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Web-based interventions to improve blood pressure control in patients with Hypertension: Protocol for a Systematic Review

PROTOCOLO DE REVISÃO SISTEMÁTICA

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Trabalho realizado sob a orientação de:
PROFESSORA DOUTORA INÊS ROSENDO DE CARVALHO E SILVA
DOUTORA BEATRIZ ROSENDO DE CARVALHO E SILVA

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Title Page

Title of Paper

Web-based interventions to improve blood pressure control in patients with Hypertension: Protocol for a Systematic Review

Running Head

Improving blood pressure control in patients with hypertension

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Contents

Abbreviations

% - Percentage

ABPM – Ambulatory Blood Pressure Monitoring

BP – Blood Pressure

BPC – Blood Pressure Control

BS – Doutora Beatriz Rosendo de Carvalho e Silva

CENTRAL - The Cochrane Central Register of Controlled Trials

CI – Confidence Interval

DBP – Diastolic Blood Pressure

EU – European Union

HBPM – Home Blood Pressure Monitoring

IR – Professora Doutora Inês Rosendo de Carvalho e Silva

MB – Maria Leonor Matias Bernardes

MD – Mean Difference

MS – Doutora Matilde Monteiro-Soares

mmHg – Millimeter of Mercury

PRISMA – Preferred Reporting Items for Systematic Review and Meta-analyses

PROSPERO - International Prospective Register of Systematic Reviews

RCT – Randomized Control Trial

RR – Risk Ratio

SBP – Systolic Blood Pressure

SMD – Standardized Mean Differences

Abstract

Introduction: Hypertension is the major cause of cardiovascular disease and mortality in the world. Blood Pressure Control (BPC) is recognized as a key measure in the management of hypertension. Several studies have been conducted assessing the impact of specific web-based interventions in improving BPC. Our systematic review intends to identify all the available web-based interventions and determine if and which are more effective than the usual care in improving BPC.

Methods and analysis: We will include randomized control trials conducted, until October 2020, on patients diagnosed with hypertension comparing the effect of receiving usual care versus web-based interventions in blood pressure. No language restriction will be applied. We will start by an extensive electronic database search, in The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Scopus, Clinical Trials Register EU and ClinicalTrials.gov. We will conduct a narrative description and meta-analysis of the results of the included studies, structured according to type of intervention, characteristics of the population, and outcome measurement. We will extract features of the web-based interventions, selecting the ones with the best outcomes regarding BPC, to later propose an ideal web-based intervention to improve BPC in hypertensive patients.

Ethics and dissemination: Ethical approval is not required given it is a protocol for a systematic review. The findings of this study will be disseminated through peer-reviewed publications and national or international conference presentations. Updates of the review will be conducted, as necessary.

Keywords: Hypertension, Blood Pressure Control, Systematic Review, Web-Based

Trial registration number: PROSPERO CRD42020184166

Introduction

Hypertension is the major cause of cardiovascular disease and mortality worldwide.(1,2) This condition is responsible for 10,4 million deaths per year (2) and is now considered the major cardiovascular risk factor.(3,4) Hypertension is defined as office systolic blood pressure (SBP) values ≥ 140 mmHg and/or diastolic blood pressure (DBP) values ≥ 90 mmHg or equivalents (home blood pressure monitoring (HBPM) ≥ 135/85 mmHg or ambulatory blood pressure monitoring (ABPM) ≥ 130/80 mmHg over 24h, with a daytime average of ≥ 135/85 mmHg and a night-time average of ≥ 120/70 mmHg) and, in adults, it is typically asymptomatic.(3,5)

The epidemiology, pathophysiology and associated risk of hypertension are now widely known and it is clearly demonstrated by several studies that lowering BP can substantially reduce premature morbidity and mortality.(5–9)

However, besides the fact that studies show a high effectiveness in several strategies to control blood pressure (BP),(5,10) the rates of BPC in the population have been described in several studies as very poor.(11–13) In a 2013 study, only 46,5% of the patients with hypertension were aware of their condition; of those, 87,5% were medicated with at least one drug. Despite the wide variety of drugs available, only 32,5% of the medicated patients had their blood pressure under control.(13)

One of the major barriers to improve blood pressure control is the poor adherence to therapy.(9,14) Studies have shown an increase in the quality of life and a decrease of cardiovascular risk in patients with controlled blood pressure and high adherence to therapy.(9,15)

