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## Educational Intervention for improving control of blood pressure in patients with hypertension: A Systematic Review Protocol

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# EDUCATIONAL INTERVENTION FOR IMPROVING CONTROL OF BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION: A SYSTEMATIC REVIEW PROTOCOL

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*Key words:* hypertension, blood pressure, educational interventions, randomized controlled trial, systematic review

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## Abstract

**Introduction:** The aim of this review is to evaluate the effectiveness of educational interventions on improving the control of blood pressure in patients with hypertension.

**Methods:** Patients aged over eighteen years old regardless of sex, ethnicity with a diagnosis of hypertension (either treated or not treated with antihypertensive medications) will be included in our analysis. We will electronically search four databases: MEDLINE, CINAHL, PEDro, ScienceDirect. There will be no language restrictions in the search for studies. The data will be extracted independently by two authors using predefined criteria. Disagreements will be resolved between the authors. The risk of bias will be assessed using the Cochrane risk of bias tool. After searching and screening of the studies, we will run a meta-analysis of the included randomised controlled trials. We will summarise the results as risk ratio for dichotomous data and mean differences and weighted mean differences for continuous data.

**Ethics and dissemination:** The protocol for the systematic review has been registered in PROSPERO. The review will be published in a journal. The findings from the review will also be disseminated electronically and conferences presentations.

**Trial registration number:** Ribeiro C, Resqueti V, Lima I, Dias F, Glynn L, Fregonezi G. Educational interventions for improving control of blood pressure in patients with hypertension. PROSPERO: International prospective register of systematic reviews. 2014: CRD4201401071 Available from:

[http://www.crd.york.ac.uk/PROSPERO/register\\_new\\_review.asp?RecordID=10171](http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp?RecordID=10171)

### Strengths and limitations of this study:

- The trial screening and data extraction will be conducted independently by two authors.
- The results of this systematic review will help clinicians in making decisions in clinical practice, and help patients to better understand their conditions and also can heighten awareness about disease progression and complications.

## INTRODUCTION

### Description of the condition

Hypertension is a major health problem worldwide and is estimated to cause more than 13% of deaths annually,[1]. It is a multifactorial clinical condition characterized by high and sustained levels of blood pressure,[2]. It is one of the most important public health problems in the world and an important modifiable risk factor for the development of cardiovascular diseases. Adoption of healthy lifestyles by all individuals is critical for the prevention of high blood pressure and an indispensable part of the management of those with hypertension,[3].

A recent epidemiological worldwide study estimated that the high blood pressure causes approximately 7.6 million premature deaths (54% for stroke and 47% for ischaemic heart disease) and contributes to the functional disability of 92 million people in numbers adjusted for years of life in 2001,[4]. A recent systematic review reporting data performed in 35 different countries between the years 2003 and 2008 demonstrated an overall prevalence of 37.8% for men and 32.1% for women,[5].

Due to the fact that the prevalence of hypertension increases with age,[6] the management of hypertension and the prevention and treatment of major complications related to hypertension will continue to be a challenge for all health care professionals.

### Description of the intervention

Hypertension is a condition almost entirely managed by the primary care team, composed by physicians, nurses, pharmacists and other health care professionals such as physiotherapists. All cited professional can play an important role on lowering the blood pressure. It is important to show patients that lowering a high blood pressure, has been showing in drug trials, and has been

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3 associated with a reduction in many complications such as stroke (35-40%), heart attack (20-  
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5 25%) and heart failure (over 50%)[3]. The majority of patients require a combination of  
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8 antihypertensive drugs to reach target blood pressure.  
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11 A study had been showed that educational intervention led to an increase in the participants'  
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13 levels of knowledge about hypertension and a positive influence on their beliefs about  
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15 medicines,[7]. Educational interventions create opportunities for patients to better understand  
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17 their conditions and the role of therapies and also can bring awareness about disease progression  
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19 and complications. Through patient education, misconceptions that patients have about their  
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21 therapy can be cleared. This can influence adherence to therapy,[8] and consequently blood  
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23 pressure levels.  
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### 27 28 **How the intervention might work**

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30 Different health professionals have become more involved in delivering interventions to the  
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32 patients with the objective of preventing complications caused by high blood pressure. Patients  
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34 expectations have a significant effect on the treatment they get from their doctor or any other  
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36 health professional involved,[9]. Educational intervention is one of the proposed interventions  
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38 applied to hypertensive patients.  
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44 Educational interventions can positively modify patients' beliefs which in turn can lead to a  
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46 change in patient behavior, adherence to a therapy proposed by the responsible health care  
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48 professional,[8] and a possible effect on variables related to the disease such as blood pressure  
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50 levels. It may also affect in long term the progression of the disease and the prevalence of  
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52 associated conditions related to hypertension such as heart attacks and cerebrovascular artery  
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54 disease.  
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## Why is important to do this review

Due to the high morbidity and mortality caused by hypertension and the global scale of this important public health, it is important to continue to investigate interventions that can improve blood pressure control. It is striking that blood pressure goals continue to be achieved in only 25-40% of the patients who take antihypertensive drug treatment,[3,10], which is something that has remained unchanged for the last 40 years,[11].

A recent Cochrane review demonstrated that there are many categories of interventions that together reduce blood pressure in patients with hypertension,[12]. One of them was educational interventions directed to patient and physician. This kind of intervention demonstrated to be beneficial on lowering blood pressure; however, not alone and was recommended to be an adjunct additional therapy along other types of interventions such as antihypertensive drug therapy.

Due to the fact that there has been an increasing number of studies showing the importance of prevention in patients with hypertension,[13-15] this review will evaluate the current evidence of the effects of educational interventions on the control of blood pressure in patients with hypertension.

## METHODS AND ANALYSIS

### Criteria for considering studies for the review

#### *Types of studies*

We plan to include randomized clinical trials (RCTs) that have evaluated the effects of different models of educational interventions with the overall aim of improving blood pressure control in patients with hypertension, irrespective of language. The review will include RCTs where educational intervention used as the main or adjunct treatment was compared with no educational intervention or different types of educational strategies. We will exclude studies that use educational interventions not intended to improve blood pressure control.

### *Types of participants*

We will include participants with age over 18 years regardless of sex, ethnicity with a diagnosis of hypertension either treated or not treated with antihypertensive medications in a primary care, outpatient or community setting.)

### *Types of interventions*

The intervention of interest will include all educational interventions strategies designed to improve the control of blood pressure in patients with hypertension (e.g. educational interventions direct to the patient; educational interventions direct to the health professional). Comparators will be any educational intervention used as the main or adjunct treatment to improve the control of blood pressure compared with either no educational intervention or different types of educational strategies aimed to improve blood pressure control.

### *Types of outcomes assessments*

The primary outcome of this review will be any changes in mean systolic blood pressure (SBP) and/or mean diastolic blood pressure (DBP) in any care setting as well as number of patients under control of blood pressure (BP) or proportion of controlled BP defined by each randomized trial's investigators. The secondary outcomes will be: number of hospitalizations during treatment (e.g. increase of BP) or mortality from cardiovascular disease as an adverse events; the costs and cost effectiveness of interventions; the adherence to intervention (dropout rate) or adherence to medication and the outcome QOL will be measured using standardized generic questionnaire.

## **Search methods for identification of studies**

### *Electronic searches*



We will electronically search the following databases: MEDLINE, CINAHL, PEDro, ScienceDirect, WHO International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov. without any language restrictions. The search strategy will be developed after discussion among reviewers, according to the guidance of the Cochrane handbook (colocar ref.). The MEDLINE search strategy will be translated into the other databases using the appropriate controlled vocabulary as applicable for each database.

#### *Other sources*

The bibliographies of all retrieved and relevant publications identified by the above strategies will be searched for further studies. In addition, we will search the WHO International Clinical Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>). We will attempt to contact researchers to obtain additional information when needed.

### **Data collection and analysis**

#### *Selection of studies*

Before the selection of studies, a procedure for screening will be developed by discussion among all the reviewers. We will extract data into Review Manager 5.3,[16] and summarize details using a standard data extraction sheet. Two reviewers (CR and VR) will independently assess the titles and abstracts of the studies identified from the search strategy against the inclusion criteria. Full versions of articles that appear to fulfil the inclusion criteria will be obtained for further assessment. Another review author (IL) will evaluate any discrepancies, if necessary, and will advise in case of disagreement. We will record all reasons for exclusion and we will exclude studies that not use the educational interventional to improve blood pressure control.

#### *Data extraction and management*

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3 Two review authors (CR and VR), working independently, will extract data and summarize  
4 details of trials using a standard data extraction sheet. According to methods described in the  
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Two review authors (CR and VR), working independently, will extract data and summarize details of trials using a standard data extraction sheet. According to methods described in the Cochrane Handbook for Systematic Reviews of Interventions,[17] the extraction sheet includes information such as study design, methodology, participants, interventions, duration of treatment, outcomes, conclusions and potential sources of bias. We will resolve any discrepancies by discussion with a third review author (IL). If studies report more than one outcome time (e.g. 6 and 12 months), data concerning the longest follow up will be extracted. Where data are found to be missing, we will contact the corresponding author of studies to request the missing data or to clarify study details.

#### *Assessment of risk of bias in included studies*

For assessment of study quality and reporting bias two reviewers (CR and VR) will independently assess the risk of bias, using the Cochrane collaboration's tool for assessing risk of bias of the included trials,[18] which is composed of six domains of a trial, such as random sequence generation (selection bias), allocation concealment (selection bias), blinding (performance bias and detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias) and other bias. After assessing all the domains, the reviewers will summarize the assessments and categorize the included trials into three levels of bias: low, unclear and high risk of bias and high risk of bias. We will resolve any disagreements by discussion with a third author (IL).

