UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE MEDICINA

PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE:

CARDIOLOGIA E CIÊNCIAS CARDIOVASCULARES

TESE DE DOUTORADO

PREVALÊNCIA DE HIPERTENSÃO ARTERIAL SISTÊMICA NO BRASIL E MANEJO USUAL DA DOENÇA NA ATENÇÃO PRIMÁRIA

RAFAEL DA VEIGA CHAVES PICON

Orientadora: Prof.ª Dr.ª Sandra Costa Fuchs

Porto Alegre, dezembro de 2012

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"... je n'eusse pas cru me devoir contenter des opinions d'autrui un seul moment, si je ne me fusse proposé d'employer mon propre jugement à les examiner lorsqu'il serait temps;..."

"... eu não acreditaria dever contentar-me com as opiniões de outrem um só momento, se não tivesse me proposto a empregar meu próprio juízo em examiná-las quando fosse apropriado;..."

Discurso do método

René Descartes (1596–1650)

À minha mãe, Patrícia, por seu infinito amor, carinho e dedicação aos seus filhos, por impulsionar-nos a fazer mais e melhor, pelo exemplo de ética, competência, determinação e pelo modelo de enfrentamento das perdas e percalços da vida.

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LISTA DE ABREVIATURAS

95% CI: *95% confidence interval*

ACCOMPLISH: *Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension*

AES: avaliações econômicas em saúde

AIT: ataque isquêmico transitório

ALLHAT: *Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial*

ARR: aumento de risco relativo

ATS: avaliação de tecnologias em saúde

AVE: acidente vascular encefálico

BB: β-bloqueador(es)

BCC: bloqueador(es) do canal de cálcio

BP: *blood pressure*

BRA: bloqueador(es) do receptor de angiotensina

CVD: *cardiovascular disease*

DAC: doença arterial coronariana

DASH: *Dietary Approaches to Stop Hypertension*

DBH: Diretrizes Brasileiras de Hipertensão

DCV: doença(s) cardiovascular(es)

DM: *diabetes mellitus*

ECR(s): ensaio(s) clínico(s) randomizado(s)

HAS: hipertensão arterial sistêmica

HCT: hidroclorotiazida

HEE: *health economic evaluation(s)*

HT: *hypertension*

IAM: infarto agudo do miocárdio

IC 95%: intervalo de confiança de 95%

ICC: insuficiência cardíaca congestiva

IECA: inibidor(es) da enzima de conversão da angiotensina

IV-DBH: IV Diretrizes Brasileiras de Hipertensão Arterial

JNC: *Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure*

JNC-7: *The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure*

MAPA: monitorização ambulatorial de pressão arterial

MEV: modificação do estilo de vida

NNT: número necessário para tratar

PA: pressão arterial

PAD: pressão arterial diastólica

PAS: pressão arterial sistólica

PNAD: Pesquisa Nacional por Amostra de Domicílios

PROGRESS: *Perindopril Protection Against Recurrent Stroke Study*

PSF: Programa Saúde da Família

RR: risco relativo

RRR: redução de risco relativo

SHEP: *Systolic Hypertension in the Elderly Program*

SD: standard deviation

SQ: *status quo*

SUS: Sistema Único de Saúde

VI-DBH: VI Diretrizes Brasileiras de Hipertensão

VIGITEL: Vigilância para Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico

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RESUMO EM PORTUGUÊS

Introdução

Hipertensão arterial sistêmica (HAS) é atualmente definida pela média de pressão arterial (PA) de consultório maior ou igual a 140/90 mmHg em ao menos duas aferições realizadas em duas ou mais consultas. É conhecido fator de risco para doença cardiovascular, explicando cerca de metade dos casos de acidente vascular encefálico e de doença arterial coronariana. Também é notório contundente o acúmulo de evidências que apontam para correlação positiva entre os níveis pressóricos arteriais e o risco para eventos cardiovasculares.

Estimativas internacionais revelam o aumento na prevalência de HAS no mundo, apesar de, paradoxalmente, ter ocorrido aparente redução na média de PA sistólica nas últimas décadas. Segundo projeções publicadas, até 2025, 1,17 bilhão de pessoas serão portadoras de HAS, sendo que três quartos delas viverão em países em desenvolvimento e os idosos serão os mais acometidos. Mesmo assim, há carência de dados de prevalência da doença no mundo em desenvolvimento, inclusive no Brasil, e, sobretudo entre os idosos. Em nosso país, não existem estudos com amostras representativas da nação que tenham avaliado a frequência de HAS por meio de aferição de PA.