Blood Pressure control can be improved by various tools, one of which is a daily home self-monitoring of blood pressure.(16–18) This tool also helps decision making by health care providers.(5) Nevertheless, home self-monitoring of blood pressure faces problems in its practical implementation as, for example, BP values handwritten by patients are often inaccurate and/or illegible to physicians.(19) These limitations led to the conduction of several studies assessing the effect of web-based interventions in BPC.(18,20)

Objectives

We've created a protocol of a systematic review with meta-analysis of studies analyzing if web-based interventions have greater benefits than usual care in improving BPC in patients with hypertension and to identify the intervention with the most successful outcomes on BPC. As secondary outcomes, we aim to understand if web-based interventions also have an impact on improving adherence to pharmacological therapy and quality of life in patients with hypertension.

Methods

1. Protocol and registration:

This systematic review protocol was conducted in accordance to PRISMA recommendations (Appendix I – PRISMA checklist) for systematic reviews and meta-analysis. It was submitted for approval on PROSPERO on October 5th 2020 and published in the same platform on November 5th 2020 with the registration number CRD42020184166 (Appendix II).

2. Study selection (Fig. 1):

Types of studies: We will include RCTs comparing web-based interventions versus usual care to improve BPC in patients with hypertension.

Types of participants: The studies' participants will be adults with diagnosed hypertension (5,21) or taking at least one medicine for hypertension at the beginning of the study, non-regarding race, ethnicity or co-morbidity.

Types of interventions: We will consider all published and unpublished RCTs that evaluate web-based interventions to improve BPC in patients with hypertension. We will consider as a web-based intervention any intervention using the internet to facilitate the dissemination of health-related information and to connect patients to support. These can include interventions involving medical devices (electronic monitorization of medication, packaging with alarms, equipment to measure BP at home or telehealth devices) as well as communication and information technologies (computers, telephones, cell-phones, email, text messages). There will be no restrictions regarding date and language. Studies whose aim is to prevent hypertension will be excluded.

Types of settings: We will include any studies performed in ambulatory, either from public or private hospitals and clinics, and either from hospital appointments or primary care. Studies performed in hospitalized patients will be excluded.

Types of outcome measures: Our primary outcome will be BPC in patients with hypertension; change in BP values will be measured in mmHg. We will consider two secondary outcomes: adherence to pharmacological therapy, measured though 1-6 questionaries, pill count, electronic monitoring devices, biochemical urine analysis and algorithms; and quality of life in patients with hypertension, measured through validated questionaries, usually 0-100 scores and Lickert scale.

