U.PORTO
FMUP FACULDADE DE MEDICINA
UNIVERSIDADE DO PORTO

MESTRADO INTEGRADO EM MEDICINA

2020/2021

Simão Alves Pinho

Improving medication adherence in hypertensive patients: A scoping review

Março, 2021

Simão Alves Pinho

Improving medication adherence in hypertensive patients: A scoping review

Mestrado Integrado em Medicina

Área: Ciências Médicas e da Saúde

Tipologia: Dissertação

Trabalho efetuado sob a Orientação de:

Professora Doutora Rute Sofia Monteiro Sampaio

E sob a Coorientação de:

Dr. André Luís Charro Ramalho

Trabalho organizado de acordo com as normas da revista:

Preventive Medicine

Março, 2021

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

UC Dissertação/Projeto (6º Ano) - DECLARAÇÃO DE INTEGRIDADE

Eu, **Simão Alves Pinho**, abaixo assinado, nº mecanográfico **201503312**, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter atuado com absoluta integridade na elaboração deste projeto de opção.

Neste sentido, confirmo que **NÃO** incorri em plágio (ato pelo qual um indivíduo, mesmo por omissão, assume a autoria de um determinado trabalho intelectual, ou partes dele). Mais declaro que todas as frases que retirei de trabalhos anteriores pertencentes a outros autores, foram referenciadas, ou redigidas com novas palavras, tendo colocado, neste caso, a citação da fonte bibliográfica.

Faculdade de Medicina da Universidade do Porto, 20/03/2021

Assinatura conforme cartão de identificação:

Simão Alves Pinho

U.PORTO
FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

UC Dissertação/Projeto (6º Ano) – DECLARAÇÃO DE REPRODUÇÃO

NOME

Simão Alves Pinho

NÚMERO DE ESTUDANTE	E-MAIL
201503312	simao.pinho@hotmail.com

DESIGNAÇÃO DA ÁREA DO PROJECTO

Ciências Médicas e da Saúde

TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

Improving medication adherence in hypertensive patients: A scoping review

ORIENTADOR

Professora Doutora Rute Sofia Monteiro Sampaio

COORIENTADOR (se aplicável)

Dr. André Luís Charro Ramalho

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☒
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTE TRABALHO (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTE TRABALHO.	☐

Faculdade de Medicina da Universidade do Porto, 20/03/2021

Assinatura conforme cartão de identificação:

À minha família.

À Filipa.

Aos meus amigos, em particular à Mariana, que tanto me ajudou neste trabalho.

À minha orientadora, a Professora Doutora Rute Sampaio, pela sua confiança e apoio incondicionais, e ao meu coorientador, o Doutor André Ramalho, que muito me ensinou.

Improving medication adherence in hypertensive patients: A scoping review

Simão Pinho[a] BSc, Mariana Cruz[a] MSc, Filipa Ferreira[b] BSc, André Ramalho[c,d] MD MBA MSc, Rute Sampaio[a,c] PhD

a. Department of Biomedicine, Faculty of Medicine, University of Porto. Alameda Hernâni Monteiro, 4200-319, Porto, Portugal.
b. Department of Anatomy, Instituto de Ciências Biomédicas Abel Salazar - ICBAS, University of Porto. R. Jorge de Viterbo Ferreira 228, 4050-313, Porto, Portugal.
c. CINTESIS - Centre for Health Technology and Services Research, Porto, Portugal. R. Dr. Plácido da Costa, 4200-450 Porto, Portugal.
d. MEDCIDS - Department of Community Medicine, Information and Health Decision Sciences, Faculty of Medicine, University of Porto, Porto, Portugal. Rua Dr. Plácido da Costa, 4200-450, Porto, Portugal.

Authors' email addresses:

simao.pinho@hotmail.com (Simão Pinho)

m.belo.cruz@gmail.com (Mariana Cruz)

filipa.p.ferreira@gmail.com (Filipa Ferreira)

alramalho@med.upt (André Ramalho)

rutesampaio@med.up.pt (Rute Sampaio)

Corresponding author: Simão Pinho (simao.pinho@hotmail.com)

Faculty of Medicine, University of Porto, Portugal

Department of Biomedicine – CIM building, 5th floor

Alameda Hernâni Monteiro

4200-319, Porto, Portugal

Highlights

- Medication adherence interventions in hypertensives have mixed results.
- Adherence measuring tools are diverse, showing a lack of consensus in the field.
- Well-conducted, theory-based adherence interventions are infrequent.
- Our categorization system helps define and prioritize good interventions.
- This tool facilitates clinicians' and stakeholders' decision-making on adherence.

Abstract

In recent years, interest in medication adherence has greatly increased. Adherence has been particularly well studied in the context of arterial hypertension treatment. Numerous interventions have addressed this issue, however, the effort to improve adherence has been often frustrating and frequently disorganized. The aim of present study was to perform a scoping review of medication adherence interventions in hypertensive patients, so that a clear overview was achieved. Moreover, an evidence-based categorization of interventions was developed.

The review was performed according to the PRISMA-ScR statement. MEDLINE and Web of Science were searched, and studies published from database inception until August 17, 2020 were included. A total of 2994 non-duplicate studies were retrieved. After screening and eligibility phases, a total of 45 articles were included. Studies were analyzed regarding their design, participant characteristics and management of adherence strategies employed. Furthermore, medication adherence and blood pressure outcomes, as well as adherence measuring tools were evaluated. Each study's intervention was then categorized using a novel evidence-based system of categorization, derived from the conceptual clustering framework used in machine learning.

This work is an important step in pushing for better informed and more efficient future research efforts, both by providing an overview of the research field and by creating a new, evidence-based intervention categorization tool. It also provides valuable information to clinicians about medication adherence to antihypertensive therapy.

Keywords: Scoping review Arterial hypertension Medication adherence Prevention Intervention

1. Introduction

Inadequate medication adherence is a worldwide problem with an impact that, though undoubtedly very significant, is quite difficult to estimate when its pervasiveness is taken into account (1, 2). The World Health Organization defines adherence to medications as a *multidimensional phenomenon determined by the interplay of five sets of factors* (1). These are the following: *social/economic, therapy-related, patient-related, condition-related* and *health system/healthcare team* (1).

Medication adherence is a seemingly simple, but, in reality, extremely complex entity. In fact, a review of systematic reviews published by Kardas et al. in 2013 (3) found 711 individual determinants of adherence to chronic medications. In an attempt to uniformize the discourse in this area, the authors of the ABC (Ascertaining Barriers to Compliance) project's medication adherence taxonomy proposed new definitions, based on both behavioral and pharmacological sciences (4). As such, medication adherence was conceptualized as a continuous entity, divided in 3 distinct, quantifiable phases: *Initiation* (the act of taking the first dose of medication as prescribed), *Implementation* (the extent to which a patient takes their medication as prescribed) and Discontinuation (the moment when the patient completely stops taking the medication). In addition, *Persistence* was defined as the time period between *Initiation* and *Discontinuation* (4). This taxonomy was later used to create the ESPACOMP (European Society for Patient Adherence, Compliance, and Persistence) Medication Adherence Reporting Guideline (EMERGE) (5), which is of great utility and pertinence.

Another very important conceptualization is the division of medication nonadherence in intentional and unintentional. This stems from the fact that not all nonadherence behaviors are conscious and intentional: patients can be passively inconsistent in their medication taking habits, i.e. unintentionally nonadherent (due to forgetfulness, for example) (6). The recognition of the existence of both intentional and unintentional nonadherence behavior patterns emphasizes the need to address these, whether individually or as a whole, as they most likely coexist in the same patient (7).

Arterial hypertension (henceforth, hypertension) is a chronic health condition that requires chronic medication to control and prevent the plethora of cardiovascular and cerebrovascular morbidities related to it (8). However, despite the availability of effective treatments, the majority of patients with hypertension do not achieve satisfactory blood pressure levels (9), and it is well established that suboptimal antihypertensive medication adherence plays a crucial role (10). Likewise, poor medication adherence is an important confounder in the diagnosis of true resistant hypertension (11), further demonstrating its pertinency and need to be addressed (1, 2, 12, 13). As a matter of fact, improving medication adherence is a key factor not only in preventing hypertension complications, but also in

relieving the condition's healthcare burden and socioeconomic sequelae, positively modifying health system overall effectiveness (14).

Indeed, increasing the rate of adherence to hypertensive medication to 70% in just 5 European countries (England, France, Germany, Italy, and Spain) would lead to 82,235 less cardiovascular events and save over €330 million over 10 years (15).

This problem's relevance has long been well-recognized (16) and, consequently, several interventions addressing medication nonadherence in hypertensive patients have been described and/or implemented (13). Despite a great variety, there is a lack of evidence to support any specific intervention to improve medication adherence (1, 3, 6, 10, 13). Moreover, interventions are often complex, multimodal and, yet, vaguely detailed, which means that few are reported beyond the academic research setting and can be replicated in real-life scenarios. This issue is highlighted in a 2015 review of interventions to improve adherence to antihypertensives, in which Conn et al. found that less than 25% of the studies included were theory-based (13). More recently, in a systematic overview of systematic reviews, Anderson et al. (2020) concluded that the vast majority of primary studies describing interventions on medication adherence are of very low or low quality (17), cementing the fact that the search for effective interventions has been an often frustrating, frequently disorganized and misguided effort so far (1, 3, 18).

In light of this paradigm, a scoping review with the aim to summarize and clarify the evidence on medication adherence interventions in hypertensive patients was performed. Besides this, the present study proposes an intervention categorization that allows a clear, systematized, and reliable approach to their interpretation and development. The ABC taxonomy (4) and EMERGE (5) were used as theoretical frameworks in our study.

2. Methods

This scoping review was conducted following the PRISMA Extension for Scoping Reviews (19), thus employing a systematic approach to mapping the evidence on interventions to improve medication adherence in hypertensive patients (Figure 1). Its main objectives were to identify and categorize interventions, analyzing their outcomes and adherence measuring tools used. The protocol was drafted by the research team (Pinho, Cruz and Ferreira) and revised by the advisory board (Sampaio and Ramalho). It was based on the PROSPERO database's protocol model (20); however, it was not submitted, as scoping reviews are not eligible for registration. All the study selection phases were performed by 2 independent reviewers, with consensus meetings as tiebreakers, ensuring the eligibility criteria were rigorously applied.

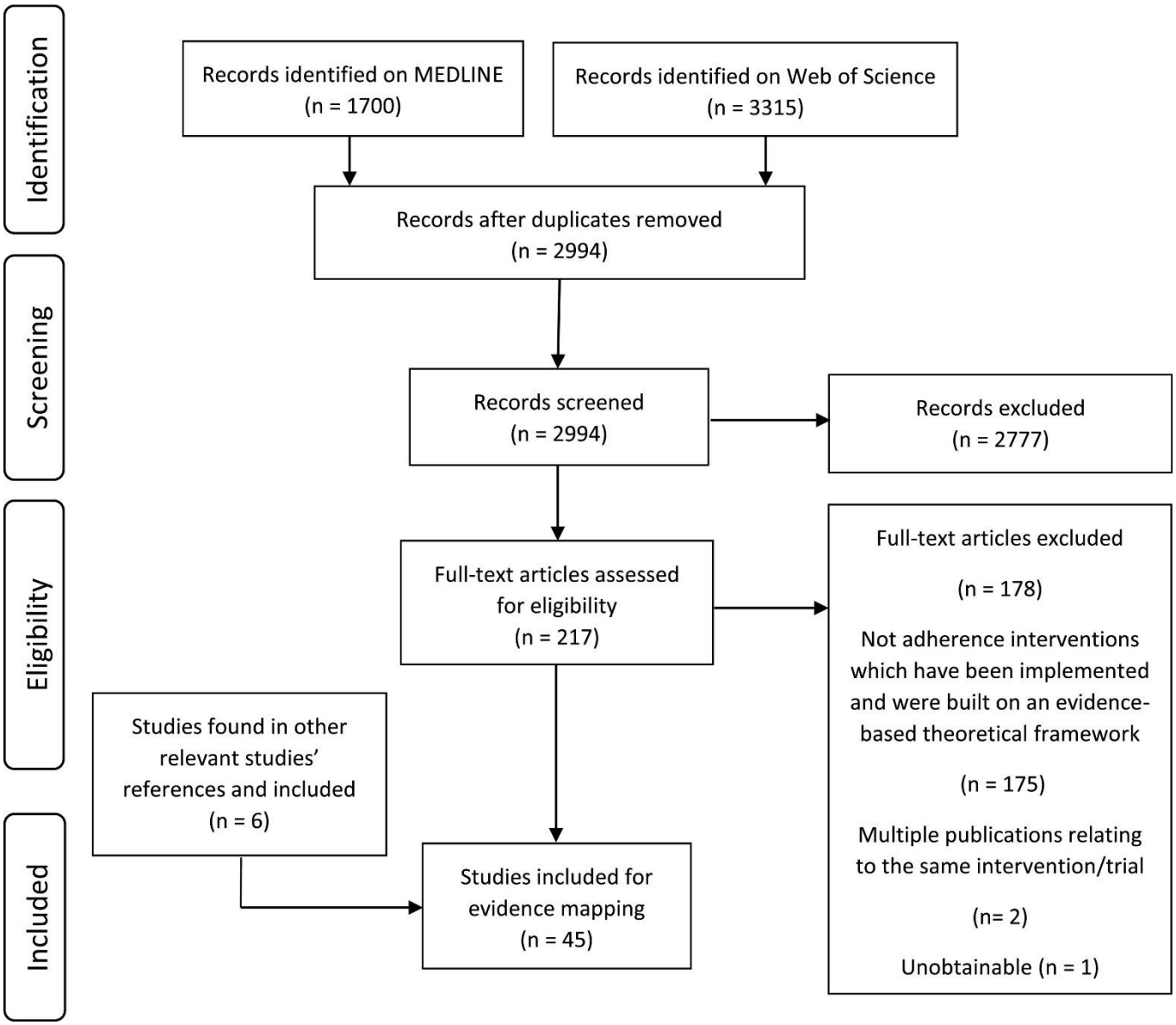

Figure 1 – Study Selection (based on the PRISMA Flow Diagram (40))

2.1 Data Sources and Searches

From an initial set of relevant studies, a search expression was defined and calibrated in electronic databases, through test rounds for individual and combined terms. The database eligible for calibration was MEDLINE. There were no restrictions on publication period or language. The terms in the search expression were selected using information from the ABC taxonomy (4) and EMERGE (5), and following an evidence-based methodology for planning and creating a multi-database search strategy (21).