O impacto da HAS sobre a saúde da população e seus desdobramentos econômicos, apesar de serem, presumivelmente, substanciais, nunca foram estimados de forma ampla assumindo a perspectiva do Sistema Único de Saúde (SUS). Existem estimações de custos diretos associados ao tratamento farmacológico da doença, provenientes de raras avaliações econômicas realizadas e de bancos de dados administrativos como o DATASUS. No

entanto, as próprias análises de custo-efetividade se limitam ao estudo da eficiência do tratamento medicamentoso no controle ou redução da PA. Não há, portanto, conhecimento, no cenário nacional, a respeito da custo-efetividade das diferentes intervenções disponíveis no tratamento da HAS sobre prevenção de doença cardiovascular ou morte. Também não se conhece em profundidade o *status quo* do tratamento da HAS na atenção primária brasileira, ou seja, as práticas usualmente empregadas no manejo ambulatorial dos pacientes hipertensos atendidos pelo SUS. O *status quo* é o caso-base contra o qual, idealmente, nas tecnologias ou programas de saúde deveriam ser comparados antes de se decidir pela sua incorporação, ou não, no Sistema.

As dificuldades normalmente encontradas durante a realização de avaliações econômicas em saúde – instrumento de pesquisa maior das avaliações de tecnologia em saúde – costumam ser fruto não do excesso, mas da escassez de informações necessárias para condução dessas análises. Com isso em mente, o presente trabalho pretende auxiliar na ampliação do conhecimento de parâmetro indispensável para o planejamento em saúde pública e estimativa de ônus econômico da HAS: a prevalência de doença; e ainda traçar um panorama da real assistência dispensada aos indivíduos hipertensos no âmbito da atenção primária brasileira.

Métodos

Três revisões sistemáticas foram delineadas para responder as seguintes questões de pesquisa: i) qual a prevalência nacional de HAS em adultos e o comportamento da mesma

nos últimos 30 anos? i) qual a prevalência nacional de HAS em idosos? iii) como os hipertensos são usualmente manejados na atenção primária brasileira?

Foram empregadas as bases de dados do PubMed, Embase, Biblioteca Virtual em Saúde, LILACS, Scielo e o Banco de Teses da CAPES. Busca manual entre as referências dos artigos encontrados e busca por trabalhos publicados em congressos nacionais de cardiologia também foram realizadas. Não se aplicou nenhuma restrição de língua.

Estudos de coorte ou transversais de base populacional, realizados a partir de 1980 e realizados em amostras probabilísticas eram elegíveis para as análises. Para o estudo do manejo usual da HAS na atenção primária, trabalhos conduzidos com amostras oriundas de Unidades Básicas de Saúde e centros de referência ligados ao SUS também foram incluídos.

Para as meta-análises, foi utilizado modelo de efeitos aleatórios. Meta-regressão foi usada para avaliar o comportamento da prevalência de HT ao longo do tempo.

Resultados

A prevalência de hipertensão arterial pelos critérios do JNC (BP ≥140/90 mmHg) em 1980, 1990 e 2000 foram 36,1 (IC 95% 28,7–44,2), 32,9% (29,9–36,0%) e 28,7% (26,2 – 31,4%), respectivamente (P <0,001). Em 2000, as estimativas de prevalência por autorrelato de hipertensão em inquéritos telefônicos foi de 20,6% (19,0–22,4%) e em inquéritos domiciliares foi de 25,2% (23,3–27,2%).

Entre os idosos, a prevalência de HT para o período de 1980 a 2010, segundo os critérios JNC, foi 68,0% (65,1–69,4%). Em 2000, a prevalência pelos mesmos critérios foi de

68,9% (64.1–73.3%). Prevalência autorreferida através de visitas domiciliares foi 49,9% (46,8–51,2%) e por meio de inquéritos telefônicos foi 53,8% (44,8–62,6%).

Indivíduos hipertensos tinham em média 2,6 consultas médicas por ano e metade afirmou ter usado os serviços do SUS na maioria das vezes. Três quartos estavam usando ao menos um anti-hipertensivo e um terço dos indivíduos estavam em uso de duas medicações. Diuréticos tiazídicos (18,2%) e inibidores de enzima conversora de angiotensina (16,2%) foram os medicamentos mais frequentemente utilizados em monoterapia e combinados um com o outro (14,9%). Aproximadamente um terço dos hipertensos foram submetidos a medidas de colesterol total, triglicerídeos, glicemia de jejum e creatinina sérica nos últimos 12 meses. Fumantes representaram 21,7% de indivíduos com hipertensão e 13,5% de hipertensos eram também diabéticos.

Conclusões

A prevalência de HAS no Brasil parece ter diminuído 6% nas últimas três décadas, mas ainda é aproximadamente 30%. Prevalência de hipertensão arterial é elevada entre os idosos, e há considerável subestimação da prevalência da doença através de avaliações por autorrelato. Nossa meta-análise foi uma maneira alternativa para estabelecer a prevalência de HAS no Brasil, é necessária para avaliar o ônus da doença e implantar programas de saúde custo-efetivos. No entanto, estudo de prevalência com amostra representativa nacional é necessário para confirmar as estimativas e determinar prevalências mais precisas para populações específicas.