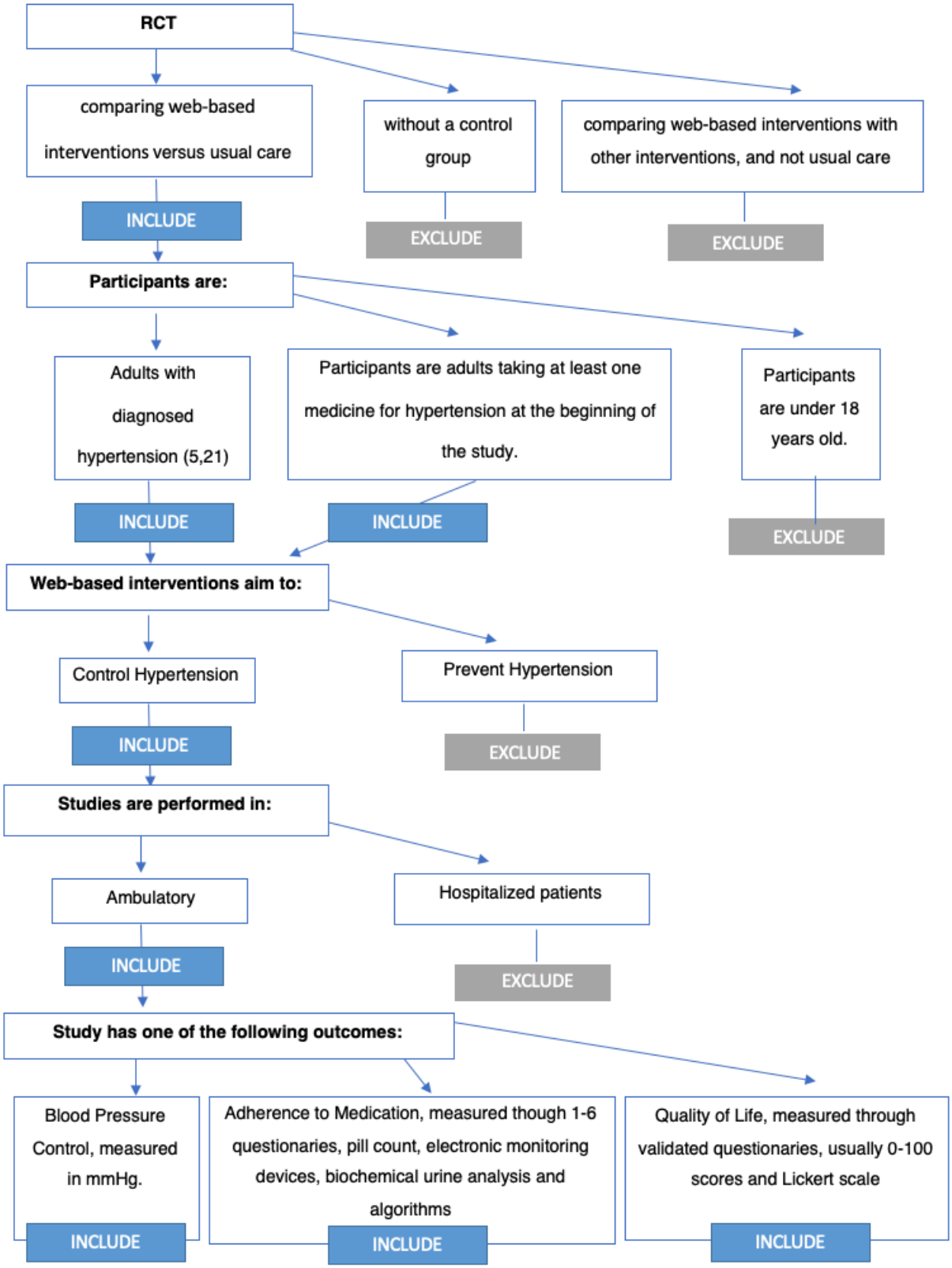

Figure 1 – Inclusion and exclusion criteria.

3. Search methods and identification of studies:

Electronic searches: The following databases will be consulted: The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Scopus, EU Clinical Trials Register and ClinicalTrials.gov. We will search the data bases for any-language studies published from inception to October 2020. The search strategy (Table 1) is deliberately broad in an effort to gather all eligible studies. Reference lists of all included studies will be hand-searched for additional records, which will also be included.

Search Strategy: See Table 1.

Table 1 - Search Strategies

Pubmed
(Hypertension[MeSH Terms] OR Hyperten*[Title/Abstract] OR (Blood Pressure[Title/Abstract] AND (High[Title/Abstract] OR Elevated[Title/Abstract] OR Uncontrolled[Title/Abstract] OR Marked[Title/Abstract] OR Essential[Title/Abstract] OR Escalated[Title/Abstract] OR Persistent[Title/Abstract] OR Abnormal[Title/Abstract]))) AND ((Mobile Applications[MeSH Terms] OR ((Mobile[Title/Abstract] OR Portable[Title/Abstract]) AND (Application*[Title/Abstract] OR Software[Title/Abstract] OR Electronic[Title/Abstract])) OR Multimed*[Text Word] OR Multimedia[MeSH Terms] OR Internet[Text Word] OR Internet[MeSH Terms] OR Email[Text Word] OR Web[Text Word] OR Cyberspace[Text Word] OR Online[Text Word] OR Multimedia[Text Word] OR Cell Phone[Text Word] OR Smart Phone[Text Word] OR Digital[Text Word] OR Computer[Text Word] OR Educational Technology[MeSH Terms] OR (Instruction[Title/Abstract] AND Tech*[Title/Abstract]) OR telemedicine[MeSH Terms] OR mobile[Title/Abstract] OR mHealth[Title/Abstract] OR telehealth[Title/Abstract] OR eHealth[Title/Abstract]) AND (Randomized Controlled Trial[Publication Type] OR Controlled Clinical Trial[Publication Type] OR Randomized[Title/Abstract] OR Placebo[Title/Abstract] OR Drug Therapy[MeSH Subheading] OR Randomly[Title/Abstract] OR Trial[Title/Abstract] OR Groups[Title/Abstract]) NOT (Animals[MeSH Terms] NOT Humans[MeSH Terms])) AND ((usual[Text Word] OR common[Text Word] OR traditional[Text Word] OR standard[Text Word]) AND (care[Text Word] OR management[Text Word] OR (intervention[Text Word] NOT intensive[Title/Abstract]))
Clinical Trials.Gov
Condition: Hypertension OR (Blood Pressure AND (High OR Elevated OR Uncontrolled OR Marked OR Essential OR Escalated OR Persistent OR Abnormal)) Other Terms: Mobile Applications OR ((Mobile OR Portable) AND (Application OR Software OR Electronic)) OR Multimedia OR Internet OR Email OR Web OR Cyberspace OR Online OR Multimedia OR Cell Phone OR Smart Phone OR Digital OR Computer OR Educational Technology OR (Instruction AND technology) OR telemedicine OR mobile OR mHealth OR telehealth OR eHealth Filters: **Study Type:** Interventional Studies (Clinical Trials)