After calibration, the most relevant search expression (Supplementary Material 1) was selected. Two databases (MEDLINE and Web of Science) were then queried, and studies from inception until 17th August 2020, the date when the search was performed, were considered.

2.2 Study Selection

Eligibility criteria

Studies included were:

1) written in English or Portuguese;
2) peer-reviewed and literature-indexed, guaranteeing their quality;
3) focused on a population of patients with arterial hypertension;
4) presenting structured, clearly described and replicable interventions addressing medication adherence – according to the recommendations of Professor Susan Michie and other authors (17, 22-25), for reasons further detailed in the discussion section, when analysing educational interventions, only those whose educational component was designed using an evidence-based theoretical framework were included;
5) describing technologies or interventions that are not merely conceptual and have been implemented in an academic and/or real-life setting.

Studies that did not have an abstract on the screening phase or which, in the eligibility phase, did not have the full-text version available (after direct contact with the authors), were excluded. There were no exclusions regarding study type or design.

Screening phase

After searching the databases, conducting a consistency check, and extracting all the articles, duplicates were identified and excluded using EndnoteX9. From 5015 starting articles, a total of 2994 remained and were assessed for eligibility (reading of title and abstracts) by two independent reviewers and a third as a tiebreaker, ensuring methodological rigor. A kappa statistic was calculated to ensure inter-rater reliability and determined to be 0.528 (95% CI 0.309-0.746).

Eligibility phase

Full texts of all the articles included in the previous phase were extracted (n= 217). The eligibility criteria were then reapplied by 2 independent reviewers and a third as a tiebreaker. The reference lists of each eligible article were scrutinized for any relevant studies omitted in the previous phases. A kappa statistic was again calculated to ensure that inter-rater reliability was maintained.

2.3 Data Extraction

A standard data extraction form was created, and the following data was extracted from each study: article title; name of first author; country of origin; publication year; publication type; aims of the study; participants of the study; adherence to medications components addressed (when mentioned, as EMERGE recommends (5)); management of adherence strategies (5); adherence-related sciences involved (fields of science the intervention encompasses, either due to its nature or the background of the people implementing it (5)); adherence measurement tools used; statistic methods used; study limitations; intervention category (according to the systematic categorization method detailed in the section below); key findings.

Two reviewers independently extracted the data. Differences in the data extracted were resolved by the reviewer team and supervisor board on a consensus meeting.

2.4 Data Synthesis and Analysis

A system for the categorization of interventions was designed and, to prevent biases in its creation, the conceptual clustering framework was adopted. According to this framework, a group of objects (in this case interventions) forms a category only if it is describable by a concept from a predefined group of concepts (26).

A previous intervention classification system found in a Cochrane Review (27) was used as a starting point for establishing a group of concepts. Subsequently, this group was updated using data from EMERGE (5), the moderator analyses done in a widely cited systematic review of medication adherence interventions in hypertensive patients (13), the intervention type classification in a recent overview of systematic reviews of medication adherence interventions (17) and the Necessity-Concerns Framework (28). These works were sources for concepts and definitions because they provide clear, useful, and extensive information on interventions and modifiable adherence behaviors. Finally, from the resultant group of concepts 8 different categories were described (Table 1).

When performing the study categorization itself, the reviewers were instructed on biases in categorization (29) and followed general recommendations on preventing information biases (30). Differences in study categorization were solved by investigation team consensus meeting.

This novel categorization system aims to sort interventions on medication adherence according to the feature they intend to modify. Multimodal interventions are part of more than one category; this system is especially useful in these cases as it allows them to be summarized and easier to interpret.

Table 1 – Intervention categories.

Category	Concept (26)
Education of caregivers	Health professionals are taught strategies to improve patient's adherence, following a clear, evidence-based educational framework.
Education of patients	Patients are given health information, following a clear, evidence-based educational framework.
Financial or other material incentives	Patients are provided some sort of material incentive to motivate them to be adherent.
Involvement of allied health professionals	Beyond the expected patient-caregiver relationship, a health professional is assigned to personally accompany and help one or a group of patients, attending their individual needs.
Medication adherence intentional factors	Patients' motivation and beliefs regarding treatment and illness perception are addressed, tackling intentional nonadherence.
Medication adherence unintentional factors	The intervention's purpose is improving patients' skills and personal competences, such as memory, tackling unintentional nonadherence.
Simplification of treatment regimens	Patient's medication regimen is simplified, using strategies that make it easier to adhere to.
Special monitoring	Patients are monitored (or self-monitor), in a way they normally would not be.

3. Results

The results summarized below are presented in Table 2.

3.1. Study Characteristics

The database searches conducted in August 2020 yielded 5015 potentially relevant studies. After duplicate removal, 2994 articles were screened. Following title and abstract screening, 217 full-text articles were selected. After applying the eligibility criteria to the full-text articles, 45 articles were included for analysis. From 45 articles included, 6 were not present in the original 2994 articles and were added after scrutinizing the reference list of other relevant articles. Of the included studies, 34 are randomized controlled trials, 6 are quasi-experimental studies, 4 are observational studies and 1 is a secondary data analysis.

Regarding the article's country of origin, 20 studies were from the USA, 3 each were from Australia, China and France, 2 each were from Canada and the Netherlands, and, finally, Brazil, Chile, Denmark, Iran, Japan, Malaysia, Poland, South Africa, South Korea, Spain, Taiwan and the UK had 1 study each.

3.2 Medication Adherence Measuring Tools

There were 33 individually different tools used to measure adherence. Likewise, 33 studies used a single adherence measuring tool, 10 studies used two different tools, 1 study used three and another used four.

Most studies included used self-reporting tools for measuring adherence, with 19 different self-report tools used. In fact, 21 studies used self-reporting tools as the only medication adherence outcome measure, 8 studies used a self-reporting tool in conjunction with a different type of measure and 16 studies did not use any form of self-reporting as a medication adherence outcome. The majority of studies (14 of them) used the Morisky Medication Adherence Scale, in its different versions (6 studies used the 4-MMAS (32), another 6 the 8-MMAS (33) and 1 the MMS (34)). Furthermore, 8 studies (35-42) developed their own self-reporting tools, often developed based on undefined assumptions. Finally, 9 studies used other self-reporting tools found in literature (43-50).

As for objective measurements of adherence based on pharmacy records or pill counts, Proportion of Days Covered (51) pill was the most frequent method, with 7 studies using it. It was followed by pill count, as 5 studies measured this outcome, and Medication Possession Ratio (51) (4 studies). It should be noted that 2 studies used pill count based tools, described in the study (52, 53). One study also used time to discontinuation and time to refill as adherence outcomes, and another evaluated the percentage of patients that refilled prescriptions on time.

Regarding the use of electronic or digital data for measuring adherence, 9 studies used data collected with some variation of a sensor-enabled pill or pill bottle (54-58). In this group, the Medication Event Monitoring System pill cap (54) was used most frequently, with 5 studies employing it. Lastly, 1 study used data from the mobile application it implemented as an adherence outcome (59).

3.3 Study Categorization

Most studies (26 of them) presented multimodal interventions, implementing approaches from 2 or more different categories; the remaining studies (19 of them) focused on a single category of intervention. The most frequently tested categories, with 20 studies each, were medication adherence intentional factors and medication adherence unintentional factors. Education of patients was present in 17 interventions and special monitoring in 16. There was involvement of allied health professionals in 6 studies, 5 studies implemented simplification of treatment regimens and 3 studies had interventions that fit the education of caregivers category. Finally, only 1 study tested the effect of financial or other material incentives.

3.4 Study Outcomes

Most included studies (30 of them) found that their interventions significantly improved medication adherence; however, 15 studies found no significant impact in any of the measured adherence outcomes. Concerning impact on blood pressure, the paradigm is different: of the 38 studies reporting blood pressure outcomes, less than half (18 of them) found their intervention had any significant impact; the remaining 20 reported nonsignificant results.

Regarding the categorization of interventions with significant results on adherence, most tested interventions fit either the medication adherence intentional factors category or the medication adherence unintentional factors one, with 11 studies each (55% of interventions in each category). The following most frequent category was education of patients, with 10 interventions (approximately 59% of interventions), after which came the special monitoring category, with 9 (56% of interventions). The involvement of allied professionals and simplification of treatment regimens categories had 5 interventions each (83% and 100%, respectively). Finally, there were 2 interventions in the education of caregivers category (66% of interventions in this category) and 1 in the financial or other material incentives category (100% of interventions).

The number of multimodal interventions that were successful in improving was close to the number of unimodal ones, as there were 16 of the former (approximately 60%) and 14 of the latter (approximately 70%). Of the unimodal interventions, 5 fit the simplification of treatment regimens category, 2 (each) fit the special monitoring, education of patients and medication adherence unintentional factors categories and 1 (each) fit the financial or other material incentives, involvement of allied health professionals and education of caregivers categories.

The most frequently mentioned study limitation was a short follow-up, making it impossible to evaluate long-term outcomes. This is a frequent limitation which is also often mentioned in previous reviews (3, 60, 61).

Table 2- Studies Included.

First Author; Year; Country	Publication Type; Participants	Management of Adherence Strategies (5) (Intervention)	Adherence Measurement Tools	Key Findings	Intervention Category
Abughosh, S; 2018; USA (62)	RCT; 11 pharmacy students and 743 nonadherent patients with DM and HT.	6 MI (63) phone calls made by pharmacy students, trained in the Transtheoretical Model of Behavioral Change (64).	PDC. (51)	MA was significantly better in the intervention group.	Involvement of allied health professionals; MA intentional factors.
Andrejak, M; 2000; France (65)	RCT; 162 hypertensive patients, aged ≥ 18 years.	Trandolapril once daily, instead of captopril twice daily.	Pill count; MEMS pill caps (54).	MA with the once daily regimen was significantly higher. BP control between groups was not significantly different.	Simplification of dosage regimens.
Bajorek, B; 2016; Australia (66)	Cluster RCT; 15 pharmacists and 53 patients, aged ≥ 18 years, with uncontrolled HT.	Pharmacist-led service based on the Health Collaboration Model (67), employing BP measurements, MA barrier identification, medication reviews and recommendations.	MMAS-8 (33).	MA and BP control significantly improved in the 3-month follow-up group. No significant MA or BP changes in the 12-month follow-up group.	Education of patients; MA intentional factors.
Becker, LA; 1986; USA (35)	RCT; 180 patients, aged 20-80 years, with poor BP control.	Pill blister with medication taking schedule printed on it.	Self-report; Pill count.	No significant improvements in MA or BP control.	MA unintentional factors.
Bobrow, K; 2016; South Africa (40)	RCT; 1372 hypertensive patients, aged ≥ 21 years.	Interactive messages, based on behavior change techniques (26), designed to improve MA, provide HT education and allow appointment rescheduling.	PDC (51); Self-report.	MA measured by PDC was significantly better. Self-reported MA did not significantly change. Systolic BP was statistically better.	Education of patients; MA intentional factors; MA unintentional factors.
Boissel, JP; 1996; France (36)	RCT; 7274 hypertensive patients, aged ≥ 18 years.	Slow-release nicardipine 2 times a day, instead of nicardipine 3 times a day.	Standardized interview.	MA in the twice daily regimen group was significantly better. No significant differences in BP control.	Simplification of dosage regimens.
Bosworth, HB; 2005; USA (68)	RCT; 588 hypertensive veterans.	Phone calls based on the Health Decision Model (69), providing predefined health information (namely about medication taking memory aids) and emphasizing positive, motivating messages.	MMAS-4 (32).	MA did not significantly change at 6 months. BP control at 24 months significantly improved in the intervention group, but there was no between-group significant difference (70).	Education of patients; MA intentional factors; MA unintentional factors.