#### *Measures of treatment effect*

We will present the effects on blood pressure between interventions at follow-up (systolic and diastolic blood pressure) according to the educational intervention proposed in each study. We will present the outcome results for each trial with 95% confidence intervals (CI). Continuous

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3 outcomes (such as changes in systolic and diastolic blood pressure) will be expressed and  
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5 calculated as mean difference (MD) and overall effect size between intervention and control  
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7 groups. We will use Relative Risk (RR) or Odds Ratio (OR) depending on measurements indices  
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9 in individual studies for other primary and secondary outcomes.  
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### 12 *Unit of analysis issues*

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14 We will treat the number of individual participants as the unit of analysis in this review. We will  
15  
16 include cluster-randomized trials in the analysis. For cluster-randomized trials, we will adjust  
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18 results when the unit of analysis in the trial is presented as the total number of individual  
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20 participants instead of number of clusters. Results will be adjusted using the mean cluster size  
21  
22 and intracluster correlation coefficient,[19]. For meta-analysis, data will be combined to  
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24 individually randomized trials using the generic inverse-variance method as described on  
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26 Chapter 16.3 of the Cochrane Handbook for Systematic Reviews of Interventions,[19].  
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### 32 *Dealing with missing data*

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34 In the case of missing data, we will contact the original investigators to request missing data  
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36 whenever possible. If trial does not specify participant group number prior to dropout, we will  
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38 present only complete case analysis for primary and secondary outcomes.  
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### 41 *Assessment of heterogeneity*

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43 Whenever studies appear to be similar in terms of level of participants, intervention type and  
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45 duration and outcome type we will pool data using meta-analysis (using RevMan 5.3). We will  
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47 test statistical heterogeneity using the Chi<sup>2</sup> test (considering a value of P < 0.1 to indicate  
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49 heterogeneity) and estimate the amount of heterogeneity using the I<sup>2</sup> statistic,[20]. If I<sup>2</sup> is over  
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3 50% indicating a high level of heterogeneity data will not be pooled. In the absence of clinical  
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6 and statistical heterogeneity we will use a fixed-effect model.  
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#### 8 9 *Assessment of reporting biases*

10 We will present the overall risk of bias (random sequence generation, allocation concealment,  
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12 blinding of participants and personnel, blinding of outcome assessment, incomplete outcome  
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14 data, selective reporting) in a risk of bias summary table per study. If sufficient studies (more  
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16 than ten) are identified an attempt will be made to examine for publication bias using funnel plot  
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18 as described in the Cochrane Handbook for Systematic Reviews of Interventions,[21]. If  
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20 asymmetry is present we will explore possible causes including publication bias, poor  
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22 methodological quality and true heterogeneity.  
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#### 27 28 *Data synthesis*

29 We will present a narrative overview of the combined studies with meta-analysis of outcome  
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31 data using the software Review Manager version 5.3 where appropriate. The decision to include  
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33 studies in a meta-analysis will depend on the availability of treatment effect data and assessment  
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35 of heterogeneity. Intervention effects will be calculated as relative risks with 95% confidence  
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37 intervals for dichotomous data. For continuous data, we will calculate mean differences and  
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39 weighted mean differences with 95% confidence intervals using a conservative fixed-effects  
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41 meta-analysis model in the absence of significant heterogeneity ( $p > 0.05$  or  $I^2 < 50\%$ ). If there is  
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43 high level of heterogeneity ( $I^2 > 50\%$ ) we will not pool data and we will perform sensitivity  
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45 analysis of data.  
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#### 50 51 52 *Subgroup analysis* 53 54 55 56 57 58 59 60

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3 Subgroup analysis will be carried out according to the following variables: age and gender of  
4 participants, professional delivering intervention (e.g. nurse).  
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### 8 *Sensitivity analysis*

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10 If sufficient trials are identified, we plan to conduct sensitivity analyses in order to explore the  
11 influence on the results of the following factors: assessor blinding (high risk of bias versus low  
12 risk of bias). We will restrict analyses to studies at low risk of bias.  
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### 17 *Ethics and dissemination*

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19 This systematic review does not need ethical approval. Findings of this review will be  
20 disseminated via peer-reviewed journals and conference presentations.  
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## 25 **DISCUSSION**

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27 This is the protocol for a review and there is no primary data collection. The systematic review  
28 will be published in a peer-reviewed journal and disseminated electronically or in print. This  
29 review also will benefit patients with hypertension as they will better understand and accept the  
30 therapy and change their behavior about the treatment.  
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4 *Author's Contributions:* The search strategy will be developed and run by IL. Copies of studies  
5 will be obtained by CR and VR. Selection of the studies to include will be performed by CR and  
6 VR. Extraction data from studies and entering data into RevMan will be conducted by CR and  
7 VR. The analysis will be carried out by CR, VR and IL. Interpretation of the analysis will be  
8 carried out by all authors. The final review will be drafted by all authors. The protocol was  
9 revised, and the final version was approved by all authors.  
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23 Assessment in Health: Comparative Effectiveness Research.  
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32 *Competing interests:* None.  
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# EDUCATIONAL INTERVENTION FOR IMPROVING CONTROL OF BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION: A SYSTEMATIC REVIEW PROTOCOL

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**Running Title:** Educational intervention in hypertension - systematic review.

*Key words:* hypertension, blood pressure, educational interventions, randomized controlled trial, systematic review

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For peer review only

## Abstract

**Introduction:** The aim of this review is to evaluate the effectiveness of educational interventions on improving the control of blood pressure in patients with hypertension.

**Methods:** Randomized controlled trials including patients aged over eighteen years old regardless of sex, ethnicity with a diagnosis of hypertension (either treated or not treated with antihypertensive medications) will be assessed in our analysis. We will electronically search four databases: MEDLINE, CINAHL, PEDro, ScienceDirect. There will be no language restrictions in the search for studies. The data will be extracted independently by two authors using predefined criteria. Disagreements will be resolved between the authors. The risk of bias will be assessed using the Cochrane risk of bias tool. After searching and screening of the studies, we will run a meta-analysis of the included randomised controlled trials. We will summarise the results as risk ratio for dichotomous data and mean differences for continuous data.

**Ethics and dissemination:** The protocol for the systematic review has been registered in PROSPERO. The review will be published in a journal. The findings from the review will also be disseminated electronically and conferences presentations.

**Trial registration number:** Ribeiro C, Resqueti V, Lima I, Dias F, Glynn L, Fregonezi G. Educational interventions for improving control of blood pressure in patients with hypertension. PROSPERO: International prospective register of systematic reviews. 2014: CRD4201401071 Available from:

[http://www.crd.york.ac.uk/PROSPERO/register\\_new\\_review.asp?RecordID=10171](http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp?RecordID=10171)

### Strengths and limitations of this study:

- The results of this systematic review will help clinicians in making decisions in clinical practice, and help patients to better understand their conditions and also can heighten awareness about disease progression and complications.

## INTRODUCTION

### Description of the condition

Hypertension is a major health problem worldwide and is estimated to cause more than 13% of deaths annually,[1]. It is a multifactorial clinical condition characterized by high and sustained levels of blood pressure,[2]. It is one of the most important public health problems in the world and an important modifiable risk factor for the development of cardiovascular diseases. Adoption of healthy lifestyles by all individuals is critical for the prevention of high blood pressure and an indispensable part of the management of those with hypertension,[3]. Uncontrolled hypertension is associated with high risk for development of heart disease, stroke, chronic kidney disease, retinopathy, peripheral vascular disease.

A recent epidemiological worldwide study estimated that the high blood pressure causes approximately 7.6 million premature deaths (54% for stroke and 47% for ischaemic heart disease),[4]. A recent systematic review reporting data from studies in 35 different countries between the years 2003 and 2008 demonstrated an overall prevalence of 37.8% for men and 32.1% for women,[5].

Due to the fact that the prevalence of hypertension increases with age,[6] the management of hypertension and the prevention and treatment of major complications related to hypertension will continue to be a global challenge for health care professionals.

### Description of the intervention

Hypertension is a condition almost entirely managed by the primary care team by a variety of health professionals such as physicians, nurses, pharmacists and other allied health care professionals such as physiotherapists that frequently work in cardiac rehabilitation. All



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3 professionals can potentially play an important role in lowering blood pressure. It is important  
4 that patients understand the benefits of blood pressure lowering which include a reduction in  
5 many complications such as stroke (35-40%), heart attack (20-25%) and heart failure (over  
6 50%)[3]. The majority of patients will require a combination of antihypertensive drugs to reach  
7 target blood pressure.  
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16 A previous study demonstrated that educational interventions increased participants' levels of  
17 knowledge about hypertension and had a positive influence on their beliefs about medicines,[7].  
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### **How the intervention might work**

Different health professionals have become more involved in delivering interventions to the patients with the objective of preventing complications caused by high blood pressure. Patients expectations have a significant effect on the treatment they get from their doctor or any other health professional involved,[9]. Many previous trials in blood pressure control have used educational interventions on patients, physicians or both in an attempt to improve blood pressure control.