Mais informações sobre manejo de hipertensão dentro da configuração brasileira de atenção primária são necessárias. No entanto, nossa revisão alcançou seus objetivos de descrever aspectos relevantes da atenção primária usual no Brasil. Futuras avaliações econômicas são necessárias para analisar a custo-efetividade de futuras de diretrizes clínicas frente ao *status quo*.

ABSTRACT IN ENGLISH

Introduction

Hypertension (HT) is currently defined by the mean office blood pressure (BP) of 140/90 mmHg or greater in at least two measurements made in two or more visits. It is known risk factor for cardiovascular disease (CVD), explaining about half of the cases of stroke and coronary artery disease. There is also a considerable body of evidence pointing to positive correlation between BP levels and the risk for cardiovascular events.

International estimates reveal an increase in prevalence of HT in the world, although, paradoxically, there has been apparent reduction in average systolic BP in recent decades. According to published projections, until 2025, 1.17 billion people will have high blood pressure, three-quarters of those with HT will be living in developing countries, and the elderly will be the most affected. Even so, there is a lack of data on prevalence of the disease in the developing world, including in Brazil, and especially among the elderly. In our country, there are no studies with representative samples of the nation that have assessed the prevalence of HT through BP measurements.

The impact of HT over the health of our population and its economic consequences, even though they are, presumably, substantial, were never broadly evaluated assuming the perspective of the Brazilian Unified Health System (SUS). There are estimates of direct costs associated with the pharmacological treatment of the disease from rare economic evaluations and administrative databases as the DATASUS. However, cost-effectiveness analyses were limited to the assessment of the efficiency of the medical therapy over BP reduction or control. Therefore there is no information, on a national basis, regarding the cost-effectiveness of various available interventions for HT treatment on CVD prevention and

mortality. Also, there is no in-depth knowledge of the *status quo* of HT treatment in primary care, that is, the standard of care usually provided by the SUS in the outpatient management HT. The *status quo* is the base-case scenario against which, ideally, any new technology or health program should be compared before deciding for its incorporation, or not, into the healthcare system.

The difficulties frequently encountered during the undertaken of health economic evaluations – the main research tool for health technology assessments – are the result not of excess, but of scarcity of information necessary to carry these analyses. Bearing that in mind, the present work aims to assist in the expansion of knowledge of an essential parameter for public health planning and economic burden of disease estimation: the prevalence of HT; and still, draw a panorama of the real assistance provided to hypertensive subjects within the framework of primary health care.

Methods

Three systematic reviews were outlined to answer the following research questions: i) what is the national prevalence HT in adults and the trends of this prevalence over the last 30 years? i) what is the national prevalence of HT among the elderly? iii) how the hypertensive patients are usually managed in the primary care setting in Brazil?

The PubMed, Embase, Virtual Health Library, LILACS, Scielo, and the CAPES Theses databases were employed for searches. Manual search inside references of the articles and search for works published in national cardiology meetings also were held. We did not apply any language restriction.

Population-based cohort or cross-sectional studies with probabilistic samples were eligible for the analyses. For the usual management HAS in primary care study, works carried-out on samples from primary health units or reference centers affiliated to the SUS were also included.

For the meta-analyses, random effects model was used. Meta-regression was used to evaluate the trends of HT prevalence over time.

Results

The prevalence of hypertension by the JNC criteria (BP ≥140/90 mmHg) in the 1980's, 1990's and 2000's were 36.1% (95% CI 28.7–44.2%), 32.9% (29.9–36.0%), and 28.7% (26.2 – 31.4%), respectively (P <0.001). In the 2000's, the pooled prevalence estimates of self-reported hypertension on telephone inquiries was 20.6% (19.0–22.4%), and of self-reported hypertension in home surveys was 25.2% (23.3–27.2%).

Among the elderly, the prevalence of HT for the period from 1980 to 2010, according to the JNC criteria, was 68.0% (95% CI 65.1%–69.4%). In the 2000's, prevalence following the same criteria was 68.9% (95% CI 64.1%–73.3%), whereas self-reported prevalence through household surveys was 49.0% (95% CI 46.8%–51.2%) and through telephone surveys was 53.8% (95% CI 44.8%–62.6%).

Hypertensive individuals had on average 2.6 medical appointments per year and half stated using the Brazilian public healthcare services most of the time. Three quarters were using al least one blood pressure medication and a third of individuals were in use of two drugs. Thiazide type diuretics (18.2%) and angiotensin-converting enzyme inhibitors (16.2%) were the most often used medications in single-drug therapy and combined with each other

(14.9%). Approximately one third of hypertensives were tested for total serum cholesterol, triglycerides, fasting plasma glucose, and serum creatinine in the last 12 months. Current smokers accounted for 21.7% of subjects with hypertension and 13.5% of hypertensives were also diabetics.