Bosworth, HB; 2009; USA (71)	Factorial RCT; 656 hypertensive patients.	Phone intervention based on the Health Decision Model (69) and Transtheoretical Model of Behavior Change (64), designed to improve MA and health behaviors; or BP self-monitoring 3 times a week; or both.	MMAS-4 (32).	Self-reported MA was not significantly better in intervention groups. BP control was significantly better in the combined intervention group than in the control group. The difference was not significant between either of the other intervention groups and the control group.	Education of patients; MA intentional factors; MA unintentional factors; Special monitoring.
Buis, L; 2017; USA (72)	Factorial RCT; 123 hypertensive African American patients, aged ≥ 18 years.	BPMED, an automated text-messaging system aligned with the Health Belief Model (73), that sends users medication taking reminders and evidence-based educational material.	MMAS-8 (33); Pill count.	No significant changes in MA or BP control. On linear regression, baseline systolic BP was the only predictor of BP change.	Education of patients; MA unintentional factors.
Buis, LR; 2020; USA (74)	Non-randomized, uncontrolled trial; 15 patients, aged ≥ 18 years, with uncontrolled HT.	BPTrack: 2 apps, one patient-directed and another pharmacist-directed. The patient-directed app allows patients to register their BP, receive medication taking reminders, record MA and send messages to the pharmacist. The pharmacist-directed app allows patient data tracking, goal-setting and sending messages to patients.	ARMS (46).	MA did not significantly change. BP control was significantly better.	Involvement of allied health professionals; MA unintentional factors; Special monitoring.
Chabot, I; 2003; Canada (75)	Non-randomized, controlled trial; 100 patients, aged 18–80 years.	Decision aid software, integrated in the pharmacy system, based on the PRECEDE–PROCEED model (76), using data from patient's BP measurements and PDC. With the software's guidance, the pharmacist could then provide lifestyle changing recommendations for patients, their GPs, or both and patient education, addressing MA.	PDC (51); MMAS-4 (32).	MA measured by MMAS significantly improved in high-income patients. No significant overall group differences regarding MA or BP. In high-income patients, there was a significant improvement in systolic BP. In low-income patients, there was no significant BP differences.	Education of caregivers; Education of patients; MA intentional factors.
Christensen, A; 2010; Poland (41)	Crossover RCT; 1577 patients, aged ≥ 18 years, with untreated or ineffectively treated HT.	Helping Hand Data Capture (HHDC), a blister-operated device that provides audiovisual medication taking reminders. The time of each blister removal is monitored.	HHDC data (58); Self-report.	Self-reported MA did not significantly change. MA measured by HDDC was overall significantly better in the group using the device from the start than in the group that started used it after crossover. No significant differences in BP control.	MA unintentional factors; Special monitoring.

de Souza, AC; 2016; Brazil (77)	Non-randomized, uncontrolled trial; 116 hypertensive patients, aged ≥ 18 years.	Evidence-based educational flipchart, implemented in 3 workshop sessions.	QATSH (44).	MA improved significantly.	Education of patients.
Dupclay, L; 2012; USA (78)	Observational, retrospective, propensity-score matched cohort study; 9266 patients, aged ≥ 18 years.	Special pill container.	MPR (51); PDC (51); Time to refill and time to discontinuation.	MA was significantly better, regardless of MA measure. MA in patients with the lowest MPR did not significantly improve.	MA unintentional factors.
Hedegaard, U; 2015; Denmark (79)	RCT; 532 hypertensive patients, aged ≥ 18 years.	Pharmacy intervention consisting of a medication review, followed by advice to the patient's GP, a patient MI (63) session and follow-up phone calls.	MPR (51).	MA improved significantly. No significant changes in BP control.	Involvement of allied health professionals; MA intentional factors.
Ho, CT; 2018; Taiwan (80)	Observational, retrospective, cohort study; 17568 hypertensive patients, aged ≥ 18 years.	Single-pill fixed-dose drug combination.	PDC (51).	MA was significantly better and there was a significant reduction of major adverse cardiovascular events.	Simplification of dosage regimens.
Kang, H; 2016; South Korea (81)	Non-randomized, uncontrolled trial; 38 hypertensive patients.	HT management app (HMA), providing medication taking reminders, evidence-based lifestyle recommendations, health goals and medication education.	MMS. (34)	MA improved significantly.	Education of patients; MA unintentional factors.
Logan, AG; 1979; Canada (52)	RCT; 457 hypertensive patients, aged 18-69 years.	Two nurses were taught to manage HT according to a standard protocol, which involved MA evaluation. They then sent the patient's GP a summary of every visit.	Pill count-based tool.	MA and BP were significantly better.	Involvement of allied health professionals.
Ma, CH; 2014; China (82)	RCT; 120 hypertensive patients, aged ≥ 18 years.	8 MI (63) sessions; goal-setting diary.	TAQPH (45).	MA and BP control improved significantly.	MA intentional factors.
Marquez-Contreras, E; 2006; Spain (83)	RCT; 250 patients, aged 18-80 years, with newly diagnosed or uncontrolled HT.	BP self-monitoring, 3 times a week.	MEMS pill caps (54).	MA was significantly better. BP significantly improved but was not significantly different between groups.	Special monitoring.

Matsumura, K; 2012; Japan (84)	RCT; 207 hypertensive patients, aged ≥ 20 years.	Single-pill fixed-dose drug combination.	Pill count.	MA and BP control did not significantly change.	Simplification of dosage regimens.
McKenney, JM; 1992; USA (85)	RCT; 70 hypertensive patients, aged ≥ 50 years.	Medication vial cap that displays when the container was last opened (Prescript TimeCap) (86). BP self-measurement.	Pill count.	MA and BP control were significantly better.	MA unintentional factors; Special monitoring.
McManus, RJ; 2018; UK (87)	Factorial RCT; 1182 patients, aged ≥ 35 years, with uncontrolled HT.	BP self-monitoring 4 times a day, with or without a SMS-based telemonitoring service associated.	MARS (49).	MA did not significantly change. Systolic BP was significantly better in both intervention groups, with no significant difference between them.	Special monitoring.
Mehta, SJ; 2019; USA (37)	Factorial RCT; 151 hypertensive patients, aged 18-75 years.	Medication taking reminder messages, automated by the Way to Health software. Daily medication taking reminder text messages, with bidirectional texting or not.	Smart pill cap (AdhereTech) (56); Self-report.	No significant improvements in MA or BP control.	MA unintentional factors; Special monitoring.
Moorhead, P; 2017; USA (88)	Cluster RCT; 57 patients, aged ≥ 18 years, with uncontrolled HT and DM.	Proteus Discover, a digital health system that incorporates sensor-enabled medication and a mobile app that provides medication taking reminders and gathers user data, connected to a wearable sensor.	Data from the digital health system (57).	MA was significantly better. Subjects with lower levels of MA at baseline had the greatest MA improvement.	MA unintentional factors; Special monitoring.
Morawski, K; 2018; USA (89)	RCT; 412 hypertensive patients, aged 18-75 years.	Smartphone app Medisafe, providing medication taking reminders, MA tracking and weekly MA reports and optional peer support.	MMAS-8 (33).	Nonsignificant increase in MA in the intervention group, with no change in the control group. The between-group difference was statistically significant. Systolic BP did not significantly change.	MA intentional factors; MA unintentional factors; Special monitoring.
Mounier-Vehier, C; 1998; France (90)	RCT; 103 hypertensive patients aged 18-75 years.	Amlodipine 1 time a day instead of nifedipine 2 times a day.	MEMS pill caps (54).	MA was significantly better. BP control was not significantly different between groups overall, but at night it was significantly better in the amlodipine group.	Simplification of dosage regimens.
Muhammad, J; 2019; Malaysia (39)	RCT; 88 hypertensive patients, aged ≥ 18 years.	BP self-measurement, 2 times per day.	New MA Scale Questionnaire.	MA did not significantly change. BP significantly improved in both groups; the between-group difference significant.	Special monitoring.

Odusola, A; 2015; Netherlands (91)	Observational, one group pre-test, post-test study; 149 patients, aged ≥ 18 years, with uncontrolled HT or poor self-reported MA.	3 group education sessions with culturally tailored written and audio-visual educational materials.	MMAS-8 (33).	MA and BP control significantly improved.	Education of patients.
Ogedegbe, G; 2008; USA (92)	RCT; 190 African Americans, aged ≥ 18 years, with uncontrolled BP.	4 MI (63) sessions.	MEMS pill caps (54).	MA significantly worsened in the control group and did not significantly change with the intervention. The group difference was not significant. BP significantly lowered in both groups; the between-group difference was not significant.	MA intentional factors.
Patel, S; 2013; USA (59)	Non-randomized, uncontrolled trial; 50 hypertensive patients, aged 18-80 years.	Pill Book, an app providing information on commonly prescribed medications and audiovisual medication taking prompts, with MA tracking.	PDC (51); MMAS-4 (32); Tracking data from the application.	MA measured by PDC significantly increased at 3 months. At the 6-month visit (3 months after the phone app was turned off), MA was significantly lower than baseline. MA measured by MMAS significantly improved at 6 months. BP control improved significantly.	MA unintentional factors; Special monitoring.
Persell, SD; 2020; USA (42)	RCT; 333 hypertensive patients, aged 18-84 years.	Hypertension Personal Control Program, an AI-based app connected to a BP self-measuring device, providing evidence-based HT education and coaching on lifestyle and diet, based on DASH (93); BP data tracking and medication taking reminders.	Self-report.	No significant improvements in MA or BP control.	Education of patients; MA intentional factors; MA unintentional factors; Special Monitoring.
Sany, SB; 2020; Iran (94)	RCT; 35 physicians and 242 patients, aged ≥ 18 years, with uncontrolled HT.	Physicians participated in 2 full-day workshops, based on the Health Literacy in Practice model (95) and standard treatment algorithms for HT.	Adult Primary Care Questionnaire (50).	MA and BP control were significantly better.	Education of caregivers.
Schneider, PJ; 2008; USA (96)	RCT; 85 hypertensive patients, aged ≥ 65 years.	Pill Calendar: medication blister in the form of a calendar, with information on what to do if a dose is missed.	Percentage of prescriptions refilled on time; MPR (51).	MA and BP control were significantly better.	MA unintentional factors.

Schoenthaler, A; 2020; USA (97)	RCT; 119 non-adherent hypertensive Latino patients, aged ≥ 18 years.	9 counseling sessions based on the teamlet mode (98), conducted in person or via telephone.	MMAS-8 (33); Smart pill bottle eCAP ECM (55).	MA measured by eCAP device significantly worsened in both groups, with no between-group significant difference. MA measured by MMAS-8 was significantly better in the intervention group. No significant differences in systolic BP.	Involvement of allied health professionals; MA intentional factors.
Schroeder, EB; 2020; USA (99)	RCT; 295 hypertensive patients, aged 21-79 years.	Interactive voice response and text message, providing appointment reminders, with prompts to reschedule missed appointments and refill medications and weekly messages encouraging self-care and medication taking.	Voils instrument (48).	No significant improvements in MA or BP control.	MA intentional factors; MA unintentional factors.
Stewart, K; 2014; Australia (100)	Cluster RCT; 395 hypertensive patients aged ≥ 18 years.	Package of interventions, involving BP self-monitoring; MI (63) and evidence-based health education; pharmacy-based medications review and GP referral when needed and optional medication refill reminders.	MMAS-4 (32); TABS (43).	MA significantly improved in both groups, with no significant between-group difference. Systolic BP was significantly better.	Education of patients; MA intentional factors; MA unintentional factors; Special monitoring.
Svarstad, BL; 2013; USA (101)	Cluster RCT; 576 hypertensive black patients, aged ≥ 18 years.	Multimodal intervention, based on the Health Collaboration Model (67), involving training session for pharmacists and technicians, with provision of guiding clinical toolkits; patient toolkits with card for recording self-monitored BP, a 7-day medication box and a pedometer and monthly patient assessment with identification of MA barriers.	PDC (51).	MA and BP control were significantly better at 6 months. 6 months after intervention discontinuation, improvements in MA and systolic BP were sustained, though the difference in diastolic BP and overall BP control was no longer significant.	Education of patients; Education of caregivers; MA intentional factors; MA unintentional factors; Special monitoring.
Tu, Q; 2020; Australia (102)	Cluster RCT; 270 diabetic patients, aged ≥ 60 years, with uncontrolled HT, recently discharged from the hospital.	Hospital-home transitional care program, based on the integrated care model (103), involving goal-setting, action plan and individualized treatment plan and 6 months post-discharge support.	TAPQH (45).	MA and BP were significantly better.	Education of patients; Involvement of allied health professionals; MA intentional factors.
van Onzenoort, HAW; 2010; Netherlands (104)	RCT; 228 hypertensive patients, aged ≥ 18 years.	BP self-monitoring, 6 times a day.	MEMS pill caps (54).	MA was significantly better. BP control did not significantly change.	Special monitoring.

Varleta, P; 2017; Chile (105)	RCT; 314 hypertensive patients, aged 30-80 years.	Patients received text messages developed using social-cognitive theory data (106), containing educational information about lifestyle choices and MA.	MMAS-4 (32).	MA significantly decreased in the control group and significantly improved in the intervention group. There was a BP reduction in both groups, but not enough power to make statistical comparisons.	Education of patients; MA intentional factors.
Wang, MY; 2020; China (107)	RCT; 174 hypertensive patients, hospitalized after an ischemic stroke.	Comprehensive Reminder System, based on the Health Belief Model (73), comprising a health education session before hospital discharge, along with the provision of a goal-setting calendar; an automated message service of prewritten medication taking reminder messages and 4 follow-up telephone calls.	Adapted version of Health Promoting Lifestyle Profile II (47).	MA significantly increased in both groups at 3 months. At 6 months, it significantly decreased in the control group and stayed identical in the intervention group, as such, MA was significantly better in the intervention group. Systolic BP levels were significantly better as well.	Education of patients; MA intentional factors; MA unintentional factors.
Webb, PA; 1980; USA (53)	Factorial RCT; 123 low-income black patients, aged 20-80 years, with uncontrolled HT.	Educational Intervention: 3 group education sessions based on group decision making techniques (108), discussing management of HT and importance of MA. Counseling Intervention: 3 individual counseling sessions, focused on overall psychosocial well-being.	Pill count-based tool.	No significant improvements in MA or BP control.	Education of patients; MA intentional factors.
Wu, JR; 2018; USA (109)	Secondary data analysis; 477 hypertensive patients, aged ≥ 18 years.	BP self-monitoring, 3 times per week. Phone health-coaching program, modelled after the Health decision Model (69) and the Transtheoretical Model of Behavior Change (64), conveying lifestyle and HT information and MI (63) goal-setting strategies.	MMAS-8 (33).	MA and BP significantly improved. However, MA significantly decreased in patients with high MA at baseline.	Education of patients; MA intentional factors; Special monitoring.
Yu, BR; 2013; China (38)	Observational, retrospective cohort study; 351 hypertensive patients.	Subsidy program that provided free medication and HT management to patients in low-income families.	Survey.	MA was significantly better. BP control did not significantly change.	Financial or other material incentives.