Educational interventions can positively modify patients' beliefs which in turn can lead to a change in patient behavior such as improvement in adherence to a therapy proposed by the health care professional,[8] and a possible effect on variables related to the disease such as blood

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3 pressure levels. This may also affect in long term the progression of the disease and the  
4 prevalence of associated conditions related to hypertension such as heart attacks and stroke.  
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### 8 9 **Why is important to do this review**

10  
11 Due to the high morbidity and mortality caused by hypertension and the global scale of this  
12 important public health issue, it is important to continue to investigate interventions that can  
13 improve blood pressure control. It is striking that blood pressure goals continue to be a achieved  
14 in only 25-40% of the patients who take antihypertensive drug treatment,[3,10], which is  
15 something that has remained unchanged for the last 40 years,[11].  
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24 A recent Cochrane review demonstrated that there are many categories of interventions that  
25 singly or in unison have the potential to reduce blood pressure in patients with hypertension,[12].  
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29 In this review educational interventions directed to patient and physician were examined;  
30 however, the focus of the review and protocol was not the educational intervention alone.  
31 Educational interventions either to health professionals or patients, did not appear to be  
32 associated with large net reductions in blood pressure but were recommended as an adjunct  
33 additional therapy along other types of interventions.  
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41 Due to the fact that there has been an increasing number of recent studies showing the  
42 importance of prevention in patients with hypertension,[13-15] this review will determine the  
43 current evidence of the effects of educational interventions to improve control of blood pressure  
44 in patients with hypertension, potentially updating the recommendation for clinical practice.  
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## 51 **METHODS AND ANALYSIS**

### 52 **Criteria for considering studies for the review**

### *Types of studies*

We plan to include randomized clinical trials (RCTs) that have evaluated the effects of different models of educational interventions with the overall aim of improving blood pressure control in patients with hypertension, irrespective of language. The review will include RCTs where educational intervention used as the main or adjunct treatment was compared with no educational intervention or different types of educational strategies. We will exclude studies that use educational interventions not intended to improve blood pressure control.

### *Types of participants*

We will include studies that participants have age over 18 years regardless of sex, ethnicity with a diagnosis of hypertension either treated or not treated with antihypertensive medications in a primary care, outpatient or community setting.)

### *Types of interventions*

The intervention of interest will include all educational interventions strategies designed to improve the control of blood pressure in patients with hypertension (e.g. educational interventions direct to the patient; educational interventions direct to the health professional). Comparators will be any educational intervention used as the main or adjunct treatment to improve the control of blood pressure compared with either no educational intervention or different types of educational strategies aimed to improve blood pressure control.

### *Types of outcomes assessments*

The primary outcome of this review will be any changes in mean systolic blood pressure (SBP) and/or mean diastolic blood pressure (DBP) in any care setting as well as number of patients under control of blood pressure (BP) or proportion of controlled BP defined by each randomized

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3 trial's investigators. The secondary outcomes will be: number of hospitalizations during  
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5 treatment (e.g. increase of BP) or mortality from cardiovascular disease as an adverse events; the  
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7 costs and cost effectiveness of interventions; the adherence to intervention (dropout rate) or  
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9 adherence to medication and the outcome QOL will be measured using standardized generic  
10  
11 questionnaire.  
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## 14 15 16 **Search methods for identification of studies**

### 17 18 *Electronic searches*

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20 We will electronically search the following databases: MEDLINE, CINAHL, PEDro,  
21  
22 ScienceDirect, WHO International Clinical Trials Registry Platform (ICTRP) and  
23  
24 ClinicalTrials.gov. without any language restrictions. The search strategy will be developed after  
25  
26 discussion among reviewers, according to the guidance of the Cochrane handbook[16].The  
27  
28 MEDLINE search strategy will be translated into the other databases using the appropriate  
29  
30 controlled vocabulary as applicable for each database.  
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### 34 35 *Other sources*

36  
37 The bibliographies of all retrieved and relevant publications identified by the above strategies  
38  
39 will be searched for further studies. In addition, we will search the WHO International Clinical  
40  
41 Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>). We will attempt to contact  
42  
43 researchers to obtain additional information when needed.  
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## 47 48 **Data collection and analysis**

### 49 50 *Selection of studies*

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52 Before the selection of studies, a procedure for screening will be developed by discussion among  
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54 all the reviewers. We will extract data into Review Manager 5.3,[17] and summarize details  
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3 using a standard data extraction sheet. Two reviewers (CR and VR) will independently assess the  
4 titles and abstracts of the studies identified from the search strategy against the inclusion criteria.  
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6 Full versions of articles that appear to fulfil the inclusion criteria will be obtained for further  
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8 assessment. Another review author (IL) will evaluate any discrepancies, if necessary, and will  
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10 advise in case of disagreement. We will record all reasons for exclusion and we will exclude  
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12 studies that not use the educational interventional to improve blood pressure control.  
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### 15 16 17 18 *Data extraction and management*

19  
20 Two review authors (CR and VR), working independently, will extract data and summarize  
21  
22 details of trials using a standard data extraction sheet. According to methods described in the  
23  
24 Cochrane Handbook for Systematic Reviews of Interventions,[18] the extraction sheet includes  
25  
26 information such as study design, methodology, participants, interventions, duration of  
27  
28 treatment, outcomes, conclusions and potential sources of bias. We will resolve any  
29  
30 discrepancies by discussion with a third review author (IL). If studies report more than one  
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32 outcome time (e.g. 6 and 12 months), data concerning the longest follow up will be extracted.  
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34 Where data are found to be missing, we will contact the corresponding author of studies to  
35  
36 request the missing data or to clarify study details.  
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### 39 40 41 42 *Assessment of risk of bias in included studies*

43  
44 For assessment of study quality and reporting bias two reviewers (CR and VR) will  
45  
46 independently assess the risk of bias, using the Cochrane collaboration's tool for assessing risk  
47  
48 of bias of the included trials,[19] which is composed of six domains of a trial, such as random  
49  
50 sequence generation (selection bias), allocation concealment (selection bias), blinding  
51  
52 (performance bias and detection bias), incomplete outcome data (attrition bias), selective  
53  
54 outcome reporting (reporting bias) and other bias. After assessing all the domains, the reviewers  
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3 will summarize the assessments and categorize the included trials into three levels of bias: low,  
4 unclear and high risk of bias and high risk of bias. We will resolve any disagreements by  
5 discussion with a third author (IL).  
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### 10 *Measures of treatment effect*

11 We will present the effects on blood pressure between interventions at follow-up (systolic and  
12 diastolic blood pressure) according to the educational intervention proposed in each study. We  
13 will present the outcome results for each trial with 95% confidence intervals (CI). Continuous  
14 outcomes (such as changes in systolic and diastolic blood pressure) will be expressed and  
15 calculated as mean difference (MD) and overall effect size between intervention and control  
16 groups. We will use Relative Risk (RR) or Odds Ratio (OR) depending on measurements indices  
17 in individual studies for other primary and secondary outcomes.  
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### 30 *Dealing with missing data*

31 In the case of missing data, we will contact the original investigators to request missing data  
32 whenever possible. If trial does not specify participant group number prior to dropout, we will  
33 present only complete case analysis for primary and secondary outcomes.  
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### 40 *Assessment of heterogeneity*

41 Whenever studies appear to be similar in terms of participants characteristics (established  
42 hypertensive, people with diabetes or other chronic disease), intervention type and duration and  
43 outcome type we will pool data using meta-analysis (using RevMan 5.3). We will test statistical  
44 heterogeneity using the Chi<sup>2</sup> test (considering a value of P < 0.1 to indicate heterogeneity) and  
45 estimate the amount of heterogeneity using the I<sup>2</sup> statistic,[20]. If I<sup>2</sup> is over 50% indicating a high  
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3 level of heterogeneity data will not be pooled. In the absence of clinical and statistical  
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5 heterogeneity we will use a fixed-effect model.  
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### 8 *Assessment of reporting biases*

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10 We will present the overall risk of bias (random sequence generation, allocation concealment,  
11  
12 blinding of participants and personnel, blinding of outcome assessment, incomplete outcome  
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14 data, selective reporting) in a risk of bias summary table per study. If sufficient studies (more  
15  
16 than ten) are identified an attempt will be made to examine for publication bias using funnel plot  
17  
18 as described in the Cochrane Handbook for Systematic Reviews of Interventions,[21]. If  
19  
20 asymmetry is present we will explore possible causes including publication bias, poor  
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22 methodological quality and true heterogeneity.  
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### 26 *Data synthesis*

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28 We will present a narrative overview of the combined studies with meta-analysis of outcome  
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30 data using the software Review Manager version 5.3 where appropriate.  
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34 We will include cluster-randomized trials in the analysis. For cluster-randomized trials, we will  
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36 adjust results when the unit of analysis in the trial is presented as the total number of individual  
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38 participants instead of number of clusters. Results will be adjusted using the mean cluster size  
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40 and intracluster correlation coefficient,[22]. For meta-analysis, data will be combined to  
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42 individually randomized trials using the generic inverse-variance method as described on  
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44 Chapter 16.3 of the Cochrane Handbook for Systematic Reviews of Interventions,[22].  
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49 The decision to include studies in a meta-analysis will depend on the availability of treatment  
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51 effect data and assessment of heterogeneity. Intervention effects will be calculated as relative  
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53 risks with 95% confidence intervals for dichotomous data. For continuous data, we will calculate  
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55 mean differences with 95% confidence intervals using a conservative fixed-effects meta-analysis  
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3 model in the absence of significant heterogeneity ( $p > 0.05$  or  $I^2 < 50\%$ ). If there is high level of  
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5 heterogeneity ( $I^2 > 50\%$ ) we will not pool data and we will perform sensitivity analysis of data.  
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### 8 9 *Subgroup analysis*

10 Subgroup analysis will be carried out according to the following variables: age and gender of  
11  
12 participants, professional delivering intervention (e.g. nurse).  
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### 15 16 *Sensitivity analysis*

17 If sufficient trials are identified, we plan to conduct sensitivity analyses in order to explore the  
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19 influence on the results of the following factors: assessor blinding (high risk of bias versus low  
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21 risk of bias). We will restrict analyses to studies at low risk of bias.  
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### 25 26 *Ethics and dissemination*

27 This systematic review does not need ethical approval. Findings of this review will be  
28  
29 disseminated via peer-reviewed journals and conference presentations.  
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## 32 33 **DISCUSSION**

34 This is the protocol for a review and there is no primary data collection. The systematic review  
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36 will be published in a peer-reviewed journal and disseminated electronically or in print. This  
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38 review also will benefit patients with hypertension as they will better understand and accept the  
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40 therapy and change their behavior about the treatment.  
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4 *Author's Contributions:* The search strategy will be developed and run by IL. Copies of studies  
5 will be obtained by CR and VR. Selection of the studies to include will be performed by CR and  
6 VR. Extraction data from studies and entering data into RevMan will be conducted by CR and  
7 VR. The analysis will be carried out by CR, VR and IL. Interpretation of the analysis will be  
8 carried out by all authors. The final review will be drafted by all authors. The protocol was  
9 revised, and the final version was approved by all authors.  
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23 Assessment in Health: Comparative Effectiveness Research.  
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32 *Competing interests:* None.  
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# EDUCATIONAL INTERVENTION FOR IMPROVING CONTROL OF BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION: A SYSTEMATIC REVIEW PROTOCOL

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**Running Title:** Educational intervention in hypertension - systematic review.