Conclusions

The prevalence of hypertension in Brazil seems to have diminished 6% in the last three decades, but it still is approximately 30%. Prevalence of hypertension is high among the elderly and there is considerable underestimation of disease prevalence through self-reported estimates. Our meta-analysis was an alternative way to establishing the hypertension prevalence in Brazil, which is necessary to assess the hypertension burden and to implement cost-effective interventions. Nonetheless, a nationwide prevalence study is still needed to confirm the estimates and determine more accurate rates for specific populations.

More information on hypertension management inside the Brazilian primary care setting is still needed. Nonetheless, our assessment achieved its goals of describing relevant aspects of usual primary care in Brazil. Future economical evaluations are needed to assess forthcoming clinical guidelines' cost-effectiveness over the *status quo*.

1. Apresentação

O presente trabalho versa sobre a prevalência nacional (atual e pregressa) de hipertensão arterial sistêmica (HAS) no Brasil e descreve o tratamento usualmente dispensado aos pacientes hipertensos na atenção primária do país. Os resultados foram organizados e descritos em três artigos.

Os dois primeiros estudos são revisões sistemáticas com meta-análise: o primeiro aborda a prevalência de HAS em adultos, o segundo, nos idosos. O terceiro artigo é uma revisão quantitativa da prática assistencial usual prestada aos hipertensos na atenção primária brasileira. Juntos, os três artigos traçam um panorama propositalmente amplo da HAS no país, caracterizando a dimensão dessa doença no Brasil e ilustrando, da maneira mais sistemática possível, a forma como esta é habitualmente manejada a nível ambulatorial.

Em seu conjunto, este trabalho pretende contribuir para o desenvolvimento da pesquisa em avaliação de tecnologias em saúde (ATS) com foco em avaliações econômicas em saúde (AES), campos de investigação em desenvolvimento no Brasil. Esta tese tem o intuito de auxiliar os pesquisadores da área, fornecendo subsídios para futuros estudos.

2. Introdução e Revisão da Literatura

2.1. Definição de HAS

Hipertensão assumiu diversas definições ao longo do século XX. Correntemente, define-se HAS como a média de pressão arterial (PA) – aferida pelo método auscultatório ou oscilométrico por pelo menos duas vezes [1] em pelo menos duas consultas com uma semana de intervalo [2] – maior ou igual a 140 mmHg para pressão sistólica ou 90 mmHg para pressão diastólica [1]. O acréscimo de uso de medicamentos anti-hipertensivos à definição permite detectar os indivíduos hipertensos em tratamento com pressão controlada. Existem outras definições de HAS, como, por exemplo, aquela determinada pela monitorização ambulatorial da pressão arterial (MAPA) ou monitorização residencial, mas essas estão fora do escopo deste trabalho.

2.2. HAS: risco cardiovascular, prevalência e controle da doença

Hipertensão é notório fator de risco para doença cardiovascular (DCV), responsável por grande parte das mortes atribuídas a DCV e explica cerca de 45,0% dos casos de doença arterial coronariana (DAC) e 51,0% de acidente vascular encefálico (AVE) [3–5]. Risco aumentado para DCV é detectado a partir de PA maior do que 115/75 mmHg, sendo que o risco de morte dobra a cada aumento de 10 mmHg de PA diastólica (PAD) e 20 mmHg de PA sistólica (PAS) [3]. A PAS, no entanto, tem se mostrado melhor preditora de eventos cardiovasculares do que a PAD [4,6].

Revisão sistemática com meta-análise evidenciou redução da média de PAS mundial de 0,8 e 1,0 mmHg por década para homens e mulheres, respectivamente, no período de

1980 a 2008; e queda da média da PAS da América Latina Tropical (Brasil e Paraguai) de 1,8 e 3,5 mmHg por década para homens e mulheres, respectivamente, para o mesmo período [6]. Mesmo assim, a prevalência mundial de HAS, no ano 2000, foi estimada em 26,4% com projeção de aumento para 29,2% (ou 1,17 bilhão de indivíduos) até 2025, sendo que dois terços dos hipertensos hoje vivem em países em desenvolvimento como o Brasil – proporção que alcançará quase 75,0% até 2025 [7]. Revisão recentemente publicada por Ibrahim e Damasceno demonstra o claro aumento de prevalência de HAS nos países em desenvolvimento; são relatados incrementos de até 29,8%, como é o caso da Índia, em um horizonte temporal de apenas 15 anos, com predomínio de hipertensos em zonas urbanas em relação às rurais [6]. Proporção de controle pressórico (PA <140/90 mmHg, ou PA <130/80 mmHg para hipertensos diabéticos) dentre pacientes hipertensos tratados farmacologicamente foi tão baixa quanto 1,0%, como na Tanzânia [8].