Abbreviations AI - artificial intelligence; BP - blood pressure; DM - diabetes mellitus; GP - general practitioner; HT - arterial hypertension; MA - medication adherence; MI - motivational interviewing; UK - United Kingdom; USA - United States of America.

4. Discussion

We are not aware of any other studies that have produced such a comprehensive, evidence-based mapping and categorization of all the existing types of medication adherence interventions in hypertensive patients. The present study, besides an extensive overview of the area, provides a much-needed new perspective, as our work highlights major limitations in the search for effective interventions to improve medication adherence in hypertensive patients.

Throughout the review, we were very conscious of considerations on what an appropriately developed intervention is and, as such, traced every step of an intervention to the theoretical framework it was based on, when possible. Hoffmann et al. demonstrated in 2014 that interventions that are shown to be useful cannot be reliably implemented, replicated or built on without a completely published, clear description (110). Additionally, as Breitenstein et al. (2010) emphasized, an improper description of an intervention's structure challenges the work's implementation fidelity itself (111). As such, developing a well-structured, accurately conducted health intervention requires it to be evidence-based and fully described, not only concerning the materials it used, but the intervention's framework itself (17, 23, 24).

These observations were particularly relevant when analyzing multimodal interventions that included an educational or behavior-changing component. Often, the authors do not specify how the behavior-changing approach was developed, which educational materials were used, or even whether the intervention was based on established psychological and health education models. One might argue that educational or behavioral interventions that are not based in theory do not represent true scientific interventions, as their design is not clearly described or based on a psychological, behavioral or educational theoretical framework (22, 112). In fact, frequently these interventions equate to the mere act of providing information to participants in a non-systematic way. This, however, is simply an aspect of the shared decision-making clinical practice model, that nowadays is widely recommended accepted as the most ethical (113). A lot of potentially relevant studies were excluded because of these considerations.

Furthermore, even after selecting for only demonstrably evidence-based studies, none of the studies included in the present study follow the EMERGE checklist on medication adherence reporting (5). In fact, only 1 (97) of the 10 included studies (37, 39, 42, 74, 80, 94, 97, 102, 107, 114) that were published after the EMERGE went as far as even mentioning the medication adherence phase its intervention addressed, which is the first item on the checklist.

Another highlighted problem in the medication adherence research field is the fact that tools used to measure adherence are very diverse and difficult, if not impossible, to compare to each other. This is not a new remark, as the difficulty of reliably measuring adherence is well-established, with some authors suggesting the best solution to be the combined use of at least 2 methods (115, 116). It should be noted, however, that most studies included in this review used a single adherence measurement tool. Besides this, the great variety of adherence measuring tools used is a good testament to the yet (to our knowledge) unaddressed need for an academic consensus on what the best tools are specifically.

An interesting and somewhat unexpected result of our work is that the numbers of multimodal and unimodal interventions that had a significant impact on adherence were very similar, even though there were less unimodal interventions overall. This seems to suggest that, when an intervention is evidence-based and well implemented, unimodal interventions might have as much potential for success as multimodal ones.

Another fact that should be highlighted is that interventions that fit the involvement of allied professionals and financial or other material incentives categories were all successful. One must be cautions interpreting these results though, as there were few interventions in these categories. In fact, the categories with the largest percentages of successful studies were the ones with fewer interventions in them. Thus, our study's findings are still consistent with the established notion that there is no single intervention or category of interventions that can reliably and predictably have a positive impact on adherence (1, 3, 10, 13). Furthermore, they highlight categories that are less explored in well-conducted, evidence-based interventions, namely: involvement of allied professionals, simplification of treatment regimens, education of caregivers and financial or other material incentives.

Even though the present review employed a clear, rigorous method, it is not without limitations. The most important one is likely to be the fact that excluding studies which did not fully describe their intervention's theoretical framework may have led to the exclusion of a few studies that were, nevertheless, evidence-based and well-supported, but did not sufficiently detail their methods. When the eligibility criteria were delineated, this possibility was acknowledged and interpreted as an unavoidable consequence of guaranteeing all included studies were well-described. In fact, an evidence-based, well-conducted but poorly described study would not be possible to replicate, making its relevance questionable.

Another caveat of the review is that the search was restricted to 2 databases, which may have prevented the identification of other potentially relevant studies in different databases. Likewise, grey literature was not included, which makes our work more vulnerable to publication bias. However, the exclusion of non-

indexed literature was a calculated choice, so that only peer-reviewed, minimally biased works were included.

Finally, the search expression was designed to be as broad as possible, while balancing its terms' sensitivity and specificity. Even though an evidence-based methodology was followed, one cannot exclude the possibility of a better search expression. Scouring all relevant studies' references for other potentially relevant studies, as mentioned in the methods section, may have contributed to mitigate this drawback.

Our study contributes to shedding light on the current state of medication adherence research, namely regarding interventions with hypertensive patients. It promotes a more open, transparent discussion and the furthering of research in this field, highlighting what has already been addressed and which aspects need to be improved on. This work is an important step in defining and prioritizing good, evidence-based research, allowing for better decision-making by stakeholders and healthcare professionals, and, accordingly, the improvement of patients' clinical outcomes.

5. Funding Source

None.

6. Conflicts of Interest

The authors declare no conflicts of interest.

7. Author Contributions

Simão Pinho: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Writing – Review & Editing, Visualization.

Mariana Cruz: Formal analysis, Investigation, Writing – Review & Editing.

Filipa Ferreira: Formal analysis, Investigation, Writing – Review & Editing.

André Ramalho: Conceptualization, Methodology, Validation, Resources, Writing – Review & Editing, Supervision.

Rute Sampaio: Conceptualization, Methodology, Validation, Resources, Writing – Review & Editing, Supervision, Project Administration.

8. References

1. WHO. Adherence to long-term therapies: Evidence for action WHO full report. 2003.
2. Zullig LL, Blalock DV, Dougherty S, Henderson R, Ha CC, Oakes MM, et al. The new landscape of medication adherence improvement: where population health science meets precision medicine. Patient Prefer Adherence. 2018;12:1225-30. Epub 2018/07/24. doi: 10.2147/PPA.S165404. PubMed PMID: 30034226; PubMed Central PMCID: PMCPMC6049050.
3. Kardas P, Lewek P, Matyjaszczyk M. Determinants of patient adherence: a review of systematic reviews. Frontiers in pharmacology. 2013;4:91. Epub 2013/07/31. doi: 10.3389/fphar.2013.00091. PubMed PMID: 23898295; PubMed Central PMCID: PMCPMC3722478.
4. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. Br J Clin Pharmacol. 2012;73(5):691-705. Epub 2012/04/11. doi: 10.1111/j.1365-2125.2012.04167.x. PubMed PMID: 22486599; PubMed Central PMCID: PMCPMC3403197.
5. De Geest S, Zullig LL, Dunbar-Jacob J, Helmy R, Hughes DA, Wilson IB, et al. ESPACOMP Medication Adherence Reporting Guideline (EMERGE). Ann Intern Med. 2018;169(1):30-5. Epub 2018/06/28. doi: 10.7326/m18-0543. PubMed PMID: 29946690.
6. Lehane E, McCarthy G. Intentional and unintentional medication non-adherence: A comprehensive framework for clinical research and practice? A discussion paper. International Journal of Nursing Studies. 2007;44(8):1468-77. doi: 10.1016/j.ijnurstu.2006.07.010.
7. Mukhtar O, Weinman J, Jackson SH. Intentional non-adherence to medications by older adults. Drugs & aging. 2014;31(3):149-57. Epub 2014/02/26. doi: 10.1007/s40266-014-0153-9. PubMed PMID: 24566876.
8. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 Practice Guidelines for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. Blood Press. 2018;27(6):314-40. doi: 10.1080/08037051.2018.1527177. PubMed PMID: 30380928.
9. Kotseva K, De Backer G, De Bacquer D, Rydén L, Hoes A, Grobbee D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: Results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. European Journal of Preventive Cardiology. 2019;26(8):824-35. doi: 10.1177/2047487318825350.
10. Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keepanasseril A, et al. Interventions for enhancing medication adherence. Cochrane Database Syst Rev. 2014(11):CD000011. Epub 2014/11/21. doi: 10.1002/14651858.CD000011.pub4. PubMed PMID: 25412402.
11. Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, Dennison-Himmelfarb CR, et al. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension. 2018;72(5):e53-e90. doi: 10.1161/HYP.0000000000000084. PubMed PMID: 30354828.
12. Lee HJ, Jang SI, Park EC. Effect of adherence to antihypertensive medication on stroke incidence in patients with hypertension: a population-based retrospective cohort study. BMJ Open. 2017;7(6):e014486. Epub 2017/07/05. doi: 10.1136/bmjopen-2016-014486. PubMed PMID: 28674133; PubMed Central PMCID: PMCPMC5734476.
13. Conn VS, Ruppar TM, Chase JA, Enriquez M, Cooper PS. Interventions to Improve Medication Adherence in Hypertensive Patients: Systematic Review and Meta-analysis. Current hypertension reports. 2015;17(12):94. Epub 2015/11/13. doi: 10.1007/s11906-015-0606-5. PubMed PMID: 26560139; PubMed Central PMCID: PMCPMC5662945.
14. Will JC, Zhang Z, Ritchey MD, Loustalot F. Medication Adherence and Incident Preventable Hospitalizations for Hypertension. American journal of preventive medicine. 2016;50(4):489-99. Epub 2015/11/04. doi: 10.1016/j.amepre.2015.08.021. PubMed PMID: 26526163.
15. Mennini FS, Marcellusi A, von der Schulenburg JM, Gray A, Levy P, Sciattella P, et al. Cost of poor adherence to anti-hypertensive therapy in five European countries. The European journal of health economics : HEPAC : health economics in prevention and care. 2015;16(1):65-72. Epub 2014/01/07. doi: 10.1007/s10198-013-0554-4. PubMed PMID: 24390212.
16. Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J, et al. A meta-analysis of the association between adherence to drug therapy and mortality. BMJ. 2006;333(7557):15. doi: 10.1136/bmj.38875.675486.55.
17. Anderson LJ, Nuckols TK, Coles C, Le MM, Schnipper JL, Shane R, et al. A systematic overview of systematic reviews evaluating medication adherence interventions. American Journal of Health-System Pharmacy. 2020;77(2):138-47. doi: 10.1093/ajhp/zxz284.

18. Kini V, Ho PM. Interventions to Improve Medication Adherence: A Review. Jama. 2018;320(23):2461-73. doi: 10.1001/jama.2018.19271.
19. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Annals of Internal Medicine. 2018;169(7):467-73. doi: 10.7326/M18-0850.
20. Moher D, Booth A, Stewart L. How to reduce unnecessary duplication: use PROSPERO. BJOG : an international journal of obstetrics and gynaecology. 2014;121(7):784-6. Epub 2014/03/19. doi: 10.1111/1471-0528.12657. PubMed PMID: 24629162.
21. Bramer WM, de Jonge GB, Rethlefsen ML, Mast F, Kleijnen J. A systematic approach to searching: an efficient and complete method to develop literature searches. J Med Libr Assoc. 2018;106(4):531-41. Epub 2018/10/01. doi: 10.5195/jmla.2018.283. PubMed PMID: 30271302.
22. Michie S, Prestwich A. Are interventions theory-based? Development of a theory coding scheme. Health psychology : official journal of the Division of Health Psychology, American Psychological Association. 2010;29(1):1-8. Epub 2010/01/13. doi: 10.1037/a0016939. PubMed PMID: 20063930.
23. Bartholomew LK, Mullen PD. Five roles for using theory and evidence in the design and testing of behavior change interventions. Journal of Public Health Dentistry. 2011;71(s1):S20-S33. doi: 10.1111/j.1752-7325.2011.00223.x.
24. Whitlock EP, Orleans CT, Pender N, Allan J. Evaluating primary care behavioral counseling interventions: an evidence-based approach. American journal of preventive medicine. 2002;22(4):267-84. Epub 2002/05/04. doi: 10.1016/s0749-3797(02)00415-4. PubMed PMID: 11988383.
25. Abraham C, Michie S. A taxonomy of behavior change techniques used in interventions. Health psychology : official journal of the Division of Health Psychology, American Psychological Association. 2008;27(3):379-87. Epub 2008/07/16. doi: 10.1037/0278-6133.27.3.379. PubMed PMID: 18624603.
26. Kaufman KA. Conceptual Clustering. In: Seel NM, editor. Encyclopedia of the Sciences of Learning. Boston, MA: Springer US; 2012. p. 738-40.
27. Schroeder K, Fahey T, Ebrahim S. Interventions for improving adherence to treatment in patients with high blood pressure in ambulatory settings. Cochrane Database Syst Rev. 2004(2):Cd004804. Epub 2004/04/24. doi: 10.1002/14651858.Cd004804. PubMed PMID: 15106262.
28. Horne R, Chapman SC, Parham R, Freemantle N, Forbes A, Cooper V. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the Necessity-Concerns Framework. PloS one. 2013;8(12):e80633. Epub 2013/12/07. doi: 10.1371/journal.pone.0080633. PubMed PMID: 24312488; PubMed Central PMCID: PMCPMC3846635.
29. Das-Smaal EA. Biases in Categorization. In: Caverni J-P, Fabre J-M, Gonzalez M, editors. Advances in Psychology. 68: North-Holland; 1990. p. 349-86.
30. Althubaiti A. Information bias in health research: definition, pitfalls, and adjustment methods. Journal of multidisciplinary healthcare. 2016;9:211-7. doi: 10.2147/JMDH.S104807. PubMed PMID: 27217764.
31. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Medicine. 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097.
32. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical care. 1986;24(1):67-74. Epub 1986/01/01. doi: 10.1097/00005650-198601000-00007. PubMed PMID: 3945130.
33. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008;10(5):348-54. doi: 10.1111/j.1751-7176.2008.07572.x. PubMed PMID: 18453793.
34. (CMSA) CMSoA. Case Management Adherence Guidelines (CMAG) 2.0 - Guidelines from the Case Management Society of America for improving patient adherence to medication therapies. 2006 [cited September 30, 2020]. [cited September 30, 2020]. Available from: https://www.miccsi.org/wp-content/uploads/2016/01/CMAG2.pdf.
35. Becker LA, Glanz K, Sobel E, Mossey J, Zinn SL, Knott KA. A randomized trial of special packaging of antihypertensive medications. The Journal of family practice. 1986;22(4):357-61. Epub 1986/04/01. PubMed PMID: 3958683.
36. Boissel JP, Meillard O, Perrin-Fayolle E, Ducruet T, Alamercery Y, Sassano P, et al. Comparison between a bid and a tid regimen: improved compliance with no improved antihypertensive effect. European Journal of Clinical Pharmacology. 1996;50(1):63-7. doi: 10.1007/s002280050070.