*Key words:* hypertension, blood pressure, educational interventions, randomized controlled trial, systematic review

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## Abstract

**Introduction:** The aim of this review is to evaluate the effectiveness of educational interventions on improving the control of blood pressure in patients with hypertension.

**Methods:** Randomized controlled trials including patients aged over eighteen years old regardless of sex, ethnicity with a diagnosis of hypertension (either treated or not treated with antihypertensive medications) will be assessed in our analysis. We will electronically search four databases: MEDLINE, CINAHL, PEDro, ScienceDirect. There will be no language restrictions in the search for studies. The data will be extracted independently by two authors using predefined criteria. Disagreements will be resolved between the authors. The risk of bias will be assessed using the Cochrane risk of bias tool. After searching and screening of the studies, we will run a meta-analysis of the included randomised controlled trials. We will summarise the results as risk ratio for dichotomous data and mean differences and weighted mean differences for continuous data.

**Ethics and dissemination:** The protocol for the systematic review has been registered in PROSPERO. The review will be published in a journal. The findings from the review will also be disseminated electronically and conferences presentations.

**Trial registration number:** Ribeiro C, Resqueti V, Lima I, Dias F, Glynn L, Fregonezi G. Educational interventions for improving control of blood pressure in patients with hypertension. PROSPERO: International prospective register of systematic reviews. 2014: CRD4201401071 Available from: [http://www.crd.york.ac.uk/PROSPERO/register\\_new\\_review.asp?RecordID=10171](http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp?RecordID=10171)

### Strengths and limitations of this study:

- The trial screening and data extraction will be conducted independently by two authors.

- The results of this systematic review will help clinicians in making decisions in clinical practice, and help patients to better understand their conditions and also can heighten awareness about disease progression and complications.

## INTRODUCTION

### Description of the condition

Hypertension is a major health problem worldwide and is estimated to cause more than 13% of deaths annually,[1]. It is a multifactorial clinical condition characterized by high and sustained levels of blood pressure,[2]. It is one of the most important public health problems in the world and an important modifiable risk factor for the development of cardiovascular diseases. Adoption of healthy lifestyles by all individuals is critical for the prevention of high blood pressure and an indispensable part of the management of those with hypertension,[3]. Uncontrolled hypertension is associated with high risk for development of heart disease, stroke, chronic kidney disease, retinopathy, peripheral vascular disease.

A recent epidemiological worldwide study estimated that the high blood pressure causes approximately 7.6 million premature deaths (54% for stroke and 47% for ischaemic heart disease),[4]. A recent systematic review reporting data from studies performed in 35 different countries between the years 2003 and 2008 demonstrated an overall prevalence of 37.8% for men and 32.1% for women,[5].

Due to the fact that the prevalence of hypertension increases with age,[6] the management of hypertension and the prevention and treatment of major complications related to hypertension will continue to be a global challenge for health care professionals.

### Description of the intervention

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2  
3 Hypertension is a condition almost entirely managed by the primary care team by a variety of  
4 health professionals such as physicians, nurses, pharmacists and other allied health care  
5 professionals such as physiotherapists that frequently work in cardiac rehabilitation. All  
6 professionals can potentially play an important role in lowering blood pressure. It is important  
7 that patients understand the benefits of blood pressure lowering which include a reduction in  
8 many complications such as stroke (35-40%), heart attack (20-25%) and heart failure (over  
9 50%)[3]. The majority of patients will require a combination of antihypertensive drugs to reach  
10 target blood pressure.  
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13 A previous study demonstrated that educational interventions increased participants' levels of  
14 knowledge about hypertension and had a positive influence on their beliefs about medicines,[7].  
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17 Educational interventions can also create opportunities for patients to better understand their  
18 conditions and the role of therapies and also can heighten awareness about disease progression  
19 and complications. Through patient education, misconceptions that patients have about their  
20 therapy can be clarified. This can influence adherence to therapy,[8] and therefore potentially  
21 may lead to improve blood pressure control.  
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### 24 **How the intervention might work**

25 Different health professionals have become more involved in delivering interventions to the  
26 patients with the objective of preventing complications caused by high blood pressure. Patients  
27 expectations have a significant effect on the treatment they get from their doctor or any other  
28 health professional involved,[9]. Many previous trials in blood pressure control have used  
29 educational interventions on patients, physicians or both in an attempt to improve blood pressure  
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3 Educational interventions can positively modify patients' beliefs which in turn can lead to a  
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5 change in patient behavior such as improvement in adherence to a therapy proposed by the health  
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7 care professional,[8] and a possible effect on variables related to the disease such as blood  
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9 pressure levels. This may also affect in long term the progression of the disease and the  
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11 prevalence of associated conditions related to hypertension such as heart attacks and stroke.  
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### 14 15 16 **Why is important to do this review**

17  
18 Due to the high morbidity and mortality caused by hypertension and the global scale of this  
19  
20 important public health issue, it is important to continue to investigate interventions that can  
21  
22 improve blood pressure control. It is striking that blood pressure goals continue to be achieved  
23  
24 in only 25-40% of the patients who take antihypertensive drug treatment,[3,10], which is  
25  
26 something that has remained unchanged for the last 40 years,[11].  
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28  
29 A recent Cochrane review demonstrated that there are many categories of interventions that  
30  
31 singly or in unison have the potential to reduce blood pressure in patients with hypertension,[12].  
32  
33 In this review educational interventions directed to patient and physician were examined;  
34  
35 **however, the focus of the review and protocol was not the educational intervention alone.**  
36  
37 Educational interventions either to health professionals or patients, did not appear to be  
38  
39 associated with large net reductions in blood pressure but were recommended as an adjunct  
40  
41 additional therapy along other types of interventions.

42  
43 **Due to the fact that there has been an increasing number of recent studies showing the**  
44  
45 **importance of prevention in patients with hypertension,[13-15] this review will determine the**  
46  
47 **current evidence of the effects of educational interventions to improve control of blood pressure**  
48  
49 **in patients with hypertension, potentially updating the recommendation for clinical practice.**

## 50 51 **METHODS AND ANALYSIS**

### 52 53 **Criteria for considering studies for the review**

#### 54 55 *Types of studies*

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3 We plan to include randomized clinical trials (RCTs) that have evaluated the effects of different  
4 models of educational interventions with the overall aim of improving blood pressure control in  
5 patients with hypertension, irrespective of language. The review will include RCTs where  
6 educational intervention used as the main or adjunct treatment was compared with no  
7 educational intervention or different types of educational strategies. We will exclude studies that  
8 use educational interventions not intended to improve blood pressure control.  
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### 17 *Types of participants*

18 We will include studies that participants have age over 18 years regardless of sex, ethnicity with  
19 a diagnosis of hypertension either treated or not treated with antihypertensive medications in a  
20 primary care, outpatient or community setting.)  
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### 28 *Types of interventions*

29 The intervention of interest will include all educational interventions strategies designed to  
30 improve the control of blood pressure in patients with hypertension (e.g. educational  
31 interventions direct to the patient; educational interventions direct to the health professional).  
32 Comparators will be any educational intervention used as the main or adjunct treatment to  
33 improve the control of blood pressure compared with either no educational intervention or  
34 different types of educational strategies aimed to improve blood pressure control.  
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### 45 *Types of outcomes assessments*

46 The primary outcome of this review will be any changes in mean systolic blood pressure (SBP)  
47 and/or mean diastolic blood pressure (DBP) in any care setting as well as number of patients  
48 under control of blood pressure (BP) or proportion of controlled BP defined by each randomized  
49 trial's investigators. The secondary outcomes will be: number of hospitalizations during  
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3 treatment (e.g. increase of BP) or mortality from cardiovascular disease as an adverse events; the  
4 costs and cost effectiveness of interventions; the adherence to intervention (dropout rate) or  
5 adherence to medication and the outcome QOL will be measured using standardized generic  
6 questionnaire.  
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## 12 **Search methods for identification of studies**

### 13 *Electronic searches*

14 We will electronically search the following databases: MEDLINE, CINAHL, PEDro,  
15 ScienceDirect, WHO International Clinical Trials Registry Platform (ICTRP) and  
16 ClinicalTrials.gov. without any language restrictions. The search strategy will be developed after  
17 discussion among reviewers, according to the guidance of the Cochrane handbook[16].The  
18 MEDLINE search strategy will be translated into the other databases using the appropriate  
19 controlled vocabulary as applicable for each database.  
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### 32 *Other sources*

33 The bibliographies of all retrieved and relevant publications identified by the above strategies  
34 will be searched for further studies. In addition, we will search the WHO International Clinical  
35 Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>). We will attempt to contact  
36 researchers to obtain additional information when needed.  
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## 44 **Data collection and analysis**

### 45 *Selection of studies*

46 Before the selection of studies, a procedure for screening will be developed by discussion among  
47 all the reviewers. We will extract data into Review Manager 5.3,[17] and summarize details  
48 using a standard data extraction sheet. Two reviewers (CR and VR) will independently assess the  
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3 titles and abstracts of the studies identified from the search strategy against the inclusion criteria.  
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5 Full versions of articles that appear to fulfil the inclusion criteria will be obtained for further  
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7 assessment. Another review author (IL) will evaluate any discrepancies, if necessary, and will  
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9 advise in case of disagreement. We will record all reasons for exclusion and we will exclude  
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11 studies that not use the educational interventional to improve blood pressure control.  
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#### 14 15 *Data extraction and management*