No Brasil, segundo as VI Diretrizes Brasileiras de Hipertensão (VI-DBH), 22 estudos, conduzidos em diversas localidades distintas nos últimos 20 anos, detectaram prevalência de HAS entre 22,3% e 43,9%, sendo superior a 50,0% naqueles com 60 a 69 anos e, aproximadamente, 75,0% dentre os com 70 anos ou mais [9]. Ainda de acordo com as VI-DBH, as proporções de conhecimento da doença, tratamento farmacológico e controle de PA dentre os hipertensos brasileiros – com base em somente dois estudos – comparadas às referentes estatísticas internacionais – fundamentado em 44 estudos conduzidos em 35 países – foram de 52,3%, 34,9% e 67,3% *versus* 59,1%, 13,7% e 26,1%, respectivamente [10–12]. Contudo, apesar de haver dados de prevalência de HAS e controle pressórico para países em desenvolvimento, esses ainda são escassos, logo, mais estudos são necessários para melhor estimação da frequência e controle da doença nessas nações [13].

No nosso país, não há estudos realizados em amostras representativas nacionais que tenham avaliado a prevalência e a proporção de controle de HAS através de PA aferida. Existem, contudo, inquéritos telefônicos e domiciliares que avaliaram a prevalência autorreferida de HAS: o VIGITEL (Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico) e o PNAD (Pesquisa Nacional por Amostra de Domicílios). [14–17]. O estudo VIGITEL, em 2006, estimou prevalência de HAS de 21,6% (IC 95%: 21,3–22,0%) em indivíduos maiores de 18 anos, de 26 capitais estaduais e do Distrito Federal; para o ano 2008, a estimativa foi de 23,9% (IC 95%: 23,0–24,7%); e, em 2010, a prevalência foi de 23,3% (IC 95%: 22,3–24,2%) [14–16]. Já o PNAD, em 2008, revelou prevalência de doença de 53,3% em idosos (≥60 anos) para todo o Brasil [17]. Entretanto, em nossa revisão sistemática publicada em 2012, estimamos prevalência de HAS em adultos – determinada por aferição de PA (≥140/90 mmHg) ou relato de uso de anti-hipertensivo – de 28,7% (IC 95%: 26,2–31,4%) para a década de 2000 [18]; também detectamos prevalência de HAS de 68,9% (IC 95%: 64,1–73,3%) em idosos (vide Artigo 2). Assim, parece haver subestimação da prevalência naqueles inquéritos, provavelmente em função de viés de seleção (no caso do VIGITEL) e baixa confiabilidade do autorrelato [19–24].

2.3. ATS e diretrizes clínicas

Dada a limitação de recursos dos sistemas de saúde e o impacto de decisões sobre a saúde da população, faz-se necessário escolher quais são as estratégias de saúde que devem ser incorporadas pelos sistemas e como, com a finalidade de atingir ganho máximo em saúde com os recursos disponíveis, respeitando as expectativas da população [25]. Neste sentido, a ATS surge como ferramenta para a tomada de decisão, auxiliando gestores na

área da saúde, uma vez que utiliza ferramentas de pesquisa capazes de comparar duas ou mais estratégias com base em desfechos clínicos relevantes, levando em conta o contexto econômico e social, e a perspectiva do pagador interessado ou dos usuários de um sistema de saúde [26]. O Ministério da Saúde usa a seguinte definição para ATS: "... campo multidisciplinar de análise de políticas, que estuda as implicações clínicas, sociais, éticas e econômicas do desenvolvimento, difusão e uso da tecnologia em saúde" [27]. Já AES são definidas como a comparação de opções alternativas em termos de custos e consequências [28].

Uma das grandes limitações dos estudos de ATS, especialmente das AES, é a dificuldade de generalização dos achados encontrados [29]. Fatores como os preços absolutos e relativos de recursos em saúde; as variações na prática clínica; as condições artificiais nas quais os pacientes são avaliados nos estudos – especialmente nos ensaios clínicos randomizados (ECRs) –, quando comparado com a prática usual; e a experiência do corpo clínico local comprometem a validade externa e aplicabilidade de muitos estudos internacionais [29,30]. Somado a isso, há relativa escassez de dados de custo-efetividade do tratamento de HAS no Brasil [20]. Sendo assim, mais estudos brasileiros são necessários, já que não se pode importar livremente os dados internacionais de ATS e AES.

Entretanto, algumas iniciativas nacionais merecem destaque. Em um trabalho publicado em 2000, análise de custo-efetividade comparando atenolol, captopril, anlodipino e losartana à hidroclorotiazida (HCT) demonstrou que o diurético tem melhor razão de custo-efetividade para redução de PA: R$48,00/mmHg/ano de tratamento [31]. Em estudo de base populacional conduzido em São José do Rio Preto em 2004-2005, foi estimada razão de custo-efetividade do tratamento medicamentoso da HAS para controle de PA. Diuréticos apresentaram menor razão de custo-efetividade (US$15,00 (±US$2,00) por mês), seguido de

β-bloqueadores (BB) (US$34,70 (±US$5,50)) e inibidores da enzima de conversão da angiotensina (IECA) (US$176,70 (±US$21,80)) [32].