37. Mehta SJ, Volpp KG, Troxel AB, Day SC, Lim R, Marcus N, et al. Electronic Pill Bottles or Bidirectional Text Messaging to Improve Hypertension Medication Adherence (Way 2 Text): a Randomized Clinical Trial. Journal of general internal medicine. 2019;34(11):2397-404. Epub 2019/08/10. doi: 10.1007/s11606-019-05241-x. PubMed PMID: 31396815; PubMed Central PMCID: PMCPMC6848522.
38. Yu B, Zhang X, Wang G. Full coverage for hypertension drugs in rural communities in China. Am J Manag Care. 2013;19(1):e22-e9. PubMed PMID: 23379776.
39. Muhammad J, Jamial MM, Ishak A. Home Blood Pressure Monitoring Has Similar Effects on Office Blood Pressure and Medication Compliance as Usual Care. Korean J Fam Med. 2019;40(5):335-43. Epub 2019/01/14. doi: 10.4082/kjfm.18.0026. PubMed PMID: 30636386.
40. Bobrow K, Farmer AJ, Springer D, Shanyinde M, Yu LM, Brennan T, et al. Mobile Phone Text Messages to Support Treatment Adherence in Adults With High Blood Pressure (SMS-Text Adherence Support [StAR]): A Single-Blind, Randomized Trial. Circulation. 2016;133(6):592-600. Epub 2016/01/16. doi: 10.1161/circulationaha.115.017530. PubMed PMID: 26769742; PubMed Central PMCID: PMCPMC4750295.
41. Christensen A, Christrup LL, Fabricius PE, Chrostowska M, Wronka M, Narkiewicz K, et al. The impact of an electronic monitoring and reminder device on patient compliance with antihypertensive therapy: a randomized controlled trial. Journal of hypertension. 2010;28(1):194-200. Epub 2009/09/23. doi: 10.1097/HJH.0b013e328331b718. PubMed PMID: 19770778.
42. Persell SD, Peprah YA, Lipiszko D, Lee JY, Li JJ, Ciolino JD, et al. Effect of Home Blood Pressure Monitoring via a Smartphone Hypertension Coaching Application or Tracking Application on Adults With Uncontrolled Hypertension: A Randomized Clinical Trial. JAMA network open. 2020;3(3):e200255. Epub 2020/03/03. doi: 10.1001/jamanetworkopen.2020.0255. PubMed PMID: 32119093; PubMed Central PMCID: PMCPMC7052730.
43. George J, Mackinnon A, Kong DC, Stewart K. Development and validation of the Beliefs and Behaviour Questionnaire (BBQ). Patient education and counseling. 2006;64(1-3):50-60. Epub 2006/07/18. doi: 10.1016/j.pec.2005.11.010. PubMed PMID: 16843634.
44. Rodrigues M, Moreira TM, Andrade D. Elaboration and validation of instrument to assess adherence to hypertension treatment. Revista de saude publica. 2014;48:232-40. doi: 10.1590/S0034-8910.2014048005044.
45. Ma C, Chen S, You L, Luo Z, Xing C. Development and psychometric evaluation of the Treatment Adherence Questionnaire for Patients with Hypertension. Journal of advanced nursing. 2012;68(6):1402-13. Epub 2011/10/01. doi: 10.1111/j.1365-2648.2011.05835.x. PubMed PMID: 21954893.
46. Kripalani S, Risser J, Gatti ME, Jacobson TA. Development and evaluation of the Adherence to Refills and Medications Scale (ARMS) among low-literacy patients with chronic disease. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2009;12(1):118-23. Epub 2009/11/17. doi: 10.1111/j.1524-4733.2008.00400.x. PubMed PMID: 19911444.
47. Wan LH, Zhao J, Zhang XP, Deng SF, Li L, He SZ, et al. Stroke prevention knowledge and prestroke health behaviors among hypertensive stroke patients in mainland China. The Journal of cardiovascular nursing. 2014;29(2):E1-9. Epub 2013/02/08. doi: 10.1097/JCN.0b013e31827f0ab5. PubMed PMID: 23388703.
48. Voils CI, King HA, Neelon B, Hoyle RH, Reeve BB, Maciejewski ML, et al. Characterizing weekly self-reported antihypertensive medication nonadherence across repeated occasions. Patient preference and adherence. 2014;8:643-50. doi: 10.2147/PPA.S60715. PubMed PMID: 24855340.
49. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res. 1999;47(6):555-67. Epub 2000/02/08. doi: 10.1016/s0022-3999(99)00057-4. PubMed PMID: 10661603.
50. (CAHPS®) CAoHPaS. CAHPS® Clinician & Group Survey - Adult Primary Care Questionnaire 1.0 2009. Available from: https://dirigohealth.maine.gov/Documents/CAHPS%20Adult%20primary%20care%20survey.pdf.
51. Raebel MA, Schmittdiel J, Karter AJ, Konieczny JL, Steiner JF. Standardizing terminology and definitions of medication adherence and persistence in research employing electronic databases. Medical care. 2013;51(8 Suppl 3):S11-S21. doi: 10.1097/MLR.0b013e31829b1d2a. PubMed PMID: 23774515.
52. Logan AG, Milne BJ, Achber C, Campbell WP, Haynes RB. Work-site treatment of hypertension by specially trained nurses. A controlled trial. Lancet (London, England). 1979;2(8153):1175-8. Epub 1979/12/01. doi: 10.1016/s0140-6736(79)92397-3. PubMed PMID: 91901.
53. Webb PA. Effectiveness of patient education and psychosocial counseling in promoting compliance and control among hypertensive patients. The Journal of family practice. 1980;10(6):1047-55. Epub 1980/06/01. PubMed PMID: 7373255.
54. AARDEX. MEMS® Adherence Hardware - MEMS® Cap 2019 [September 30, 2020]. Available from: https://www.aardexgroup.com/solutions/mems-adherence-hardware/.

55. IMC IMC-. eCAP™ ECM 2020 [September 30, 2020]. Available from: https://www.informationmediary.com/nfc-smart-packaging-devices/ecap-smart-pill-bottle/.
56. Inc. A. AdhereTech - How it works 2019 [September 30, 2020]. Available from: https://www.adheretech.com/how-it-works.
57. Health PD. Proteus Discover 2020 [September 30, 2020]. Available from: https://www.proteus.com/discover/.
58. DEVELOPA. The Helping-Hand from Bang & Olufsen Medicom 2020 [September 30, 2020]. Available from: https://developa.dk/projects/helping-hand-bang-olufsen-medicom/.
59. Patel S, Jacobus-Kantor L, Marshall L, Ritchie C, Kaplinski M, Khurana PS, et al. Mobilizing your medications: an automated medication reminder application for mobile phones and hypertension medication adherence in a high-risk urban population. Journal of diabetes science and technology. 2013;7(3):630-9. Epub 2013/06/14. doi: 10.1177/193229681300700307. PubMed PMID: 23759395; PubMed Central PMCID: PMCPMC3869130.
60. Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists. 2003;60(7):657-65. Epub 2003/04/19. doi: 10.1093/ajhp/60.7.657. PubMed PMID: 12701547.
61. Stirratt MJ, Curtis JR, Danila MI, Hansen R, Miller MJ, Gakumo CA. Advancing the Science and Practice of Medication Adherence. Journal of general internal medicine. 2018;33(2):216-22. Epub 2017/12/06. doi: 10.1007/s11606-017-4198-4. PubMed PMID: 29204969; PubMed Central PMCID: PMCPMC5789101.
62. Abughosh S, Wang X, Serna O, Esse T, Mann A, Masilamani S, et al. A Motivational Interviewing Intervention by Pharmacy Students to Improve Medication Adherence. Journal of managed care & specialty pharmacy. 2017;23(5):549-60. Epub 2017/04/28. doi: 10.18553/jmcp.2017.23.5.549. PubMed PMID: 28448784.
63. Rollnick S, Miller W. What is Motivational Interviewing? Behavioural and Cognitive Psychotherapy. 1995;23:325-34. doi: 10.1017/S135246580001643X.
64. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. Journal of consulting and clinical psychology. 1983;51(3):390-5. Epub 1983/06/01. doi: 10.1037//0022-006x.51.3.390. PubMed PMID: 6863699.
65. Andrejak M, Genes N, Vaur L, Poncelet P, Clerson P, Carré A. Electronic pill-boxes in the evaluation of antihypertensive treatment compliance: comparison of once daily versus twice daily regimen. American journal of hypertension. 2000;13(2):184-90. Epub 2000/03/04. doi: 10.1016/s0895-7061(99)00175-2. PubMed PMID: 10701819.
66. Bajorek B, Lemay KS, Magin P, Roberts C, Krass I, Armour CL. Implementation and evaluation of a pharmacist-led hypertension management service in primary care: outcomes and methodological challenges. Pharmacy practice. 2016;14(2):723. Epub 2016/07/07. doi: 10.18549/PharmPract.2016.02.723. PubMed PMID: 27382427; PubMed Central PMCID: PMCPMC4930861.
67. Svarstad B, Bultman D. Remington: the science and practice of pharmacy. The patient: behavioral determinants: Lippincott Williams & Wilkins; 2000.
68. Bosworth HB, Olsen MK, Gentry P, Orr M, Dudley T, McCant F, et al. Nurse administered telephone intervention for blood pressure control: a patient-tailored multifactorial intervention. Patient education and counseling. 2005;57(1):5-14. Epub 2005/03/31. doi: 10.1016/j.pec.2004.03.011. PubMed PMID: 15797147.
69. Eraker SA, Kirscht JP, Becker MH. Understanding and improving patient compliance. Ann Intern Med. 1984;100(2):258-68. Epub 1984/02/01. doi: 10.7326/0003-4819-100-2-258. PubMed PMID: 6362512.
70. Bosworth HB, Olsen MK, Dudley T, Orr M, Goldstein MK, Datta SK, et al. Patient education and provider decision support to control blood pressure in primary care: a cluster randomized trial. American heart journal. 2009;157(3):450-6. Epub 2009/03/03. doi: 10.1016/j.ahj.2008.11.003. PubMed PMID: 19249414.
71. Bosworth HB, Olsen MK, Grubber JM, Neary AM, Orr MM, Powers BJ, et al. Two self-management interventions to improve hypertension control: a randomized trial. Ann Intern Med. 2009;151(10):687-95. Epub 2009/11/19. doi: 10.7326/0003-4819-151-10-200911170-00148. PubMed PMID: 19920269; PubMed Central PMCID: PMCPMC2892337.
72. Buis L, Hirzel L, Dawood RM, Dawood KL, Nichols LP, Artinian NT, et al. Text Messaging to Improve Hypertension Medication Adherence in African Americans From Primary Care and Emergency Department Settings: Results From Two Randomized Feasibility Studies. JMIR mHealth and uHealth. 2017;5(2):e9. Epub 2017/02/06. doi: 10.2196/mhealth.6630. PubMed PMID: 28148474; PubMed Central PMCID: PMCPMC5311421.