16  
17 Two review authors (CR and VR), working independently, will extract data and summarize  
18  
19 details of trials using a standard data extraction sheet. According to methods described in the  
20  
21 Cochrane Handbook for Systematic Reviews of Interventions,[18] the extraction sheet includes  
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23 information such as study design, methodology, participants, interventions, duration of  
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25 treatment, outcomes, conclusions and potential sources of bias. We will resolve any  
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27 discrepancies by discussion with a third review author (IL). If studies report more than one  
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29 outcome time (e.g. 6 and 12 months), data concerning the longest follow up will be extracted.  
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31 Where data are found to be missing, we will contact the corresponding author of studies to  
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33 request the missing data or to clarify study details.  
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#### 39 40 *Assessment of risk of bias in included studies*

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42 For assessment of study quality and reporting bias two reviewers (CR and VR) will  
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44 independently assess the risk of bias, using the Cochrane collaboration's tool for assessing risk  
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46 of bias of the included trials,[19]which is composed of six domains of a trial, such as random  
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48 sequence generation (selection bias), allocation concealment (selection bias), blinding  
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50 (performance bias and detection bias), incomplete outcome data (attrition bias), selective  
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52 outcome reporting (reporting bias) and other bias. After assessing all the domains, the reviewers  
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54 will summarize the assessments and categorize the included trials into three levels of bias: low,  
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unclear and high risk of bias and high risk of bias. We will resolve any disagreements by discussion with a third author (IL).

### *Measures of treatment effect*

We will present the effects on blood pressure between interventions at follow-up (systolic and diastolic blood pressure) according to the educational intervention proposed in each study. We will present the outcome results for each trial with 95% confidence intervals (CI). Continuous outcomes (such as changes in systolic and diastolic blood pressure) will be expressed and calculated as mean difference (MD) and overall effect size between intervention and control groups. We will use Relative Risk (RR) or Odds Ratio (OR) depending on measurements indices in individual studies for other primary and secondary outcomes.

### *Unit of analysis issues*

We will treat the number of individual participants as the unit of analysis in this review. We will include cluster randomized trials in the analysis. For cluster randomized trials, we will adjust results when the unit of analysis in the trial is presented as the total number of individual participants instead of number of clusters. Results will be adjusted using the mean cluster size and intracluster correlation coefficient,[20]. For meta analysis, data will be combined to individually randomized trials using the generic inverse variance method as described on Chapter 16.3 of the Cochrane Handbook for Systematic Reviews of Interventions,[20].

### *Dealing with missing data*

In the case of missing data, we will contact the original investigators to request missing data whenever possible. If trial does not specify participant group number prior to dropout, we will present only complete case analysis for primary and secondary outcomes.



### *Assessment of heterogeneity*

Whenever studies appear to be similar in terms of level of participants characteristics (established hypertensive, people with diabetes or other chronic disease), OK intervention type and duration and outcome type we will pool data using meta-analysis (using RevMan 5.3). We will test statistical heterogeneity using the Chi<sup>2</sup> test (considering a value of P < 0.1 to indicate heterogeneity) and estimate the amount of heterogeneity using the I<sup>2</sup> statistic,[20]. If I<sup>2</sup> is over 50% indicating a high level of heterogeneity data will not be pooled. In the absence of clinical and statistical heterogeneity we will use a fixed-effect model.

### *Assessment of reporting biases*

We will present the overall risk of bias (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting) in a risk of bias summary table per study. If sufficient studies (more than ten) are identified an attempt will be made to examine for publication bias using funnel plot as described in the Cochrane Handbook for Systematic Reviews of Interventions,[21]. If asymmetry is present we will explore possible causes including publication bias, poor methodological quality and true heterogeneity.

### *Data synthesis*

We will present a narrative overview of the combined studies with meta-analysis of outcome data using the software Review Manager version 5.3 where appropriate.

We will include cluster-randomized trials in the analysis. For cluster-randomized trials, we will adjust results when the unit of analysis in the trial is presented as the total number of individual participants instead of number of clusters. Results will be adjusted using the mean cluster size and intracluster correlation coefficient,[22]. For meta-analysis, data will be combined to

individually randomized trials using the generic inverse-variance method as described on Chapter 16.3 of the Cochrane Handbook for Systematic Reviews of Interventions,[22].

The decision to include studies in a meta-analysis will depend on the availability of treatment effect data and assessment of heterogeneity. Intervention effects will be calculated as relative risks with 95% confidence intervals for dichotomous data. For continuous data, we will calculate mean differences with 95% confidence intervals using a conservative fixed-effects meta-analysis model in the absence of significant heterogeneity ( $p > 0.05$  or  $I^2 < 50\%$ ). If there is high level of heterogeneity ( $I^2 > 50\%$ ) we will not pool data and we will perform sensitivity analysis of data.

#### *Subgroup analysis*

Subgroup analysis will be carried out according to the following variables: age and gender of participants, professional delivering intervention (e.g. nurse).

#### *Sensitivity analysis*

If sufficient trials are identified, we plan to conduct sensitivity analyses in order to explore the influence on the results of the following factors: assessor blinding (high risk of bias versus low risk of bias). We will restrict analyses to studies at low risk of bias.

#### *Ethics and dissemination*

This systematic review does not need ethical approval. Findings of this review will be disseminated via peer-reviewed journals and conference presentations.

## **DISCUSSION**

This is the protocol for a review and there is no primary data collection. The systematic review will be published in a peer-reviewed journal and disseminated electronically or in print. This

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3 review also will benefit patients with hypertension as they will better understand and accept the  
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6 therapy and change their behavior about the treatment.  
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*Author's Contributions:* The search strategy will be developed and run by IL. Copies of studies will be obtained by CR and VR. Selection of the studies to include will be performed by CR and VR. Extraction data from studies and entering data into RevMan will be conducted by CR and VR. The analysis will be carried out by CR, VR and IL. Interpretation of the analysis will be carried out by all authors. The final review will be drafted by all authors. The protocol was revised, and the final version was approved by all authors.

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*Competing interests:* None.

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UNIVERSIDADE FEDERAL DO RIO GRANDE DO NORTE  
CENTRO DE CIÊNCIAS DA SAÚDE  
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September 05, 2014

Dear Editor

Please consider the manuscript "EDUCATIONAL INTERVENTION FOR IMPROVING CONTROL OF BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION: A SYSTEMATIC REVIEW PROTOCOL" for publication in *BMJ Open* as a study protocol. This protocol describes all the methodology to develop a systematic review that will evaluate the current evidence of the effects of educational interventions on the control of blood pressure on patients with hypertension.

All authors have contributed to the present work and have also read and approved the submission of the manuscript to this journal. This study protocol has not been published or is under consideration for publication elsewhere and the authors have no conflict of interest to report.

We appreciate your consideration and we hope we will be able to contribute to the journal.

Thank you.

Sincerely,



Guilherme Augusto de Freitas Fregonezi, PT, PhD

# BMJ Open

## Educational Interventions for improving control of blood pressure in patients with hypertension: A Systematic Review Protocol

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<b>Primary Subject Heading</b>:	Cardiovascular medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Hypertension < CARDIOLOGY, EDUCATION & TRAINING (see Medical Education & Training), Rehabilitation medicine < INTERNAL MEDICINE, PREVENTIVE MEDICINE

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Manuscripts

# EDUCATIONAL INTERVENTIONS FOR IMPROVING CONTROL OF BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION: A SYSTEMATIC REVIEW PROTOCOL

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**Running Title:** Educational intervention in hypertension - systematic review.

*Key words:* hypertension, blood pressure, educational interventions, randomized controlled trial, systematic review

Word Count: 2216

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## Abstract

**Introduction:** The aim of this review is to evaluate the effectiveness of educational interventions on improving the control of blood pressure in patients with hypertension.

**Methods:** Randomized controlled trials including patients aged over eighteen years old regardless of sex, ethnicity with a diagnosis of hypertension (either treated or not treated with antihypertensive medications) will be assessed in our analysis. We will electronically search four databases: MEDLINE, CINAHL, PEDro, ScienceDirect. There will be no language restrictions in the search for studies. The data will be extracted independently by two authors using predefined criteria. Disagreements will be resolved between the authors. The risk of bias will be assessed using the Cochrane risk of bias tool. After searching and screening of the studies, we will run a meta-analysis of the included randomised controlled trials. We will summarise the results as risk ratio for dichotomous data and mean differences for continuous data.

**Ethics and dissemination:** The protocol for the systematic review has been registered in PROSPERO. The review will be published in a journal. The findings from the review will also be disseminated electronically and conferences presentations.

**Registration:** Ribeiro C, Resqueti V, Lima I, Dias F, Glynn L, Fregonezi G. Educational interventions for improving control of blood pressure in patients with hypertension. PROSPERO: International prospective register of systematic reviews. 2014: CRD4201401071 Available from: [http://www.crd.york.ac.uk/PROSPERO/register\\_new\\_review.asp?RecordID=10171](http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp?RecordID=10171)

### Strengths and limitations of this study:

- The results of this systematic review will help clinicians in making decisions in clinical practice, and help patients to better understand their conditions and also can heighten awareness about disease progression and complications.

## INTRODUCTION

### Description of the condition

Hypertension is a major health problem worldwide and is estimated to cause more than 13% of deaths annually,[1]. It is a multifactorial clinical condition characterized by high and sustained levels of blood pressure,[2]. It is one of the most important public health problems in the world and an important modifiable risk factor for the development of cardiovascular diseases. Adoption of healthy lifestyles by all individuals is critical for the prevention of high blood pressure and an indispensable part of the management of those with hypertension,[3]. Uncontrolled hypertension is associated with high risk for development of heart disease, stroke, chronic kidney disease, retinopathy, peripheral vascular disease.