Study Results: All Studies

Status: Recruitment: Recruiting; Enrolling by invitation; Active, not recruiting; Suspended; Terminated; Completed; Withdrawn; Unknown Status

Age Group: Adult (18-64); Older Aldult (65+)

Sex: All.

EU Clinical Trials Register

Hypertension OR (“Blood Pressure” AND (High OR Elevated OR Uncontrolled OR Marked OR Essential OR Escalated OR Persistent OR Abnormal)) AND ("Mobile Applications" OR ((Mobile OR Portable) AND (Application OR Software OR Electronic)) OR Multimedia OR Internet OR Email OR Web OR Cyberspace OR Online OR Multimedia OR Cell Phone OR Smart Phone OR Digital OR Computer OR Educational Technology OR (Instruction AND technology) OR telemedicine OR mobile OR mHealth OR telehealth OR eHealth) AND ("Randomized Controlled Trial" OR "Controlled Clinical Trial" OR Randomized OR Placebo OR Drug Therapy OR Randomly OR Trial)

Filters: Age Range: Adult; Elderly.
Trial Status: Completed; Ongoing; Prematurely Ended.

Scopus

(TITLE-ABS-KEY (hypertens*) OR TITLE-ABS-KEY ("Blood Pressure" AND high OR elevated OR uncontrolled OR marked OR essential OR escalated OR persistent OR abnormal)) AND ((ABS ("Mobile Applications" OR multimed* OR internet OR email OR web OR cyberspace OR online OR "Cell Phone" OR digital OR computer OR mobile OR mhealth OR telehealth OR ehealth)) OR (KEY (telemedicine))) AND (TITLE-ABS-KEY ((clinic* W/1 trial*) OR (randomi* W/1 control*) OR (randomi* W/2 trial*) OR (random* W/1 assign*) OR (random* W/1 allocat*) OR (control* W/1 clinic*) OR (control* W/1 trial) OR placebo* OR (quantitat* W/1 stud*) OR (control* W/1 stud*) OR (randomi* W/1 stud*) OR (singl* W/1 blind*) OR (singl* W/1 mask*) OR (doubl* W/1 blind*) OR (doubl* W/1 mask*) OR (tripl* W/1 blind*) OR (tripl* W/1 mask*) OR (trebl* W/1 blind*) OR (trebl* W/1 mask*)) AND
NOT (SRCTYPE (b) OR SRCTYPE (k) OR SRCTYPE (p) OR SRCTYPE (r) OR SRCTYPE (d) OR DOCTYPE (ab) OR DOCTYPE (bk) OR DOCTYPE (ch) OR DOCTYPE (bz) OR DOCTYPE (cr) OR DOCTYPE (ed) OR DOCTYPE (er) OR DOCTYPE (le) OR DOCTYPE (no) OR DOCTYPE (pr) OR DOCTYPE (rp) OR DOCTYPE (re) OR DOCTYPE (sh)))