73. Becker MH. The Health Belief Model and Sick Role Behavior. Health Education Monographs. 1974;2(4):409-19. doi: 10.1177/109019817400200407.
74. Buis LR, Roberson DN, Kadri R, Rockey NG, Plegue MA, Danak SU, et al. Understanding the Feasibility, Acceptability, and Efficacy of a Clinical Pharmacist-led Mobile Approach (BPTrack) to Hypertension Management: Mixed Methods Pilot Study. J Med Internet Res. 2020;22(8):e19882-e. doi: 10.2196/19882. PubMed PMID: 32780026.
75. Chabot I, Moisan J, Grégoire JP, Milot A. Pharmacist intervention program for control of hypertension. The Annals of pharmacotherapy. 2003;37(9):1186-93. Epub 2003/08/19. doi: 10.1345/aph.1C267. PubMed PMID: 12921497.
76. Lusk SL. Health promotion planning: An educational and environmental approach: Lawrence W. Green and Marshall W. Kreuter Mayfield Publishing, Mountain View, California, 2nd edn. Patient education and counseling. 1992;19(3):298. doi: 10.1016/0738-3991(92)90152-9.
77. de Souza AC, Moreira TM, Oliveira ES, Menezes AV, Loureiro AM, Silva CB, et al. Effectiveness of Educational Technology in Promoting Quality of Life and Treatment Adherence in Hypertensive People. PloS one. 2016;11(11):e0165311. Epub 2016/11/17. doi: 10.1371/journal.pone.0165311. PubMed PMID: 27851752; PubMed Central PMCID: PMCPMC5112805.
78. Dupclay L, Eaddy M, Jackson J, Raju A, Shim A. Real-world impact of reminder packaging on antihypertensive treatment adherence and persistence. Patient Prefer Adherence. 2012;6:499-507. Epub 2012/08/29. doi: 10.2147/ppa.S31417. PubMed PMID: 22927746; PubMed Central PMCID: PMCPMC3422118.
79. Hedegaard U, Kjeldsen LJ, Pottegård A, Henriksen JE, Lambrechtsen J, Hangaard J, et al. Improving Medication Adherence in Patients with Hypertension: A Randomized Trial. The American journal of medicine. 2015;128(12):1351-61. Epub 2015/08/25. doi: 10.1016/j.amjmed.2015.08.011. PubMed PMID: 26302142.
80. Ho CT, Tung YC, Chou SH, Hsiao FC, Lin YS, Chang CJ, et al. Clinical outcomes in hypertensive patients treated with a single-pill fixed-dose combination of renin-angiotensin system inhibitor and thiazide diuretic. J Clin Hypertens (Greenwich). 2018;20(12):1731-8. Epub 2018/10/31. doi: 10.1111/jch.13413. PubMed PMID: 30375168.
81. Kang H, Park HA. A Mobile App for Hypertension Management Based on Clinical Practice Guidelines: Development and Deployment. JMIR mHealth and uHealth. 2016;4(1):e12. Epub 2016/02/04. doi: 10.2196/mhealth.4966. PubMed PMID: 26839283; PubMed Central PMCID: PMCPMC4756253.
82. Ma C, Zhou Y, Zhou W, Huang C. Evaluation of the effect of motivational interviewing counselling on hypertension care. Patient education and counseling. 2014;95(2):231-7. Epub 2014/02/18. doi: 10.1016/j.pec.2014.01.011. PubMed PMID: 24530144.
83. Márquez-Contreras E, Martell-Claros N, Gil-Guillén V, de la Figuera-Von Wichmann M, Casado-Martínez JJ, Martin-de Pablos JL, et al. Efficacy of a home blood pressure monitoring programme on therapeutic compliance in hypertension: the EAPACUM-HTA study. Journal of hypertension. 2006;24(1):169-75. Epub 2005/12/07. doi: 10.1097/01.hjh.0000198023.53859.a2. PubMed PMID: 16331115.
84. Matsumura K, Arima H, Tominaga M, Ohtsubo T, Sasaguri T, Fujii K, et al. Does a combination pill of antihypertensive drugs improve medication adherence in Japanese? A randomized controlled trial. Circulation journal : official journal of the Japanese Circulation Society. 2012;76(6):1415-22. Epub 2012/03/27. doi: 10.1253/circj.cj-11-1481. PubMed PMID: 22447014.
85. McKenney JM, Munroe WP, Wright JT, Jr. Impact of an electronic medication compliance aid on long-term blood pressure control. J Clin Pharmacol. 1992;32(3):277-83. Epub 1992/03/11. doi: 10.1002/j.1552-4604.1992.tb03837.x. PubMed PMID: 1564133.
86. Reminders EM. PRESCRIPT TimeCap Medication Reminder System 2020 [October 15, 2020]. Available from: https://www.epill.com/prescript.html.
87. McManus RJ, Mant J, Franssen M, Nickless A, Schwartz C, Hodgkinson J, et al. Efficacy of self-monitored blood pressure, with or without telemonitoring, for titration of antihypertensive medication (TASMINH4): an unmasked randomised controlled trial. Lancet (London, England). 2018;391(10124):949-59. Epub 2018/03/04. doi: 10.1016/s0140-6736(18)30309-x. PubMed PMID: 29499873; PubMed Central PMCID: PMCPMC5854463.
88. Moorhead P, Zavala A, Kim Y, Virdi NS. Efficacy and safety of a medication dose reminder feature in a digital health offering with the use of sensor-enabled medicines. Journal of the American Pharmacists Association : JAPhA. 2017;57(2):155-61.e1. Epub 2017/02/06. doi: 10.1016/j.japh.2016.12.067. PubMed PMID: 28159505.
89. Morawski K, Ghazinouri R, Krumme A, Lauffenburger JC, Lu Z, Durfee E, et al. Association of a Smartphone Application With Medication Adherence and Blood Pressure Control: The MedISAFE-BP Randomized Clinical Trial.

JAMA internal medicine. 2018;178(6):802-9. Epub 2018/05/02. doi: 10.1001/jamainternmed.2018.0447. PubMed PMID: 29710289; PubMed Central PMCID: PMCPMC6145760.
90. Mounier-Vehier C, Bernaud C, Carré A, Lequeuche B, Hotton JM, Charpentier JC. Compliance and antihypertensive efficacy of amlodipine compared with nifedipine slow-release. American journal of hypertension. 1998;11(4 Pt 1):478-86. Epub 1998/06/02. doi: 10.1016/s0895-7061(97)00485-8. PubMed PMID: 9607387.
91. Odusola A, Nelissen H, Hendriks M, Schultsz C, Wit F, Bolarinwa O, et al. How Group-Based Cardiovascular Health Education Affects Treatment Adherence and Blood Pressure Control among Insured Hypertensive Nigerians: A Pre-Test, Post-Test Study. World Journal of Cardiovascular Diseases. 2015;5:181-98. doi: 10.4236/wjcd.2015.57021.
92. Ogedegbe G, Chaplin W, Schoenthaler A, Statman D, Berger D, Richardson T, et al. A practice-based trial of motivational interviewing and adherence in hypertensive African Americans. American journal of hypertension. 2008;21(10):1137-43. Epub 2008/07/24. doi: 10.1038/ajh.2008.240. PubMed PMID: 18654123.
93. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. The New England journal of medicine. 1997;336(16):1117-24. Epub 1997/04/17. doi: 10.1056/nejm199704173361601. PubMed PMID: 9099655.
94. Tavakoly Sany SB, Behzhad F, Ferns G, Peyman N. Communication skills training for physicians improves health literacy and medical outcomes among patients with hypertension: a randomized controlled trial. BMC Health Services Research. 2020;20(1):60. doi: 10.1186/s12913-020-4901-8.
95. Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. Family medicine. 2004;36(8):588-94. Epub 2004/09/03. PubMed PMID: 15343421.
96. Schneider PJ, Murphy JE, Pedersen CA. Impact of medication packaging on adherence and treatment outcomes in older ambulatory patients. Journal of the American Pharmacists Association : JAPhA. 2008;48(1):58-63. Epub 2008/01/15. doi: 10.1331/JAPhA.2008.07040. PubMed PMID: 18192132.
97. Schoenthaler A, de la Calle F, Pitaro M, Lum A, Chaplin W, Mogavero J, et al. A Systems-Level Approach to Improving Medication Adherence in Hypertensive Latinos: a Randomized Control Trial. Journal of general internal medicine. 2020;35(1):182-9. Epub 2019/10/19. doi: 10.1007/s11606-019-05419-3. PubMed PMID: 31625041; PubMed Central PMCID: PMCPMC6957668.
98. Bodenheimer T, Laing BY. The teamlet model of primary care. Ann Fam Med. 2007;5(5):457-61. doi: 10.1370/afm.731. PubMed PMID: 17893389.
99. Schroeder E, Moore K, Manson S, Baldwin M, Goodrich G, Malone A, et al. A randomized clinical trial of an interactive voice response and text message intervention for individuals with hypertension. The Journal of Clinical Hypertension. 2020. doi: 10.1111/jch.13909.
100. Stewart K, George J, Mc Namara KP, Jackson SL, Peterson GM, Bereznicki LR, et al. A multifaceted pharmacist intervention to improve antihypertensive adherence: a cluster-randomized, controlled trial (HAPPy trial). Journal of clinical pharmacy and therapeutics. 2014;39(5):527-34. Epub 2014/06/20. doi: 10.1111/jcpt.12185. PubMed PMID: 24943987.
101. Svarstad BL, Kotchen JM, Shireman TI, Brown RL, Crawford SY, Mount JK, et al. Improving refill adherence and hypertension control in black patients: Wisconsin TEAM trial. Journal of the American Pharmacists Association : JAPhA. 2013;53(5):520-9. Epub 2013/09/14. doi: 10.1331/JAPhA.2013.12246. PubMed PMID: 24030130; PubMed Central PMCID: PMCPMC4930551.
102. Tu Q, Xiao LD, Ullah S, Fuller J, Du H. A transitional care intervention for hypertension control for older people with diabetes: A cluster randomized controlled trial. Journal of advanced nursing. 2020;76(10):2696-708. doi: 10.1111/jan.14466.
103. Care ICI. The Chronic Care Model 2020 [October 15, 2020]. Available from: http://www.improvingchroniccare.org/index.php?p=The_Chronic_Care_Model&s.
104. van Onzenoort HA, Verberk WJ, Kroon AA, Kessels AG, Nelemans PJ, van der Kuy PH, et al. Effect of self-measurement of blood pressure on adherence to treatment in patients with mild-to-moderate hypertension. Journal of hypertension. 2010;28(3):622-7. Epub 2009/12/03. doi: 10.1097/HJH.0b013e328334f36b. PubMed PMID: 19952780.
105. Varleta P, Acevedo M, Akel C, Salinas C, Navarrete C, García A, et al. Mobile phone text messaging improves antihypertensive drug adherence in the community. J Clin Hypertens (Greenwich). 2017;19(12):1276-84. Epub 2017/09/25. doi: 10.1111/jch.13098. PubMed PMID: 28941056.
106. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. Psychological review. 1977;84 2:191-215.

107. Wang MY, Shen MJ, Wan LH, Mo MM, Wu Z, Li LL, et al. Effects of a Comprehensive Reminder System Based on the Health Belief Model for Patients Who Have Had a Stroke on Health Behaviors, Blood Pressure, Disability, and Recurrence From Baseline to 6 Months: A Randomized Controlled Trial. The Journal of cardiovascular nursing. 2020;35(2):156-64. Epub 2020/01/07. doi: 10.1097/jcn.0000000000000631. PubMed PMID: 31904693.
108. Lewin K. Group decision and social change. 3 ed. Holt RaW, editor. New York1958.
109. Wu JR, Cummings DM, Li Q, Hinderliter A, Bosworth HB, Tillman J, et al. The effect of a practice-based multicomponent intervention that includes health coaching on medication adherence and blood pressure control in rural primary care. J Clin Hypertens (Greenwich). 2018;20(4):757-64. Epub 2018/03/27. doi: 10.1111/jch.13265. PubMed PMID: 29577574; PubMed Central PMCID: PMCPMC5908743.
110. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. Bmj. 2014;348:g1687. Epub 2014/03/13. doi: 10.1136/bmj.g1687. PubMed PMID: 24609605.
111. Breitenstein SM, Gross D, Garvey CA, Hill C, Fogg L, Resnick B. Implementation fidelity in community-based interventions. Res Nurs Health. 2010;33(2):164-73. doi: 10.1002/nur.20373. PubMed PMID: 20198637.
112. Bergeron K, Abdi S, DeCorby K, Mensah G, Rempel B, Manson H. Theories, models and frameworks used in capacity building interventions relevant to public health: a systematic review. BMC Public Health. 2017;17(1):914-. doi: 10.1186/s12889-017-4919-y. PubMed PMID: 29183296.
113. Elwyn G, Frosch D, Thomson R, Joseph-Williams N, Lloyd A, Kinnersley P, et al. Shared decision making: a model for clinical practice. Journal of general internal medicine. 2012;27(10):1361-7. Epub 2012/05/23. doi: 10.1007/s11606-012-2077-6. PubMed PMID: 22618581.
114. Schroeder EB, Moore KR, Manson SM, Baldwin MA, Goodrich GK, Malone AS, et al. A randomized clinical trial of an interactive voice response and text message intervention for individuals with hypertension. The Journal of Clinical Hypertension. 2020;22(7):1228-38. doi: 10.1111/jch.13909.
115. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Med Pharm Rep. 2019;92(2):117-22. Epub 2019/04/25. doi: 10.15386/mpr-1201. PubMed PMID: 31086837.
116. Hawkshead J, Krousel-Wood MA. Techniques for Measuring Medication Adherence in Hypertensive Patients in Outpatient Settings. Disease Management & Health Outcomes. 2007;15(2):109-18. doi: 10.2165/00115677-200715020-00006.