A recent epidemiological worldwide study estimated that the high blood pressure causes approximately 7.6 million premature deaths (54% for stroke and 47% for ischaemic heart disease),[4]. A recent systematic review reporting data from studies in 35 different countries between the years 2003 and 2008 demonstrated an overall prevalence of 37.8% for men and 32.1% for women,[5].

Due to the fact that the prevalence of hypertension increases with age,[6] the management of hypertension and the prevention and treatment of major complications related to hypertension will continue to be a global challenge for health care professionals.

### Description of the intervention

Hypertension is a condition almost entirely managed by the primary care team by a variety of health professionals such as physicians, nurses, pharmacists and other allied health care professionals such as physiotherapists that frequently work in cardiac rehabilitation. All professionals can potentially play an important role in lowering blood pressure. It is important

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3 that patients understand the benefits of blood pressure lowering which include a reduction in  
4 many complications such as stroke (35-40%), heart attack (20-25%) and heart failure (over  
5 50%)[3]. The majority of patients will require a combination of antihypertensive drugs to reach  
6 target blood pressure.  
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13 A previous study demonstrated that educational interventions increased participants' levels of  
14 knowledge about hypertension and had a positive influence on their beliefs about medicines,[7].  
15 Educational interventions can also create opportunities for patients to better understand their  
16 conditions and the role of therapies and also can heighten awareness about disease progression  
17 and complications. Through patient education, misconceptions that patients have about their  
18 therapy can be clarified. This can influence adherence to therapy,[8] and therefore potentially  
19 may lead to improve blood pressure control.  
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### 31 **How the intervention might work**

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33 Different health professionals have become more involved in delivering interventions to the  
34 patients with the objective of preventing complications caused by high blood pressure. Patients  
35 expectations have a significant effect on the treatment they get from their doctor or any other  
36 health professional involved,[9]. Many previous trials in blood pressure control have used  
37 educational interventions on patients, physicians or both in an attempt to improve blood pressure  
38 control.  
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49 Educational interventions can positively modify patients' beliefs which in turn can lead to a  
50 change in patient behavior such as improvement in adherence to a therapy proposed by the health  
51 care professional,[8] and a possible effect on variables related to the disease such as blood  
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3 pressure levels. This may also affect in long term the progression of the disease and the  
4 prevalence of associated conditions related to hypertension such as heart attacks and stroke.  
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### 8 9 **Why is important to do this review**

10  
11 Due to the high morbidity and mortality caused by hypertension and the global scale of this  
12 important public health issue, it is important to continue to investigate interventions that can  
13 improve blood pressure control. It is striking that blood pressure goals continue to be a achieved  
14 in only 25-40% of the patients who take antihypertensive drug treatment,[3,10], which is  
15 something that has remained unchanged for the last 40 years,[11].  
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24 A recent Cochrane review demonstrated that there are many categories of interventions that  
25 singly or in unison have the potential to reduce blood pressure in patients with hypertension,[12].  
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29 In this review educational interventions directed to patient and physician were examined;  
30 however, the focus of the review and protocol was not the educational intervention alone.  
31 Educational interventions either to health professionals or patients, did not appear to be  
32 associated with large net reductions in blood pressure but were recommended as an adjunct  
33 additional therapy along other types of interventions.  
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41 Due to the fact that there has been an increasing number of recent studies showing the  
42 importance of prevention in patients with hypertension,[13-15] this review will determine the  
43 current evidence of the effects of educational interventions to improve control of blood pressure  
44 in patients with hypertension, potentially updating the recommendation for clinical practice.  
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## 51 **METHODS AND ANALYSIS**

### 52 **Criteria for considering studies for the review**

### *Types of studies*

We plan to include randomized clinical trials (RCTs) that have evaluated the effects of different models of educational interventions with the overall aim of improving blood pressure control in patients with hypertension, irrespective of language. The review will include RCTs where educational interventions used as the main or adjunct treatment was compared with no educational interventions or different types of educational strategies. We will exclude studies that use educational interventions not intended to improve blood pressure control.

### *Types of participants*

We will include studies that participants have age over 18 years regardless of sex, ethnicity with a diagnosis of hypertension either treated or not treated with antihypertensive medications in a primary care, outpatient or community setting.)

### *Types of interventions*

The intervention of interest will include all educational interventions strategies designed to improve the control of blood pressure in patients with hypertension (e.g. educational interventions direct to the patient; educational interventions direct to the health professional). Comparators will be any educational intervention used as the main or adjunct treatment to improve the control of blood pressure compared with either no educational interventions or different types of educational strategies aimed to improve blood pressure control.

### *Types of outcomes assessments*

The primary outcome of this review will be any changes in mean systolic blood pressure (SBP) and/or mean diastolic blood pressure (DBP) in any care setting as well as number of patients under control of blood pressure (BP) or proportion of controlled BP defined by each randomized

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3 trial's investigators. The secondary outcomes will be: number of hospitalizations during  
4  
5 treatment (e.g. increase of BP) or mortality from cardiovascular disease as an adverse events; the  
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7 costs and cost effectiveness of interventions; the adherence to intervention (dropout rate) or  
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9 adherence to medication and the outcome QOL will be measured using standardized generic  
10  
11 questionnaire.  
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## 14 15 16 **Search methods for identification of studies**

### 17 18 *Electronic searches*

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20 We will electronically search the following databases: MEDLINE, CINAHL, PEDro,  
21  
22 ScienceDirect, without any language restrictions (in case of studies in another language, other  
23  
24 than English, we will contact companies specialized in translation). The search strategy will be  
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26 developed after discussion among reviewers, according to the guidance of the Cochrane  
27  
28 handbook[16].The MEDLINE search strategy will be translated into the other databases using  
29  
30 the appropriate controlled vocabulary as applicable for each database.  
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### 34 35 *Other sources*

36  
37 The bibliographies of all retrieved and relevant publications identified by the above strategies  
38  
39 will be searched for further studies. In addition, we will search the WHO International Clinical  
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41 Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>). We will attempt to contact  
42  
43 researchers to obtain additional information when needed.  
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## 46 47 **Data collection and analysis**

### 48 49 *Selection of studies*

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51 Before the selection of studies, a procedure for screening will be developed by discussion among  
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53 all the reviewers. We will extract data into Review Manager 5.3,[17] and summarize details  
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3 using a standard data extraction sheet. Two reviewers (CR and VR) will independently assess the  
4 titles and abstracts of the studies identified from the search strategy against the inclusion criteria.  
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6 Full versions of articles that appear to fulfil the inclusion criteria will be obtained for further  
7  
8 assessment. Another review author (IL) will evaluate any discrepancies, if necessary, and will  
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10 advise in case of disagreement. We will record all reasons for exclusion and we will exclude  
11  
12 studies that not use the educational interventional to improve blood pressure control.  
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### 15 16 17 18 *Data extraction and management*

19  
20 Two review authors (CR and VR), working independently, will extract data and summarize  
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22 details of trials using a standard data extraction sheet. According to methods described in the  
23  
24 Cochrane Handbook for Systematic Reviews of Interventions,[18] the extraction sheet includes  
25  
26 information such as study design, methodology, participants, interventions, duration of  
27  
28 treatment, outcomes, conclusions and potential sources of bias. We will resolve any  
29  
30 discrepancies by discussion with a third review author (IL). If studies report more than one  
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32 outcome time (e.g. 6 and 12 months), data concerning the longest follow up will be extracted.  
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34 Where data are found to be missing, we will contact the corresponding author of studies to  
35  
36 request the missing data or to clarify study details.  
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### 40 41 42 *Assessment of risk of bias in included studies*

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44 For assessment of study quality and reporting bias two reviewers (CR and VR) will  
45  
46 independently assess the risk of bias, using the Cochrane collaboration's tool for assessing risk  
47  
48 of bias of the included trials,[19] which is composed of six domains of a trial, such as random  
49  
50 sequence generation (selection bias), allocation concealment (selection bias), blinding  
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52 (performance bias and detection bias), incomplete outcome data (attrition bias), selective  
53  
54 outcome reporting (reporting bias) and other bias. After assessing all the domains, the reviewers  
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3 will summarize the assessments and categorize the included trials into three levels of bias: low,  
4 unclear and high risk of bias and high risk of bias. We will resolve any disagreements by  
5 discussion with a third author (IL).  
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### 10 *Measures of treatment effect*

11 We will present the effects on blood pressure between interventions at follow-up (systolic and  
12 diastolic blood pressure) according to the educational interventions proposed in each study. We  
13 will present the outcome results for each trial with 95% confidence intervals (CI). Continuous  
14 outcomes (such as changes in systolic and diastolic blood pressure) will be expressed and  
15 calculated as mean difference (MD) and overall effect size between intervention and control  
16 groups. We will use Relative Risk (RR) or Odds Ratio (OR) depending on measurements indices  
17 in individual studies for other primary and secondary outcomes.  
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### 30 *Dealing with missing data*

31 In the case of missing data, we will contact the original investigators to request missing data  
32 whenever possible. If trial does not specify participant group number prior to dropout, we will  
33 present only complete case analysis for primary and secondary outcomes.  
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### 40 *Assessment of heterogeneity*

41 Whenever studies appear to be similar in terms of participants characteristics (established  
42 hypertensive, people with diabetes or other chronic disease), intervention type and duration and  
43 outcome type we will pool data using meta-analysis (using RevMan 5.3). We will test statistical  
44 heterogeneity using the Chi<sup>2</sup> test (considering a value of P < 0.1 to indicate heterogeneity) and  
45 estimate the amount of heterogeneity using the I<sup>2</sup> statistic,[20]. If I<sup>2</sup> is over 50% indicating a high  
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3 level of heterogeneity data will not be pooled. In the absence of clinical and statistical  
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5 heterogeneity we will use a fixed-effect model.  
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### 8 *Assessment of reporting biases*