CENTRAL
([mh hypertension] OR (Hyperten*):ti,ab,kw OR [mh "Essential Hypertension"]) OR (("Blood Pressure"):ti,ab,kw AND ((high):ti,ab,kw OR (elevated):ti,ab,kw OR (uncontrolled):ti,ab,kw OR (marked):ti,ab,kw OR (essential):ti,ab,kw OR (escalated):ti,ab,kw OR (persistent):ti,ab,kw OR (abnormal):ti,ab,kw)) AND ([mh "Mobile Applications"] OR [mh Multimedia] OR [mh "Internet-Based Intervention"] OR [mh "Educational Technology"] OR [mh Telemedicine]) OR ((((mobile):ti,ab,kw OR (portable):ti,ab,kw) AND ((application):ti,ab,kw OR (software):ti,ab,kw OR (electronic):ti,ab,kw)) OR (multimed*):ti,ab,kw OR (internet):ti,ab,kw OR (email):ti,ab,kw OR (web):ti,ab,kw OR (cyberspace):ti,ab,kw OR (online):ti,ab,kw OR (phone):ti,ab,kw OR (digital):ti,ab,kw OR(mHealth):ti,ab,kw OR (telehealth*):ti,ab,kw OR (eHealth):ti,ab,kw)

Table 1 – Search Strategy in PubMed, ClinicalTrials.Gov, EU Clinical Trials Register, Scopus and CENTRAL.

Searching other resources: We will examine citations of included studies, search for studies citing included studies and examine reference lists from key reviews to identify additional studies not found in the electronic search.

Identification and selection of studies: We will use a systematic search strategy, according to the condition of interest, as it is designed in the book “Cochrane Handbook”. We will also contact the authors of the studies about non published RCTs. The team will sort the articles independently and blindly, identifying the ones that fit the inclusion criteria using *Ryyan.*(22) This process will be conducted in two phases: firstly we will sort titles and abstracts and secondly we will conduct a full-paper screening. The review team will discuss their differences and will try to obtain potentially relevant citations or full papers. The team will extract duplicate data. Any disagreement between them over the eligibility of a particular study will be sorted through discussion and, when necessary, a third author (IR) will be consulted.

4. Data extraction:

Two researchers from the review team will extract data independently and discrepancies will be solved through debate; if a consensus cannot be reached, a third researcher will be called to make a final judgement of the data. We will contact the authors every time there is critical information missing from the report. We will extract features of web-based interventions in order to describe which are the most effective.

Data will be extracted according to the following domains:

a) **Study characteristics:** title, publication year, study location, language and authors;

b) **Population characteristics:** demographic and clinical characteristics – sex, race and anti-hypertension drugs prescribed; geographic location; socio-economic status; highest education level achieved, comorbidities and diagnostic criteria used in the study;

c) **Intervention characteristics:** setting; intervention group and control group; type and description of web-based intervention; frequency and duration of web-based intervention and follow-up; primary outcome; secondary outcomes;

d) **Study results and effects:** validated measures; statistical analyses, adjustments, main findings and conclusions.

Microsoft Excel spreadsheets will be elaborated for two reviewers (MB and BS) to summarize the data from the included studies. Then, the spreadsheets will be combined into one. Disagreements will be resolved by a third investigator (IR).

e) Assessment of risk of bias:

The assessment of the risk of bias will be made by two authors, independently, using the risk assessment tool in Cochrane "The ROB Tool",(23) that considers the following domains: sequence generation, allocation concealment, blinding, outcome assessment, incomplete outcome data, selective outcome reporting and other sources of bias. This assessment will be conducted independently and blindly by two authors (BS and MB). Disagreements between the two authors will be sorted through debate and, if needed, a third author (IR) will be called in.

f) Data synthesis and statistical analysis:

A narrative synthesis will be conducted for all included studies, structured according to population, type of intervention, results, effects and conclusions. We will present effect measures of each study.

We will use a random-effects model for our meta-analysis, since it is expected that the RCTs to be included in our study will be performed in heterogeneous populations, differing in each study. Heterogeneity between the studies will be assessed through Q test and I2 heterogeneity index, where a value of 0%–40% will be considered unimportant heterogeneity, 30%–60% moderate, 50%–90% substantial and 75%–100% considerable,(24)

We expect to find mean differences (MDs) for most of the effect measures of the studies. The analysis will be performed for all variables and results will be presented with 95% confidence interval (CI). Standardized mean differences (SMD) will be used as a measure of pooled results for each outcome. The presence of publication bias will be evaluated by use of a funnel plot.

Discussion

1. Article Summary:

In this systematic review we aim to assess whether web-based interventions have greater benefits than usual care in improving blood pressure control in patients with hypertension. As hypertension becomes more prevalent worldwide, and its control remains very poor, these results will provide support to physicians when deciding about which type of care they shall offer their patients.