Supplementary Material 1 – Database Search Query

On PubMed:

("hypertension"[Title/Abstract] OR "high blood pressure*"[Title/Abstract] OR "hypertensive"[Title/Abstract] OR "hypertense"[Title/Abstract])

AND

(“intervention*”[Title/Abstract] OR “technolog*”[Title/Abstract] OR “device*”[Title/Abstract] OR “assessment”[Title/Abstract] OR “evaluation”[Title/Abstract] OR “monitoring”[Title/Abstract] OR "follow up"[Title/Abstract] OR “equipment”[Title/Abstract] OR “supplies”[Title/Abstract] OR “apparatus”[Title/Abstract] OR “instruments”[Title/Abstract] OR “control”[Title/Abstract])

AND

("medication adherence"[Title/Abstract] OR "medication compliance"[Title/Abstract] OR "drug compliance"[Title/Abstract] OR "drug discontinuation"[Title/Abstract] OR "drug persistence"[Title/Abstract] OR "medication persistence"[Title/Abstract] OR "patient* compliance"[Title/Abstract] OR "treatment refusal"[Title/Abstract] OR "treatment adherence"[Title/Abstract] OR "treatment compliance"[Title/Abstract] OR "therapy adherence"[Title/Abstract] OR "adherence measure"[Title/Abstract] OR "electronic adherence data"[Title/Abstract] OR "adherence monitor*"[Title/Abstract] OR "incomplete adherence"[Title/Abstract])

On Web of Science:

TS=("hypertension" OR "high blood pressure*" OR "hypertensive" OR "hypertense")

AND

TS=(“intervention*” OR “technolog*” OR “device*” OR “assessment” OR “evaluation” OR “monitoring” OR "follow up" OR “equipment” OR “supplies” OR “apparatus” OR “instruments” OR “control”)

AND

TS=("medication adherence" OR "medication compliance" OR "drug compliance" OR "drug discontinuation" OR "drug persistence" OR "medication persistence" OR "patient* compliance" OR "treatment refusal" OR "treatment adherence" OR "treatment compliance" OR "therapy adherence" OR "adherence measure" OR "electronic adherence data" OR "adherence monitor*" OR "incomplete adherence”

Supplementary Material 2 - Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3,4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	4
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	6
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	5,28 (Supplementary Material 1)
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	6
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	7
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Not applicable (optional)
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7, 8
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	8
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	8
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable (optional)

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	11-17 (Table 2)
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	9, 10
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	18, 19
Limitations	20	Discuss the limitations of the scoping review process.	19
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	20
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	20

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018; 169:467–473. doi: 10.7326/M18-0850.

PREVENTIVE MEDICINE

AUTHOR INFORMATION PACK

TABLE OF CONTENTS

ISSN: 0091-7435

DESCRIPTION

Founded in 1972 by Ernst Wynder, *Preventive Medicine* is an international scholarly journal that publishes original articles on the science and practice of **disease prevention**, **health promotion**, and **public health policymaking**. *Preventive Medicine* aims to reward innovation. It will favor insightful observational studies, thoughtful explorations of health data, unsuspected new angles for existing hypotheses, robust randomized controlled trials, and impartial systematic reviews. *Preventive Medicine's* ultimate goal is to publish research that will have an impact on the work of practitioners of disease prevention and health promotion, as well as of related disciplines.

Preventive Medicine is the companion title to the open access journal Preventive Medicine Reports, which publishes articles that form the building blocks of research in disease prevention and health promotion.

IMPACT FACTOR

2019: 3.788 © Clarivate Analytics Journal Citation Reports 2020

ABSTRACTING AND INDEXING

Scopus

Embase

PubMed/Medline PubMed Central

EDITORIAL BOARD

GUIDE FOR AUTHORS

Your Paper Your Way

We now differentiate between the requirements for new and revised submissions. You may choose to submit your manuscript as a single Word or PDF file to be used in the refereeing process. Only when your paper is at the revision stage, will you be requested to put your paper in to a 'correct format' for acceptance and provide the items required for the publication of your article. **To find out more, please visit the Preparation section below.**

INTRODUCTION

Founded in 1972 by Ernst Wynder, *Preventive Medicine* is an international scholarly journal that provides prompt publication of original articles on the science and practice of disease prevention, health promotion, and public health policymaking. *Preventive Medicine* aims to reward innovation. It will favor insightful observational studies, thoughtful explorations of health data, unsuspected new angles for existing hypotheses, robust randomized controlled trials, and impartial systematic reviews. The ultimate goal of *Preventive Medicine* is to publish research that will have an impact on the work of practitioners of disease prevention and health promotion, as well as of related disciplines.

Types of paper

Article types (maximum number of words in main text) include Original Research Paper (3500 words) or Brief Original Report (maximums: 2000 words, 2 tables or figures, 20 references), Commentary (or Guest Editorial) (1500 words), Review Article (4500 words), Book Review (1000 words), and Letter to the Editor (maximums: 600 words, 1 table or figure, and 10 references). Word count ranges do not include author citations within the text. Abstracts (maximum 250 words) are required for all article types except Letters to the Editor and Book Reviews.

Contact details for submission

Preventive Medicine manuscripts should be submitted using the journal's online submission and review web site, https://www.editorialmanager.com/ypmed/default.aspx.

To use this submission route, please go to the web site and upload your article and its associated artwork. A PDF is generated and the reviewing process is carried out using that PDF. All correspondence between the Editors and the corresponding author is performed on this system. Paper copies are no longer required. However, please note that source files will be required if your paper is accepted.

Contact Information:

Preventive Medicine Editorial Office

Gerald Bronfman Department of Oncology

McGill University

5100 Maisonneuve Blvd West, Suite 720

Montreal, QC, Canada H4A 3T2

For questions regarding manuscript content: prev.med@mcgill.ca

For technical details on manuscript formatting and types of files: pm@elsevier.com For Editorial Manager issues please visit our Support Center.

Submission checklist

You can use this list to carry out a final check of your submission before you send it to the journal for review. Please check the relevant section in this Guide for Authors for more details.

Ensure that the following items are present:

One author has been designated as the corresponding author with contact details:

- E-mail address
- Full postal address

All necessary files have been uploaded:

Manuscript:
- Include keywords
- All figures (include relevant captions)
- All tables (including titles, description, footnotes)
- Ensure all figure and table citations in the text match the files provided
- Indicate clearly if color should be used for any figures in print

Graphical Abstracts / Highlights files (where applicable)
Supplemental files (where applicable)

Further considerations

- Manuscript has been 'spell checked' and 'grammar checked'
- All references mentioned in the Reference List are cited in the text, and vice versa
- Permission has been obtained for use of copyrighted material from other sources (including the Internet)
- Fill out completely and sign the author's declaration form, which contains statement about authorship, conflict of interest, ethics, and funding. Download the form here
- Journal policies detailed in this guide have been reviewed
- Referee suggestions and contact details provided, based on journal requirements

For further information, visit our Support Center.

BEFORE YOU BEGIN

Ethics in publishing

Please see our information pages on Ethics in publishing and Ethical guidelines for journal publication.

Studies in humans and animals

If the work involves the use of human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The manuscript should be in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals and aim for the inclusion of representative human populations (sex, age and ethnicity) as per those recommendations. The terms sex and gender should be used correctly.

Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

All animal experiments should comply with the ARRIVE guidelines and should be carried out in accordance with the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, EU Directive 2010/63/EU for animal experiments, or the National Institutes of Health guide for the care and use of Laboratory animals (NIH Publications No. 8023, revised 1978) and the authors should clearly indicate in the manuscript that such guidelines have been followed. The sex of animals must be indicated, and where appropriate, the influence (or association) of sex on the results of the study.

Declaration of competing interest

All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/ registrations, and grants or other funding. Authors should complete the declaration of competing interest statement using this template and upload to the submission system at the Attach/Upload Files step. **Note: Please do not convert the .docx template to another file type. Author signatures are not required.** If there are no interests to declare, please choose the first option in the template. This statement will be published within the article if accepted. More information.

Submission declaration and verification

Submission of an article implies that the work described has not been published previously (except in the form of an abstract, a published lecture or academic thesis, see 'Multiple, redundant or concurrent publication' for more information), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyrightholder. To verify originality, your article may be checked by the originality detection service Crossref Similarity Check.

Preprints

Please note that preprints can be shared anywhere at any time, in line with Elsevier's sharing policy. Sharing your preprints e.g. on a preprint server will not count as prior publication (see 'Multiple, redundant or concurrent publication' for more information).

Use of inclusive language

Inclusive language acknowledges diversity, conveys respect to all people, is sensitive to differences, and promotes equal opportunities. Content should make no assumptions about the beliefs or commitments of any reader; contain nothing which might imply that one individual is superior to another on the grounds of age, gender, race, ethnicity, culture, sexual orientation, disability or health condition; and use inclusive language throughout. Authors should ensure that writing is free from bias, stereotypes, slang, reference to dominant culture and/or cultural assumptions. We advise to seek gender neutrality by using plural nouns ("clinicians, patients/clients") as default/wherever possible to avoid using "he, she," or "he/she." We recommend avoiding the use of descriptors that refer to personal attributes such as age, gender, race, ethnicity, culture, sexual orientation, disability or health condition unless they are relevant and valid. These guidelines are meant as a point of reference to help identify appropriate language but are by no means exhaustive or definitive.

Author contributions

For transparency, we encourage authors to submit an author statement file outlining their individual contributions to the paper using the relevant CRediT roles: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing. Authorship statements should be formatted with the names of authors first and CRediT role(s) following. More details and an example

Changes to authorship

Authors are expected to consider carefully the list and order of authors **before** submitting their manuscript and provide the definitive list of authors at the time of the original submission. Any addition, deletion or rearrangement of author names in the authorship list should be made only **before** the manuscript has been accepted and only if approved by the journal Editor. To request such a change, the Editor must receive the following from the

corresponding author: (a) the reason for the change in author list and (b) written confirmation (e-mail, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors, this includes confirmation from the author being added or removed.

Only in exceptional circumstances will the Editor consider the addition, deletion or rearrangement of authors **after** the manuscript has been accepted. While the Editor considers the request, publication of the manuscript will be suspended. If the manuscript has already been published in an online issue, any requests approved by the Editor will result in a corrigendum.

Clinical trial results

In line with the position of the International Committee of Medical Journal Editors, the journal will not consider results posted in the same clinical trials registry in which primary registration resides to be prior publication if the results posted are presented in the form of a brief structured (less than 500 words) abstract or table. However, divulging results in other circumstances (e.g., investors' meetings) is discouraged and may jeopardise consideration of the manuscript. Authors should fully disclose all posting in registries of results of the same or closely related work.

Reporting clinical trials

All randomised controlled trials submitted for publication should include a completed Consolidated Standards of Reporting Trials (CONSORT) flow chart and checklist. Please refer to the CONSORT statement website at http://www.consort-statement.org for more information. This journal has adopted the proposal from the International Committee of Medical Journal Editors (ICMJE) which require, as a condition of consideration for publication of clinical trials, registration in a public trials registry. Trials must register at or before the onset of patient enrolment. The clinical trial registration number should be included at the end of the abstract of the article. For this purpose, a clinical trial is defined as any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects of health outcomes. Healthrelated interventions include any intervention used to modify a biomedical or health-related outcome (for example drugs, surgical procedures, devices, behavioural treatments, dietary interventions, and process-of-care changes). Health outcomes include any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events. Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) will not require registration. Further information can be found at http://www.icmje.org.

Article transfer service

This journal is part of our Article Transfer Service. This means that if the Editor feels your article is more suitable in one of our other participating journals, then you may be asked to consider transferring the article to one of those. If you agree, your article will be transferred automatically on your behalf with no need to reformat. Please note that your article will be reviewed again by the new journal. More information.

Copyright

Upon acceptance of an article, authors will be asked to complete a 'Journal Publishing Agreement' (see more information on this). An e-mail will be sent to the corresponding author confirming receipt of the manuscript together with a 'Journal Publishing Agreement' form or a link to the online version of this agreement.

Subscribers may reproduce tables of contents or prepare lists of articles including abstracts for internal circulation within their institutions. Permission of the Publisher is required for resale or distribution outside the institution and for all other derivative works, including compilations and translations. If excerpts from other copyrighted works are included, the author(s) must obtain written permission from the copyright owners and credit the source(s) in the article. Elsevier has preprinted forms for use by authors in these cases.

For gold open access articles: Upon acceptance of an article, authors will be asked to complete a 'License Agreement' (more information). Permitted third party reuse of gold open access articles is determined by the author's choice of user license.

Author rights

As an author you (or your employer or institution) have certain rights to reuse your work. More information.

Elsevier supports responsible sharing

Find out how you can share your research published in Elsevier journals.

Role of the funding source

You are requested to identify who provided financial support for the conduct of the research and/or preparation of the article and to briefly describe the role of the sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. If the funding source(s) had no such involvement then this should be stated.

Open access

Please visit our Open Access page for more information.

Language (usage and editing services)

Please write your text in good English (American or British usage is accepted, but not a mixture of these). Authors who feel their English language manuscript may require editing to eliminate possible grammatical or spelling errors and to conform to correct scientific English may wish to use the English Language Editing service available from Elsevier's Author Services.

Submission

Our online submission system guides you stepwise through the process of entering your article details and uploading your files. The system converts your article files to a single PDF file used in the peer-review process. Editable files (e.g., Word, LaTeX) are required to typeset your article for final publication. All correspondence, including notification of the Editor's decision and requests for revision, is sent by e-mail.

PREPARATION

NEW SUBMISSIONS

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts your files to a single PDF file, which is used in the peer-review process.

As part of the Your Paper Your Way service, you may choose to submit your manuscript as a single file to be used in the refereeing process. This can be a PDF file or a Word document, in any format or layout that can be used by referees to evaluate your manuscript. It should contain high enough quality figures for refereeing. If you prefer to do so, you may still provide all or some of the source files at the initial submission. Please note that individual figure files larger than 10 MB must be uploaded separately.

References

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/ book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

Formatting requirements

There are no strict formatting requirements but all manuscripts must contain the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions.

If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes. Divide the article into clearly defined sections.