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10 We will present the overall risk of bias (random sequence generation, allocation concealment,  
11  
12 blinding of participants and personnel, blinding of outcome assessment, incomplete outcome  
13  
14 data, selective reporting) in a risk of bias summary table per study. If sufficient studies (more  
15  
16 than ten) are identified an attempt will be made to examine for publication bias using funnel plot  
17  
18 as described in the Cochrane Handbook for Systematic Reviews of Interventions,[21]. If  
19  
20 asymmetry is present we will explore possible causes including publication bias, poor  
21  
22 methodological quality and true heterogeneity.  
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### 27 *Data synthesis*

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29 We will present a narrative overview of the combined studies with meta-analysis of outcome  
30  
31 data using the software Review Manager version 5.3 where appropriate.  
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34 We will include cluster-randomized trials in the analysis. For cluster-randomized trials, we will  
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36 adjust results when the unit of analysis in the trial is presented as the total number of individual  
37  
38 participants instead of number of clusters. Results will be adjusted using the mean cluster size  
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40 and intracluster correlation coefficient,[22]. For meta-analysis, data will be combined to  
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42 individually randomized trials using the generic inverse-variance method as described on  
43  
44 Chapter 16.3 of the Cochrane Handbook for Systematic Reviews of Interventions,[22].  
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48 The decision to include studies in a meta-analysis will depend on the availability of treatment  
49  
50 effect data and assessment of heterogeneity. Intervention effects will be calculated as relative  
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52 risks with 95% confidence intervals for dichotomous data. For continuous data, we will calculate  
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54 mean differences with 95% confidence intervals using a conservative fixed-effects meta-analysis  
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3 model in the absence of significant heterogeneity ( $p > 0.05$  or  $I^2 < 50\%$ ). If there is high level of  
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5 heterogeneity ( $I^2 > 50\%$ ) we will not pool data and we will perform sensitivity analysis of data.  
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### 8 9 *Subgroup analysis*

10 Subgroup analysis will be carried out according to the following variables: age and gender of  
11  
12 participants, professional delivering intervention (e.g. nurse).  
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### 15 16 *Sensitivity analysis*

17 If sufficient trials are identified, we plan to conduct sensitivity analyses in order to explore the  
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19 influence on the results of the following factors: assessor blinding (high risk of bias versus low  
20  
21 risk of bias). We will restrict analyses to studies at low risk of bias.  
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### 25 26 *Ethics and dissemination*

27 This systematic review does not need ethical approval. Findings of this review will be  
28  
29 disseminated via peer-reviewed journals and conference presentations.  
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## 32 33 **DISCUSSION**

34 This is the protocol for a review and there is no primary data collection. The systematic review  
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36 will be published in a peer-reviewed journal and disseminated electronically or in print. This  
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38 review also will benefit patients with hypertension as they will better understand and accept the  
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40 therapy and change their behavior about the treatment.  
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4 *Author's Contributions:* The search strategy will be developed and run by IL. Copies of studies  
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6 will be obtained by CR and VR. Selection of the studies to include will be performed by CR and  
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8 VR. Extraction data from studies and entering data into RevMan will be conducted by CR and  
9  
10 VR. The analysis will be carried out by CR, VR and IL. Interpretation of the analysis will be  
11  
12 carried out by all authors. The final review will be drafted by all authors. The protocol was  
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14 revised, and the final version was approved by all authors.  
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26 Assessment in Health: Comparative Effectiveness Research.  
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31 *Competing interests:* None.  
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For peer review only

# EDUCATIONAL INTERVENTIONS FOR IMPROVING CONTROL OF BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION: A SYSTEMATIC REVIEW PROTOCOL

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**Running Title:** Educational intervention in hypertension - systematic review.

*Key words:* hypertension, blood pressure, educational interventions, randomized controlled trial, systematic review

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## Abstract

**Introduction:** The aim of this review is to evaluate the effectiveness of educational interventions on improving the control of blood pressure in patients with hypertension.

**Methods:** Randomized controlled trials including patients aged over eighteen years old regardless of sex, ethnicity with a diagnosis of hypertension (either treated or not treated with antihypertensive medications) will be assessed in our analysis. We will electronically search four databases: MEDLINE, CINAHL, PEDro, ScienceDirect. There will be no language restrictions in the search for studies. The data will be extracted independently by two authors using predefined criteria. Disagreements will be resolved between the authors. The risk of bias will be assessed using the Cochrane risk of bias tool. After searching and screening of the studies, we will run a meta-analysis of the included randomised controlled trials. We will summarise the results as risk ratio for dichotomous data and mean differences for continuous data.

**Ethics and dissemination:** The protocol for the systematic review has been registered in PROSPERO. The review will be published in a journal. The findings from the review will also be disseminated electronically and conferences presentations.

**Trial registration number:** **Registration:** Ribeiro C, Resqueti V, Lima I, Dias F, Glynn L, Fregonezi G. Educational interventions for improving control of blood pressure in patients with hypertension. PROSPERO: International prospective register of systematic reviews. 2014: CRD4201401071 Available from:

[http://www.crd.york.ac.uk/PROSPERO/register\\_new\\_review.asp?RecordID=10171](http://www.crd.york.ac.uk/PROSPERO/register_new_review.asp?RecordID=10171)

### Strengths and limitations of this study:

- The results of this systematic review will help clinicians in making decisions in clinical practice, and help patients to better understand their conditions and also can heighten awareness about disease progression and complications.



## INTRODUCTION

### Description of the condition

Hypertension is a major health problem worldwide and is estimated to cause more than 13% of deaths annually,[1]. It is a multifactorial clinical condition characterized by high and sustained levels of blood pressure,[2]. It is one of the most important public health problems in the world and an important modifiable risk factor for the development of cardiovascular diseases. Adoption of healthy lifestyles by all individuals is critical for the prevention of high blood pressure and an indispensable part of the management of those with hypertension,[3]. Uncontrolled hypertension is associated with high risk for development of heart disease, stroke, chronic kidney disease, retinopathy, peripheral vascular disease.

A recent epidemiological worldwide study estimated that the high blood pressure causes approximately 7.6 million premature deaths (54% for stroke and 47% for ischaemic heart disease),[4]. A recent systematic review reporting data from studies in 35 different countries between the years 2003 and 2008 demonstrated an overall prevalence of 37.8% for men and 32.1% for women,[5].

Due to the fact that the prevalence of hypertension increases with age,[6] the management of hypertension and the prevention and treatment of major complications related to hypertension will continue to be a global challenge for health care professionals.

### Description of the intervention

Hypertension is a condition almost entirely managed by the primary care team by a variety of health professionals such as physicians, nurses, pharmacists and other allied health care professionals such as physiotherapists that frequently work in cardiac rehabilitation. All

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2  
3 professionals can potentially play an important role in lowering blood pressure. It is important  
4 that patients understand the benefits of blood pressure lowering which include a reduction in  
5 many complications such as stroke (35-40%), heart attack (20-25%) and heart failure (over  
6 50%)[3]. The majority of patients will require a combination of antihypertensive drugs to reach  
7 target blood pressure.  
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11 A previous study demonstrated that educational interventions increased participants' levels of  
12 knowledge about hypertension and had a positive influence on their beliefs about medicines,[7].  
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14 Educational interventions can also create opportunities for patients to better understand their  
15 conditions and the role of therapies and also can heighten awareness about disease progression  
16 and complications. Through patient education, misconceptions that patients have about their  
17 therapy can be clarified. This can influence adherence to therapy,[8] and therefore potentially  
18 may lead to improve blood pressure control.  
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### 33 **How the intervention might work**

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35 Different health professionals have become more involved in delivering interventions to the  
36 patients with the objective of preventing complications caused by high blood pressure. Patients  
37 expectations have a significant effect on the treatment they get from their doctor or any other  
38 health professional involved,[9]. Many previous trials in blood pressure control have used  
39 educational interventions on patients, physicians or both in an attempt to improve blood pressure  
40 control.  
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51 Educational interventions can positively modify patients' beliefs which in turn can lead to a  
52 change in patient behavior such as improvement in adherence to a therapy proposed by the health  
53 care professional,[8] and a possible effect on variables related to the disease such as blood  
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3 pressure levels. This may also affect in long term the progression of the disease and the  
4 prevalence of associated conditions related to hypertension such as heart attacks and stroke.  
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### 8 9 **Why is important to do this review**

10  
11 Due to the high morbidity and mortality caused by hypertension and the global scale of this  
12 important public health issue, it is important to continue to investigate interventions that can  
13 improve blood pressure control. It is striking that blood pressure goals continue to be a achieved  
14 in only 25-40% of the patients who take antihypertensive drug treatment,[3,10], which is  
15 something that has remained unchanged for the last 40 years,[11].  
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24 A recent Cochrane review demonstrated that there are many categories of interventions that  
25 singly or in unison have the potential to reduce blood pressure in patients with hypertension,[12].  
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29 In this review educational interventions directed to patient and physician were examined;  
30 however, the focus of the review and protocol was not the educational intervention alone.  
31 Educational interventions either to health professionals or patients, did not appear to be  
32 associated with large net reductions in blood pressure but were recommended as an adjunct  
33 additional therapy along other types of interventions.  
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41 Due to the fact that there has been an increasing number of recent studies showing the  
42 importance of prevention in patients with hypertension,[13-15] this review will determine the  
43 current evidence of the effects of educational interventions to improve control of blood pressure  
44 in patients with hypertension, potentially updating the recommendation for clinical practice.  
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## 51 **METHODS AND ANALYSIS**

### 52 **Criteria for considering studies for the review**

### *Types of studies*

We plan to include randomized clinical trials (RCTs) that have evaluated the effects of different models of educational interventions with the overall aim of improving blood pressure control in patients with hypertension, irrespective of language. The review will include RCTs where educational **interventions** used as the main or adjunct treatment was compared with no educational **interventions** or different types of educational strategies. We will exclude studies that use educational interventions not intended to improve blood pressure control.