This study will not only compare usual care with web-based interventions, but also provide information about the type of web-based intervention with the best outcomes in hypertension control, constituting an important tool to guide physicians in the implementation of this type of interventions.

2. Strengths and Limitations:

With this review, we expect to give a new perspective in the approach of hypertension and hope it will have a very positive impact in its control. Following the PRISMA guidelines for reporting systematic reviews and meta-analysis, we expect to mee the highest scientific quality.

We are searching several databases in order to guaranty that the largest possible number of studies meeting our inclusion criteria are included in the review, strengthening our results.

Nevertheless, since web-based interventions are still a new research topic, we anticipate a shortage of RCTs, and this might potentially limit the interpretation of results. Anticipating this, the search strategy is deliberately broad in an effort to gather all eligible studies. However, despite being a strength point, this may also bring a bigger heterogeneity between studies populations, and constituting a potential limitation to our protocol.

Additionally, being a systematic review, the loss of information on outcome variables and publication bias can also limit our results.

3. Author's Statement:

Author's Contributions: All four authors (MB, BS, MS and IR) were involved in the design, construction and writing of this protocol.

Conflicts of Interest: All authors declare that they have no known conflicts of interest.

Funding: This research will receive no specific grant from any funding agency in the public commercial or not-for-profit sectors.

Chronogram (Fig.2)