Há pelo menos três determinantes que condicionam a prática clínica usual: nível das evidências científicas, contexto da prática profissional (meio acadêmico *versus* não acadêmico), e presença de facilitadores de adesão [30]. Entre os facilitadores de adesão se encontram os protocolos e as diretrizes clínicas, as rotinas assistenciais, entre outros [30,33,34]. As diretrizes *per se*, todavia, não garantem adesão às práticas baseadas em evidência [35,36]. Barreiras à incorporação das diretrizes clínicas na prática usual podem ser classificadas como: barreiras de conhecimento (falta de familiaridade ou de consciência do cenário clínico); de atitude (falta de motivação ou autoeficácia por parte do clínico, discordância ou pouca confiança nas diretrizes); e de comportamento (incapacidade de conciliar as preferências dos pacientes com as condutas das diretrizes, e restrições de tempo, de recursos ou de infraestrutura organizacional) [36]. A praticidade das diretrizes também parece exercer influência sobre o grau de aceitação por parte dos médicos [35]. Todavia, há evidências de que sessões de treinamento visando o bom uso das diretrizes pode efetivamente aumentar a proporção de pacientes com PA controlada no âmbito da atenção primária [37].

Estudo conduzido no Brasil por Mion e colaboradores revelou má adesão por parte de médicos internistas, cardiologias e nefrologias às IV Diretrizes Brasileiras de Hipertensão Arterial (IV-DBH). Nesse trabalho, 42,5% dos entrevistados referiram seguir completamente o documento, 49,8% relataram apenas adesão parcial às orientações, 2,1% referiram não seguir as sugestões, 4,5% simplesmente não leram a diretriz mesmo tendo-a recebido. Além disso, houve claro descompasso entre os níveis pressóricos diagnósticos de HAS e o alvo terapêutico preconizado pela IV-DBH em relação ao que os médicos usualmente praticavam

em seus consultórios, sendo que esses tendiam a adotar limiares menores nos pacientes com comorbidades. Contraditoriamente, a proporção de investigação, por parte dos médicos, de *diabetes mellitus* (DM) e dislipidemia nos pacientes hipertensos foi de apenas 64,7% e 56,4%, respectivamente [38].

Concluindo, diretrizes para detecção e tratamento de HAS são recomendadas há anos, internacionalmente, pelo *Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (JNC) – atualmente, no seu sétimo relatório (JNC-7) –, e, nacionalmente, pelas já citadas VI-DBH. Entretanto, as condutas preconizadas pelas VI-DBH e pelo JNC-7 para diagnóstico, classificação e controle de HAS nunca tiveram custo-efetividade formalmente avaliada sob a luz da ATS.

2.4. Ferramentas para ATS

As AES compõem, talvez, o conjunto mais importante de ferramentas de pesquisa em ATS. A descrição detalhada dos diferentes métodos de AES está fora do intento desse trabalho. Contudo, todas as AES ditas completas pressupõem uma comparação [28,39]. Deste modo, o comparador serve como cenário de caso-base contra o qual se analisarão as demais alternativas de intervenção ou de grupo de intervenções (doravante estratégias de saúde) [39]. Esses casos-base são indispensáveis para as AES, entretanto, não há nenhum modelo publicado referente ao tratamento ambulatorial de hipertensão no Brasil.

O comparador – ou *status quo* (SQ) – de uma nova estratégia de saúde em uma AES pode ser tanto uma estratégia de saúde já implantada, quanto uma estratégia não sistematizada – a chamada prática usual [39]. O manejo usual, na ausência de uma estratégia de

saúde padronizada implantada, é um comparador válido [39]. A prática usual é uma concepção realista de comparador, pois esse modelo permite a livre exclusão ou inclusão de intervenções preconizadas em diretrizes clínicas, assim como a inclusão de outras intervenções não contempladas por estas, ou seja, aceita discrepâncias entre a teoria e a prática assistencial. Assim, o SQ baseado na prática clínica usual reflete com mais fidedignidade a realidade do manejo de uma doença [29,39].

A confecção de um modelo de SQ baseado exclusivamente em ECRs parece não ser o método mais adequado [29,40,41]. ECRs são cenários de pesquisa que não expressam condições habituais da prática clínica e, portanto, podem gerar dados de custo e efeito pouco realistas [29,40,41]. Além disso, revisões sistemáticas de estudos observacionais são cada vez mais utilizados para estimar a efetividade de tratamentos, já que os ECRs não conseguem capturar todos os efeitos de uma intervenção em função do horizonte temporal limitado desses estudos [42]. Ainda, os delineamentos observacionais são a única opção de estimação de efetividade em circunstâncias em que os ECRs são inapropriados ou antiéticos [43]. A literatura também aponta que mais revisões sistemáticas em torno do manejo da HAS são necessárias para se tentar reduzir ônus cardiovascular desta doença [44].

