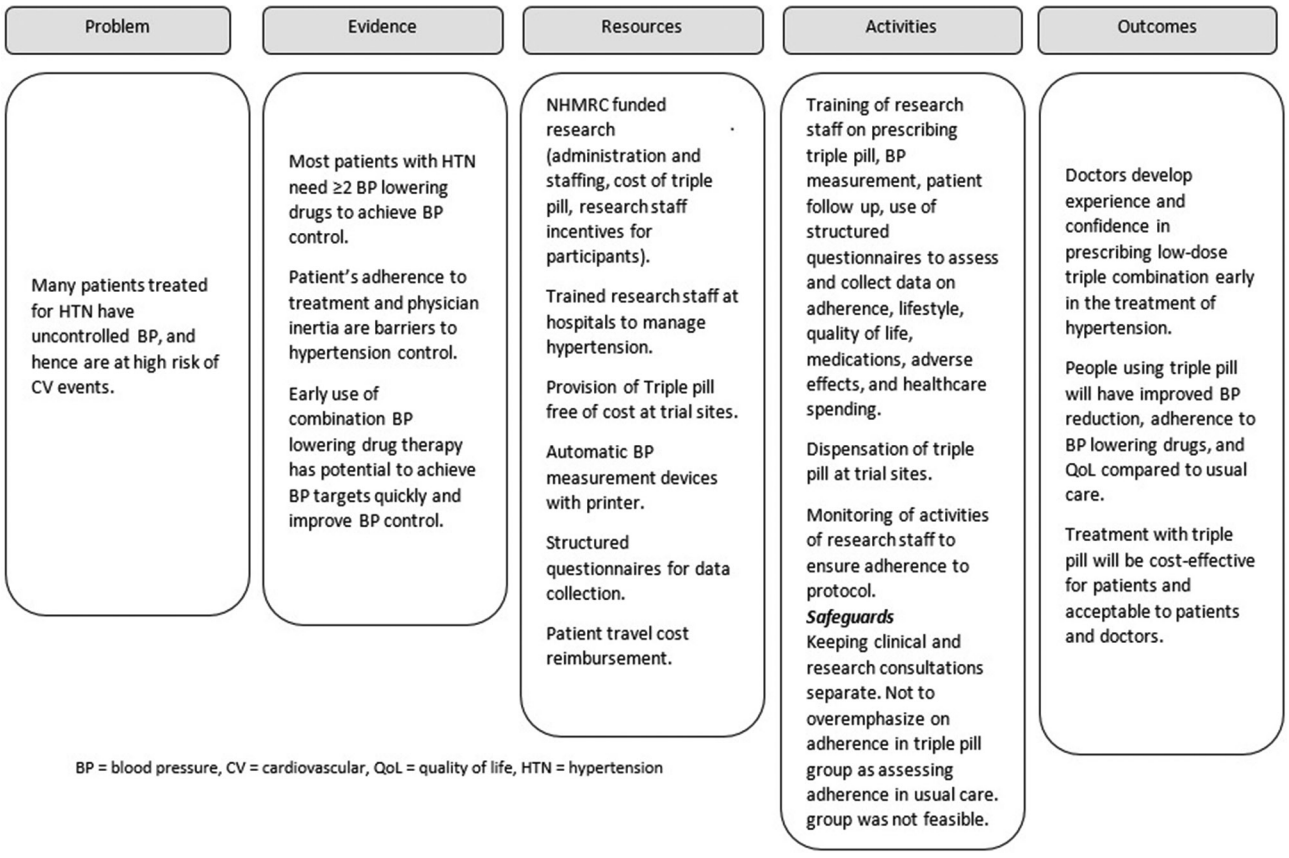

Figure 1 A logic model summarising the public health problem, evidence, resources, activities and anticipated outcomes of TRIUMPH study.

benefits and harm of participation, and provide assurances of confidentially. If willing to be interviewed, the study coordinator will organise a private place for the conduct of interview. Interviews will be conducted by trained interviewers in appropriate local language with trial participants and in English with healthcare professionals. Interviewees will be informed that there are no right or wrong answers and they are free to express their views in whichever manner they may want to. The interviewer will follow an interview guide, structuring questions based on the responses of the interviewee and ensuring that all the key areas mentioned in the interview guide are covered. Each interview is likely to last, on average, 30 min and will be audio recorded.