### *Types of participants*

We will include studies that participants have age over 18 years regardless of sex, ethnicity with a diagnosis of hypertension either treated or not treated with antihypertensive medications in a primary care, outpatient or community setting.)

### *Types of interventions*

The intervention of interest will include all educational interventions strategies designed to improve the control of blood pressure in patients with hypertension (e.g. educational interventions direct to the patient; educational interventions direct to the health professional). Comparators will be any educational intervention used as the main or adjunct treatment to improve the control of blood pressure compared with either no educational **interventions** or different types of educational strategies aimed to improve blood pressure control.

### *Types of outcomes assessments*

The primary outcome of this review will be any changes in mean systolic blood pressure (SBP) and/or mean diastolic blood pressure (DBP) in any care setting as well as number of patients under control of blood pressure (BP) or proportion of controlled BP defined by each randomized

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3 trial's investigators. The secondary outcomes will be: number of hospitalizations during  
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5 treatment (e.g. increase of BP) or mortality from cardiovascular disease as an adverse events; the  
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7 costs and cost effectiveness of interventions; the adherence to intervention (dropout rate) or  
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9 adherence to medication and the outcome QOL will be measured using standardized generic  
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11 questionnaire.  
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## 14 15 16 **Search methods for identification of studies**

### 17 18 *Electronic searches*

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20 We will electronically search the following databases: MEDLINE, CINAHL, PEDro,  
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22 ScienceDirect, ~~WHO International Clinical Trials Registry Platform (ICTRP) and~~  
23  
24 ~~ClinicalTrials.gov~~. without any language restrictions ( in case of studies in another language,  
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26 other than English, we will contact companies specialized in translation). The search strategy  
27  
28 will be developed after discussion among reviewers, according to the guidance of the Cochrane  
29  
30 handbook[16].The MEDLINE search strategy will be translated into the other databases using  
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32 the appropriate controlled vocabulary as applicable for each database.  
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### 37 38 *Other sources*

39  
40 The bibliographies of all retrieved and relevant publications identified by the above strategies  
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42 will be searched for further studies. In addition, we will search the WHO International Clinical  
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44 Trials Registry Platform (ICTRP) (<http://apps.who.int/trialsearch/>). We will attempt to contact  
45  
46 researchers to obtain additional information when needed.  
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## 49 50 **Data collection and analysis**

### 51 52 *Selection of studies*

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3 Before the selection of studies, a procedure for screening will be developed by discussion among  
4 all the reviewers. We will extract data into Review Manager 5.3,[17] and summarize details  
5 using a standard data extraction sheet. Two reviewers (CR and VR) will independently assess the  
6 titles and abstracts of the studies identified from the search strategy against the inclusion criteria.  
7  
8 Full versions of articles that appear to fulfil the inclusion criteria will be obtained for further  
9 assessment. Another review author (IL) will evaluate any discrepancies, if necessary, and will  
10 advise in case of disagreement. We will record all reasons for exclusion and we will exclude  
11 studies that not use the educational interventional to improve blood pressure control.  
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#### 14 *Data extraction and management*

15 Two review authors (CR and VR), working independently, will extract data and summarize  
16 details of trials using a standard data extraction sheet. According to methods described in the  
17 Cochrane Handbook for Systematic Reviews of Interventions,[18] the extraction sheet includes  
18 information such as study design, methodology, participants, interventions, duration of  
19 treatment, outcomes, conclusions and potential sources of bias. We will resolve any  
20 discrepancies by discussion with a third review author (IL). If studies report more than one  
21 outcome time (e.g. 6 and 12 months), data concerning the longest follow up will be extracted.  
22 Where data are found to be missing, we will contact the corresponding author of studies to  
23 request the missing data or to clarify study details.  
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#### 26 *Assessment of risk of bias in included studies*

27 For assessment of study quality and reporting bias two reviewers (CR and VR) will  
28 independently assess the risk of bias, using the Cochrane collaboration's tool for assessing risk  
29 of bias of the included trials,[19] which is composed of six domains of a trial, such as random  
30 sequence generation (selection bias), allocation concealment (selection bias), blinding  
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3 (performance bias and detection bias), incomplete outcome data (attrition bias), selective  
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6 outcome reporting (reporting bias) and other bias. After assessing all the domains, the reviewers  
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8 will summarize the assessments and categorize the included trials into three levels of bias: low,  
9  
10 unclear and high risk of bias and high risk of bias. We will resolve any disagreements by  
11  
12 discussion with a third author (IL).  
13

#### 14 15 *Measures of treatment effect*

16  
17 We will present the effects on blood pressure between interventions at follow-up (systolic and  
18  
19 diastolic blood pressure) according to the educational **interventions** proposed in each study. We  
20  
21 will present the outcome results for each trial with 95% confidence intervals (CI). Continuous  
22  
23 outcomes (such as changes in systolic and diastolic blood pressure) will be expressed and  
24  
25 calculated as mean difference (MD) and overall effect size between intervention and control  
26  
27 groups. We will use Relative Risk (RR) or Odds Ratio (OR) depending on measurements indices  
28  
29 in individual studies for other primary and secondary outcomes.  
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#### 34 35 *Dealing with missing data*

36  
37 In the case of missing data, we will contact the original investigators to request missing data  
38  
39 whenever possible. If trial does not specify participant group number prior to dropout, we will  
40  
41 present only complete case analysis for primary and secondary outcomes.  
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#### 44 45 *Assessment of heterogeneity*

46  
47 Whenever studies appear to be similar in terms of participants characteristics (established  
48  
49 hypertensive, people with diabetes or other chronic disease), intervention type and duration and  
50  
51 outcome type we will pool data using meta-analysis (using RevMan 5.3). We will test statistical  
52  
53 heterogeneity using the Chi<sup>2</sup> test (considering a value of P < 0.1 to indicate heterogeneity) and  
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3 estimate the amount of heterogeneity using the  $I^2$  statistic,[20]. If  $I^2$  is over 50% indicating a high  
4 level of heterogeneity data will not be pooled. In the absence of clinical and statistical  
5  
6 level of heterogeneity we will use a fixed-effect model.  
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### 10 *Assessment of reporting biases*

11 We will present the overall risk of bias (random sequence generation, allocation concealment,  
12  
13 blinding of participants and personnel, blinding of outcome assessment, incomplete outcome  
14  
15 data, selective reporting) in a risk of bias summary table per study. If sufficient studies (more  
16  
17 than ten) are identified an attempt will be made to examine for publication bias using funnel plot  
18  
19 as described in the Cochrane Handbook for Systematic Reviews of Interventions,[21]. If  
20  
21 asymmetry is present we will explore possible causes including publication bias, poor  
22  
23 methodological quality and true heterogeneity.  
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### 30 *Data synthesis*

31 We will present a narrative overview of the combined studies with meta-analysis of outcome  
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33 data using the software Review Manager version 5.3 where appropriate.  
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36 We will include cluster-randomized trials in the analysis. For cluster-randomized trials, we will  
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38 adjust results when the unit of analysis in the trial is presented as the total number of individual  
39  
40 participants instead of number of clusters. Results will be adjusted using the mean cluster size  
41  
42 and intracluster correlation coefficient,[22]. For meta-analysis, data will be combined to  
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44 individually randomized trials using the generic inverse-variance method as described on  
45  
46 Chapter 16.3 of the Cochrane Handbook for Systematic Reviews of Interventions,[22].  
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49 The decision to include studies in a meta-analysis will depend on the availability of treatment  
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51 effect data and assessment of heterogeneity. Intervention effects will be calculated as relative  
52  
53 risks with 95% confidence intervals for dichotomous data. For continuous data, we will calculate  
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3 mean differences with 95% confidence intervals using a conservative fixed-effects meta-analysis  
4 model in the absence of significant heterogeneity ( $p > 0.05$  or  $I^2 < 50\%$ ). If there is high level of  
5 heterogeneity ( $I^2 > 50\%$ ) we will not pool data and we will perform sensitivity analysis of data.  
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### 10 *Subgroup analysis*

11 Subgroup analysis will be carried out according to the following variables: age and gender of  
12 participants, professional delivering intervention (e.g. nurse).  
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### 17 *Sensitivity analysis*

18 If sufficient trials are identified, we plan to conduct sensitivity analyses in order to explore the  
19 influence on the results of the following factors: assessor blinding (high risk of bias versus low  
20 risk of bias). We will restrict analyses to studies at low risk of bias.  
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### 28 *Ethics and dissemination*

29 This systematic review does not need ethical approval. Findings of this review will be  
30 disseminated via peer-reviewed journals and conference presentations.  
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## 35 **DISCUSSION**

36 This is the protocol for a review and there is no primary data collection. The systematic review  
37 will be published in a peer-reviewed journal and disseminated electronically or in print. This  
38 review also will benefit patients with hypertension as they will better understand and accept the  
39 therapy and change their behavior about the treatment.  
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4 *Author's Contributions:* The search strategy will be developed and run by IL. Copies of studies  
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6 will be obtained by CR and VR. Selection of the studies to include will be performed by CR and  
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8 VR. Extraction data from studies and entering data into RevMan will be conducted by CR and  
9  
10 VR. The analysis will be carried out by CR, VR and IL. Interpretation of the analysis will be  
11  
12 carried out by all authors. The final review will be drafted by all authors. The protocol was  
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14 revised, and the final version was approved by all authors.  
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26 Assessment in Health: Comparative Effectiveness Research.  
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31 *Competing interests:* None.  
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