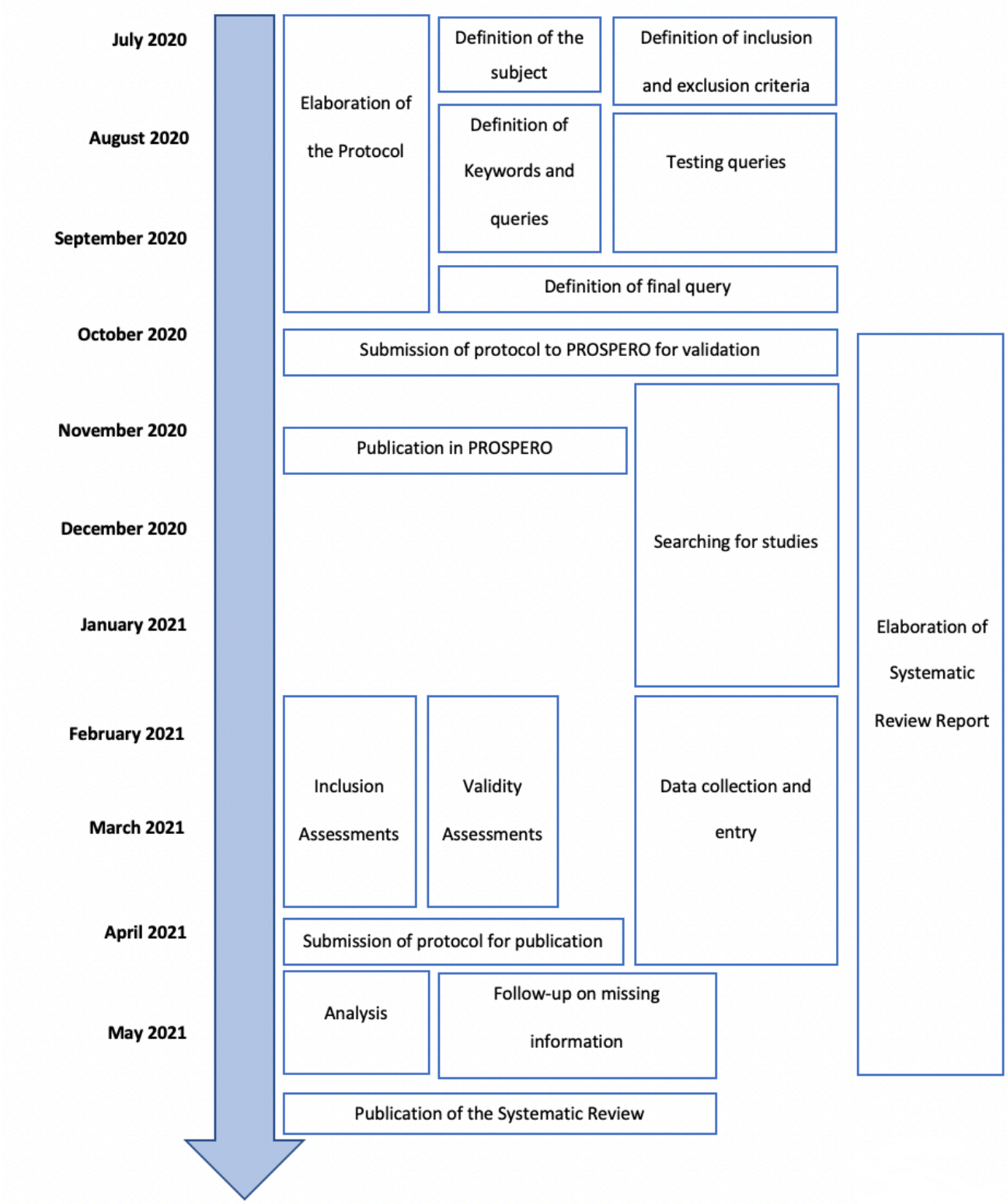

Figure 2 – Chronogram of predicted steps for the elaboration of the protocol and the systematic review.

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A big thank you to my friends, and especially to my family, who always stood by my side, through all the laughing, the crying, the conquests and the failures. Without them, this journey would not have been the same.

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Appendix I

Reporting checklist for protocol of a systematic review and meta analysis.

Based on the PRISMA-P guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA-Preporting guidelines, and cite them as:

Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.

		Reporting Item	Page Number
Title			
Identification	#1a	Identify the report as a protocol of a systematic review	1-2
Update	#1b	If the protocol is for an update of a previous systematic review, identify as such	-
Registration			
	#2	If registered, provide the name of the registry (such as PROSPERO) and registration number	5

Authors			
Contact	#3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	2
Contribution	#3b	Describe contributions of protocol authors and identify the guarantor of the review	13
Amendments			
	#4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	-
Support			
Sources	#5a	Indicate sources of financial or other support for the review	13
Sponsor	#5b	Provide name for the review funder and / or sponsor	-
Role of sponsor or funder	#5c	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	-
Introduction			
Rationale	#6	Describe the rationale for the review in the context of what is already known	6
Objectives	#7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	6

Methods

Eligibility criteria	#8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7
Information sources	#9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	9
Search strategy	#10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	9-10
Study records - data management	#11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	11-12
Study records - selection process	#11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	11
Study records - data collection process	#11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	11
Data items	#12	List and define all variables for which data will be sought (such as PICO items,	11

		funding sources), any pre-planned data assumptions and simplifications	
Outcomes and prioritization	#13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7-8
Risk of bias in individual studies	#14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	12
Data synthesis	#15a	Describe criteria under which study data will be quantitatively synthesised	12
Data synthesis	#15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I2, Kendall's τ)	12
Data synthesis	#15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	12
Data synthesis	#15d	If quantitative synthesis is not appropriate, describe the type of summary planned	12
Meta-bias(es)	#16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	-

Confidence in cumulative evidence	#17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

Appendix II

CRD-REGISTER <irss505@york.ac.uk> 5 de novembro de 2020 às 07:01
Responder a: irss505@york.ac.uk
Para: leonorbernardes1@gmail.com

Dear Ms Matias Bernardes,

We apologise for the delay in dealing with your registration, an ever-increasing number of applications has led to a backlog and substantial delays for some users.

PROSPERO is currently prioritising submissions related to COVID-19. To enable us to focus on these submissions, and to avoid additional delay, during the pandemic we will automatically publish submissions that have been waiting more than 30 days for registration.

This applies to your systematic review "Efficacy of Web-Based interventions to improve blood pressure control in patients with hypertension" which was published on our website on Nov 05, 2020.

The records will be published exactly as submitted, without review by the PROSPERO team, so the public record will indicate:

"To enable PROSPERO to focus on COVID-19 registrations during the 2020 pandemic, this registration record was automatically published exactly as submitted. The PROSPERO team has not checked eligibility"

Review owners have always been responsible for the quality and content of PROSPERO records, and high-quality well-written records will continue to speak for themselves.

Your registration number is: CRD42020184166

You are free to update the record at any time, all submitted changes will be displayed as the latest version with previous versions available to public view. Please also give brief details of the key changes in the Revision notes facility and remember to update your record when your review is published. You can log in to PROSPERO and access your records at https://www.crd.york.ac.uk/PROSPERO

Best wishes for the successful completion of your review.

Yours sincerely,

PROSPERO Administrator
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Other non-commercial resources that may be of interest
SRDR-Plus is a systematic review data management and archival tool that is available free of charge http://srdrplus.ahrq.gov.