Interview guides

The research team will develop interview guides specific for trial participant and healthcare professional interviews. Guide development will be informed by the objectives of the process evaluation, a literature review of the topic under research and brain storming among the research team. Key areas that will be covered in the interview guides include views and experience of, the TRIUMPH RCT, triple pill and BP control, adherence to treatment, hypertension and its management in Sri Lanka and translation of the intervention into practice and policy. Interview guides will be piloted before being used for data collection. During the process evaluation, based on the contemporaneous analysis of collected data, interview guides will be subjected to amendments as necessary in discussion with the research team.[21]

Data management and analysis

Translation of interviews

All interviews will be transcribed verbatim. Non-English language interviews will then be translated to English by native translators. Each transcript will be then reviewed by the interviewers against the audio for accuracy of the transcription and translation. Any content which may reveal the identity of the interviewees will be removed from the transcript.

Analysis

Framework analysis, a qualitative data analysis method, is increasingly used across multiple disciplines: psychology, social and health science. It is particularly useful in addressing four types of research questions: contextual, diagnostic, evaluative and strategic.[22] The research questions of our study fall in more than one of these categories. Further, the other aspects of our research, clearly set objectives, short time scale, makes framework analysis a preferred approach to data analysis.

Each transcript will be read thoroughly by two researchers, for data familiarisation, before coding the text. Using Nvivo,[23] two researchers will independently code the first few, same, interview transcripts. The team of investigators include experts from Sri Lanka to help understand the nuances of local language wherever required. This initial coding will involve careful review of text, line-by-line, to generate as many relevant codes as possible from different perspectives without much regard to the objectives of the study. The two coders will then compare and discuss codes to develop a framework of codes and their categories that will be applied to subsequent transcripts, without any restriction on generating new codes. The coding of the rest of the transcripts will proceed following the coding framework. The coding framework will be subjected to modification if necessary, by discussion among the coders, as the coding of interview transcripts proceed. Throughout the process of data management and analysis, researchers will draft memos of reflections, ideas and interpretations, and discuss them with the team to inform analysis.

Using Microsoft Excel, a framework matrix will be created with the names of the categories of codes as column headings and interviewee identification number on the rows. Each category of nodes will be summarised ensuring its essence is intact, and mapped in the matrix. From the framework matrix, we will compare themes across interviewees, identify patterns and connection between the categories, identify divergent themes and generate memos of the rich description of the phenomena relevant to the objectives of the study.

PATIENT AND PUBLIC INVOLVEMENT

Patients were not involved in the design of the study. Although we did not have a patient partner formally involved, the research question and outcome measures were substantially informed by our former research about patient experience and preferences for combination CVD therapies. Results of the study will be disseminated to study participants through healthcare professionals in our research network.

ETHICS AND DISSEMINATION

Dissemination

The results of this study, including the framework matrix and themes arising from the interviews, will be shared with the individuals and institutions associated with this study as well as academic audiences through peer-reviewed publication and conference presentations.

This process evaluation will complement and add value to the TRIUMPH trial by providing a better understanding of trial results. It will provide insights into the relevance, usefulness and adaptability of the strategy into clinical practice in Sri Lanka as well as other low- and middle-income settings. Improvement in BP control is dependent on several factors related to patient, provider, therapy and healthcare system. Therefore, understanding of implementation of the strategy and its interaction with these factors will also help understand determinants of BP control.

Study status

Data collection commenced in May 2017 and is likely to end in May 2018.

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Competing interests George Health Enterprises, the social enterprise arm of The George Institute for Global Health, has received investment to develop fixed-dose combination products containing aspirin, statin and blood pressure lowering drugs. George Health Enterprises has submitted patents for low-dose blood pressure combinations, on which AR is listed as one of the inventors.

Patient consent Not required.

Ethics approval Ethics Review Committee, Faculty of Medicine, University of Kelaniya, Sri Lanka, and Ethics Review Committee (RPAH Zone), Sydney, Australia.

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