Figures and tables embedded in text

Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file. The corresponding caption should be placed directly below the figure or table.

Peer review

This journal operates a single anonymized review process. All contributions will be initially assessed by the editor for suitability for the journal. Papers deemed suitable are then typically sent to a minimum of two independent expert reviewers to assess the scientific quality of the paper. The Editor is responsible for the final decision regarding acceptance or rejection of articles. The Editor's decision is final. Editors are not involved in decisions about papers which they have written themselves or have been written by family members or colleagues or which relate to products or services in which the editor has an interest. Any such submission is subject to all of the journal's usual procedures, with peer review handled independently of the relevant editor and their research groups. More information on types of peer review.

REVISED SUBMISSIONS

Use of word processing software

Regardless of the file format of the original submission, at revision you must provide us with an editable file of the entire article. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier). See also the section on Electronic artwork.

To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

LaTeX

You are recommended to use the Elsevier article class elsarticle.cls to prepare your manuscript and BibTeX to generate your bibliography.

Our LaTeX site has detailed submission instructions, templates and other information.

Article structure

Please include appropriate Cover Letter. The Title Page should include the usual - title, authors' names and affiliations, the corresponding author's name and e-mail address - as well as the word counts of the main text and abstract (word count excludes in-text citations and references). Text should be 1.5 line-spaced. Do not use footnotes in the text.

If your article is about a Randomised Controlled Trial be sure to upload a CONSORT checklist with your submission, add the trial registration number to the end of the abstract, and include a CONSORT flow chart as one of the figures in the paper. If your article is a Systematic Review of the literature please follow the PRISMA guidelines at http://www.prisma-statement.org/ and include the required content in your manuscript.

Subdivision

Main headings are Introduction, Methods, Results, Discussion, and Conclusion.

Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Methods

Provide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference: only relevant modifications should be described. The Methods section should include a separate, second-level subsection, Statistical analyses (if applicable), which concisely describes the statistical methodology.

Experimental

Provide sufficient details to allow the work to be reproduced by an independent researcher. Methods that are already published should be summarized, and indicated by a reference. If quoting directly from a previously

published method, use quotation marks and also cite the source. Any modifications to existing methods should also be described.

Theory/calculation
A Theory section should extend, not repeat, the background to the article already dealt with in the Introduction and lay the foundation for further work. In contrast, a Calculation section represents a practical development from a theoretical basis.

Results
Results should be clear and concise.

Discussion
This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature. In this section, a second-level subsection entitled Study limitations and strengths is strongly encouraged.

Conclusions
The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

Appendices
If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

- ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.
- ***Author names and affiliations.*** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. You can add your name between parentheses in your own script behind the English transliteration. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lowercase superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.
- ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**
- ***Present/permanent address.*** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

Highlights

Highlights are mandatory for this journal as they help increase the discoverability of your article via search engines. They consist of a short collection of bullet points that capture the novel results of your research as well as new methods that were used during the study (if any). Please have a look at the examples here: example Highlights.

Highlights should be submitted in a separate editable file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point).

Abstract

An un-structured abstract of 250 words or less must be part of all types of papers, except Letters to the Editor and Book Reviews. Abstracts should include sample sizes and the location of the study and the time when it was conducted. Any acronyms should be spelled out the first time they are used in the Abstract.

Abbreviations

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

Formatting of funding sources

List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Units

Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

Math formulae

Please submit math equations as editable text and not as images. Present simple formulae in line with normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, e.g., X/Y. In principle, variables are to be presented in italics. Powers of e are often more conveniently denoted by exp. Number consecutively any equations that have to be displayed separately from the text (if referred to explicitly in the text).

Footnotes

Footnotes should be used sparingly. Number them consecutively throughout the article. Many word processors build footnotes into the text, and this feature may be used. Should this not be the case, indicate the position of footnotes in the text and present the footnotes themselves separately at the end of the article.

Electronic artwork General points

- Make sure you use uniform lettering and sizing of your original artwork.
- Preferred fonts: Arial (or Helvetica), Times New Roman (or Times), Symbol, Courier.
- Number the illustrations according to their sequence in the text.
- Use a logical naming convention for your artwork files.
- Indicate per figure if it is a single, 1.5 or 2-column fitting image.
- For Word submissions only, you may still provide figures and their captions, and tables within asingle file at the revision stage.
- Please note that individual figure files larger than 10 MB must be provided in separate source files.

A detailed guide on electronic artwork is available.

You are urged to visit this site; some excerpts from the detailed information are given here. *Formats*

Regardless of the application used, when your electronic artwork is finalized, please 'save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings. Embed the font or save the text as 'graphics'.

TIFF (or JPG): Color or grayscale photographs (halftones): always use a minimum of 300 dpi.

TIFF (or JPG): Bitmapped line drawings: use a minimum of 1000 dpi.

TIFF (or JPG): Combinations bitmapped line/half-tone (color or grayscale): a minimum of 500 dpi is required.

Please do not:

- Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); the resolution is too low.
- Supply files that are too low in resolution.
- Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version. **For color reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article**. Please indicate your preference for color: in print or online only. Further information on the preparation of electronic artwork.

Figure captions

Ensure that each illustration has a caption. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Text graphics

Text graphics may be embedded in the text at the appropriate position. If you are working with LaTeX and have such features embedded in the text, these can be left. See further under Electronic artwork.

Tables

Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text. Place footnotes to tables below the table body and indicate them with superscript lowercase letters. Avoid vertical rules. Be sparing in the use of tables and ensure that the data presented in tables do not duplicate results described elsewhere in the article.

Tables should be short, single-spaced and begin on a separate page. Table legends should provide details on the location and date of the study, and the study population (if applicable). The aim of presenting tables results is not only to show adjusted effects but also to enable readers to understand the methods used, evaluate the results, and potentially integrate them into meta-analyses. Thus, presentation of sufficient detail in tables to permit readers to compute crude (unadjusted) effects is strongly encouraged. (For example, adjusted odds ratios should also be accompanied by subgroup sample sizes or percentages for each variable included in the model.)

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of

the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Reference links

Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the DOI is highly encouraged.

A DOI is guaranteed never to change, so you can use it as a permanent link to any electronic article. An example of a citation using DOI for an article not yet in an issue is: VanDecar J.C., Russo R.M., James D.E., Ambeh W.B., Franke M. (2003). Aseismic continuation of the Lesser Antilles slab beneath northeastern Venezuela. Journal of Geophysical Research, https://doi.org/10.1029/2001JB000884. Please note the format of such citations should be in the same style as all other references in the paper.

Web references

As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

Data references

This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

Reference to arXiv

As with unpublished results and personal communications, references to arXiv documents are not recommended in the reference list. Please make every effort to obtain the full reference of the published version of an arXiv document. If a reference to an arXiv document must be included in the references list it should follow the standard reference style of the journal and should include a substitution of the volume and page numbers with 'arXiv:YYMM.NNNN' or 'arXiv:arch-ive/YYMMNNN' for articles submitted to arXiv before April 2007.

References in a special issue

Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

Reference management software

Most Elsevier journals have their reference template available in many of the most popular reference management software products. These include all products that support Citation Style Language styles, such as Mendeley. Using citation plug-ins from these products, authors only need to select the appropriate journal template when preparing their article, after which citations and bibliographies will be automatically formatted in the journal's style. If no template is yet available for this journal, please follow the format of the sample references and citations as shown in this Guide. If you use reference management software, please ensure that you remove all field codes before submitting the electronic manuscript. More information on how to remove field codes from different reference management software.

Reference management software

This journal has standard templates available in key reference management packages EndNote (http://www.endnote.com/support/enstyles.asp) and Reference Manager (http://refman.com/support/rmstyles.asp). Using plug-ins to word processing packages, authors only need to select the appropriate journal template when

preparing their article and the list of references and citations to these will be formatted according to the journal style which is described above.

Users of Mendeley Desktop can easily install the reference style for this journal by clicking the following link:

http://open.mendeley.com/use-citation-style/preventive-medicine

When preparing your manuscript, you will then be able to select this style using the Mendeley plugins for Microsoft Word or LibreOffice.

Reference formatting

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/ book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct. If you do wish to format the references yourself they should be arranged according to the following examples:

Journal abbreviations source

Journal names should be abbreviated according to the List of Title Word Abbreviations.

Data visualization

Include interactive data visualizations in your publication and let your readers interact and engage more closely with your research. Follow the instructions here to find out about available data visualization options and how to include them with your article.

Supplementary material

Supplementary material such as applications, images and sound clips, can be published with your article to enhance it. Submitted supplementary items are published exactly as they are received (Excel or PowerPoint files will appear as such online). Please submit your material together with the article and supply a concise, descriptive caption for each supplementary file. If you wish to make changes to supplementary material during any stage of the process, please make sure to provide an updated file. Do not annotate any corrections on a previous version. Please switch off the 'Track Changes' option in Microsoft Office files as these will appear in the published version.

Research data

This journal encourages and enables you to share data that supports your research publication where appropriate, and enables you to interlink the data with your published articles. Research data refers to the results of observations or experimentation that validate research findings. To facilitate reproducibility and data reuse, this journal also encourages you to share your software, code, models, algorithms, protocols, methods and other useful materials related to the project.

Below are a number of ways in which you can associate data with your article or make a statement about the availability of your data when submitting your manuscript. If you are sharing data in one of these ways, you are encouraged to cite the data in your manuscript and reference list. Please refer to the "References" section for more information about data citation. For more information on depositing, sharing and using research data and other relevant research materials, visit the research data page.

Data linking

If you have made your research data available in a data repository, you can link your article directly to the dataset. Elsevier collaborates with a number of repositories to link articles on ScienceDirect with relevant repositories, giving readers access to underlying data that gives them a better understanding of the research described.

There are different ways to link your datasets to your article. When available, you can directly link your dataset to your article by providing the relevant information in the submission system. For more information, visit the database linking page.

For supported data repositories a repository banner will automatically appear next to your published article on ScienceDirect.

In addition, you can link to relevant data or entities through identifiers within the text of your manuscript, using the following format: Database: xxxx (e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN).

Mendeley Data
This journal supports Mendeley Data, enabling you to deposit any research data (including raw and processed data, video, code, software, algorithms, protocols, and methods) associated with your manuscript in a free-to-use, open access repository. During the submission process, after uploading your manuscript, you will have the opportunity to upload your relevant datasets directly to *Mendeley Data*. The datasets will be listed and directly accessible to readers next to your published article online.

For more information, visit the Mendeley Data for journals page.

Data statement
To foster transparency, we encourage you to state the availability of your data in your submission. This may be a requirement of your funding body or institution. If your data is unavailable to access or unsuitable to post, you will have the opportunity to indicate why during the submission process, for example by stating that the research data is confidential. The statement will appear with your published article on ScienceDirect. For more information, visit the Data Statement page.

AFTER ACCEPTANCE

Online proof correction

To ensure a fast publication process of the article, we kindly ask authors to provide us with their proof corrections within two days. Corresponding authors will receive an e-mail with a link to our online proofing system, allowing annotation and correction of proofs online. The environment is similar to MS Word: in addition to editing text, you can also comment on figures/tables and answer questions from the Copy Editor. Web-based proofing provides a faster and less error-prone process by allowing you to directly type your corrections, eliminating the potential introduction of errors.

If preferred, you can still choose to annotate and upload your edits on the PDF version. All instructions for proofing will be given in the e-mail we send to authors, including alternative methods to the online version and PDF.

We will do everything possible to get your article published quickly and accurately. Please use this proof only for checking the typesetting, editing, completeness and correctness of the text, tables and figures. Significant changes to the article as accepted for publication will only be considered at this stage with permission from the Editor. It is important to ensure that all corrections are sent back to us in one communication. Please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility.

Offprints

The corresponding author will, at no cost, receive a customized Share Link providing 50 days free access to the final published version of the article on ScienceDirect. The Share Link can be used for sharing the article via any communication channel, including email and social media. For an extra charge, paper offprints can be ordered via the offprint order form which is sent once the article is accepted for publication. Both corresponding and co-authors may order offprints at any time via Elsevier's Author Services. Corresponding authors who have published their article gold open access do not receive a Share Link as their final published version of the article is available open access on ScienceDirect and can be shared through the article DOI link.

AUTHOR INQUIRIES

Visit the Elsevier Support Center to find the answers you need. Here you will find everything from Frequently Asked Questions to ways to get in touch.

You can also check the status of your submitted article or find out when your accepted article will be published.

Appeal Procedure

Rejection notices are always unpleasant. Although of no consolation to authors, such decisions are also a difficult part in an editor?s job. Peer review is an imperfect process but remains the best approach to adjudicate what should be placed in the public domain. We pride ourselves at Preventive Medicine in making a good effort at identifying reviewers with content and methodological expertise for every manuscript that we send out for external evaluation. Editors reach a decision with much more information at their disposal than is apparent in the critiques that they forward to authors. Reviewers also write confidential information to editors and rate a manuscript based on additional items, such as priority, relevance, calibre of the science, perceived validity, length, and credit given to others. Authors do not see this part of the critique and may mistakenly assume that the written narrative they received is all that the editors had to reach a decision. But infelicitous editorial decisions can happen.

Reviewers often disagree on what they liked or disliked about a paper. In consequence, editors must adjudicate between opposing camps, which may end up penalizing authors with a reject decision for an article with valid scientific findings. We would welcome to hear from authors who felt that we unjustly rejected their work. Appeal letters addressed to the editor should be sent to prev.med@mcgill.ca. They should contain the reasons why our decision should be overturned, including rebuttals to specific comments made by reviewers and/or editors. We will endeavour to reply to appeal letters within 72 hours.