Conforme os postulados da ATS e da pesquisa de efetividade comparativa (do inglês *compartive effectiveness reasearh*), o emprego de dados oriundos de diferentes métodos de pesquisa clínica – isto é, estudos de intervenção e observacionais – comporiam melhor um modelo de SQ [29,39,45]. Logo, usar dados de custo, adesão, consultas, exames complementares e eventos adversos gerados em estudos observacionais, e dados de eficácia (com estimativa de efetividade por análise de intenção de tratar) originários de ECRs são um mé-

todo viável, realista, apropriado e condizente com a literatura de se construir um modelo de SQ para uso em uma AES [29,39].

2.5. Tratamento da HAS

2.5.1. Modificação de estilo de vida (MEV)

Adoção de um estilo de vida saudável é crucial para a prevenção e tratamento de HAS e a recomendação de MEV está indicada para todos os pacientes com HAS [1]. Isoladamente, dieta com calorias reduzidas é a MEV mais efetiva, com redução de 6,6 mmHg na PAS (IC 95%: 2,9–10,2 mmHg) 2,0 mmHg na PAD (IC 95%: 0,1–3,9 mmHg); seguida por dieta com restrição de sódio, com redução de 5,1 mmHg na PAS (IC 95%: 1,7—8,6 mmHg) e 2,1 mmHg na PAD (IC 95%: 0,2–3,9 mmHg) [46]. Perda de peso também tem impacto na redução da PAS: de 5 a 20 mmHg para cada 10 kg perdidos [47,48]. Redução de apenas 4,5 kg pode prevenir o surgimento de HAS em adultos com sobrepeso (índice de massa corporal ≥25 kg/m^2) [47]. Adoção da chamada dieta DASH (*Dietary Approaches to Stop Hypertension*) – rica em frutas, vegetais e laticínios magros, e pobre em gorduras – pode reduzir a PAS em até 14 mmHg [49].

Redução do consumo de álcool (no máximo até dois *drinks*, ou 30 mL de etanol, por dia para homens e um *drink*, ou 15 mL de etanol, por dia para mulheres) tem impacto modesto sobre a PAS: 2 a 4 mmHg [50]. Todavia, a inconsistência dos achados de estudos observacionais a respeito do caráter cardioprotetor do consumo moderado de álcool e a possibilidade da suposta proteção estar sendo influenciada por fatores de confusão como hábitos saudáveis e vida social ativa contraindicam o estímulo ao consumo moderado de bebi-

das alcoólicas [51,52]. Todos os pacientes tabagistas devem ser aconselhados a parar de fumar para fins de redução do risco para DCV, apesar de não haver benefício quanto à diminuição da PA [1].

Atividade física aeróbica regular (pelo menos 30 minutos por dia de caminhada na maior parte dos dias da semana) reduz a PAS em até 9 mmHg [53]. Estudo de coorte com pacientes atendidos no ambulatório de hipertensão do Hospital de Clínicas de Porto Alegre não detectou redução de PA naqueles que praticavam atividade física regular após média de 23,1 meses de seguimento [46]. O maior impacto foi observado em pacientes hipertensos que adotaram dieta com baixo teor de sal [7.0 mmHg (IC95% 2.8 to 11.2)] e com restrição calórica [8.8 mmHg (IC95% 4.4 to 13.2)] versus [3.5 mmHg (IC 95% 1.4 to 5.7)] e [2.8 mmHg (IC 95% 0.6 to 5.1)], respectivamente, para PAS e PAD [46].

Finalmente, há evidência de sinergismo de efeito das diferentes MEVs na redução da PAS: no ECR Premier, o grupo que recebeu a dieta DASH mais as recomendações para MEV experimentou maior redução na PAS em relação ao grupo alocado para aconselhamento usual (4,3 *versus* 3,7 mmHg) [43]. As MEVs devem ser recomendadas a todos os pacientes hipertensos fazendo parte da rotina assistencial de qualquer serviço médico [1,9].

2.5.2. Tratamento farmacológico

Há evidências contundentes de que o tratamento farmacológico (em monoterapia ou combinado) da HAS reduz a incidência de DCV e morte [55–60]. Existia dúvida de que o caráter protetor sobre o aparelho cardiovascular de alguns anti-hipertensivos pudesse ser atribuído a outras propriedades e efeitos, que não a redução de PA – os chamados efeitos

pleiotrópicos. Contudo, meta-regressão de 14 ECRs (envolvendo mais de 74 mil pacientes) identificou que a maior parte da redução de eventos cardiovasculares associados às diversas alternativas de tratamento medicamentoso pode ser atribuída à redução na PAS [61]. Ainda, meta-análise de 147 ECRs, avaliando 464 mil pacientes, também concluiu que o benefício associado ao tratamento da HAS está diretamente ligado à redução da PA, excluindo a possibilidade de efeito pleiotrópico dos anti-hipertensivos [59]. Assim, redução e controle da PA são cruciais para a prevenção de DCV.

2.5.2.1. Monoterapia

Em uma meta-análise em rede de ECRs, a redução de risco relativo (RRR) associada ao tratamento farmacológico da HAS, comparado a placebo ou não tratamento, foi de 14,0% para DAC, 32,0% para AVE, 46,0% para insuficiência cardíaca congestiva (ICC), 27,0% para evento cardiovascular maior, 16,0% para morte por DCV e 10,0% para morte por qualquer causa [56].

O maior ECR de tratamento de primeira linha de HAS já realizado, o estudo ALLHAT (*Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial*) demonstrou clara superioridade do tratamento baseado em diurético tiazídico (clortalidona) em relação às alternativas (anlodipino e lisinopril). A clortalidona foi superior ao anlodipino na prevenção de ICC e hospitalização por ICC ou ICC fatal, e superior ao lisinopril na prevenção de AVE, DCV, ICC e angina. O diurético também foi mais bem tolerado que os outros fármacos [57].

Além do ALLHAT, recente reanálise do estudo SHEP (*Systolic Hypertension in the Elderly Program*) revelou, após 22 anos de seguimento, aumento de 158 dias na expectativa de vida de pacientes tratados com clortalidona por 4,5 anos durante a década de 1980 em

comparação a indivíduos que receberam placebo [60]. Cada mês de tratamento com clortalidona foi associado a um ganho de, aproximadamente, um dia na expectativa de vida [60].

Recente meta-análise de 25 ECRs comparou diversos tratamentos de primeira linha na prevenção primária de DCV e morte por qualquer causa. Para o desfecho morte por qualquer causa, o estudo revelou inferioridade dos BB em relação aos bloqueadores do receptor de angiotensina (BRA), com aumento de risco relativo (ARR) de 14,0%. Para o desfecho AVE, os IECA foram inferiores aos bloqueadores do canal de cálcio (BCC) (ARR de 19,0%), entretanto, foram superiores na prevenção de ICC (RRR de 27,0%). Os diuréticos tiazídicos reduziram o risco de infarto agudo do miocárdio (IAM) em 18,0% quando comparados aos BB e diminuíram o risco de ICC em 27,0%, 27,0% e 49,0% quando comparados aos BCC, BB e α-bloqueadores, respectivamente [55]. Em função do acúmulo de evidências favorecendo os diuréticos tiazídicos, o JNC-7 recomenda o uso dessa classe de anti-hipertensivos como a primeira escolha no tratamento farmacológico da HAS, mesmo em pacientes com DM [1].

2.5.2.2. Terapia combinada

Mais de dois terços dos hipertensos precisam de mais do que um anti-hipertensivo para obter o controle da PA [62]. Mesmo assim, enquanto há uma profusão de ECRs que avaliaram o efeito do tratamento de primeira linha da HAS, existe relativa escassez de estudos para o tratamento combinado da doença e nenhuma combinação de dois fármacos demonstrou eficácia claramente superior [62]. Contudo, terapia combinada de BB com outro anti-hipertensivo parece não ser uma boa opção terapêutica, particularmente em idosos

[63,64], haja vista sua ineficácia frente a placebo no tratamento em monoterapia, conforme demonstrou uma revisão sistemática da *Cochrane Collaboration* [65].

O ECR PROGRESS (*Perindopril Protection Against Recurrent Stroke Study)* avaliou o efeito de tratamento anti-hipertensivo – baseado em perindopril mais indapamida (conforme decisão do médico assistente) – em indivíduos com história prévia de AVE e ataque isquêmico transitório (AIT). O tratamento combinado produziu RRR de 40,0%, para qualquer evento cardiovascular maior em relação a dois comprimidos de placebo, já a monoterapia com perindopril apresentou efeito equivalente a placebo [58].

O estudo ACCOMPLISH (*Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension*) comparou benazepril 20 mg mais anlodipino 5 mg *versus* benazepril 20 mg mais HCT 12,5 mg (todos os agentes com possibilidade de progressão para o dobro da dose inicial) na prevenção de evento cardiovascular maior fatal e não fatal [66]. Todos os mais de 11 mil participantes tinham pelo menos 60 anos e história de DCV em uso anti-hipertensivo ou PAS ≥160 mmHg. O grupo IECA mais BCC produziu RRR 18,4% – com número necessário para tratar (NNT) em três anos de 46. Esse ECR foi alvo de críticas, especialmente pelo o representante tiazídico utilizado e sua dose. Primeiramente, há mais evidências sustentando o uso e a eficácia de clortalidona do que de HCT [55–57,60,67]. Além disso, a dose inicial de HCT de 12,5 mg pode ser considerada subterapêutica, já que a potência hipotensora da clortalidona é duas vezes maior que da HCT e esta última é geralmente empregada com dose inicial de 25 mg [68,69].

A maioria da dos pacientes hipertensos com DM necessitarão de dois ou mais fármacos para controle da PA [70]. As recomendações atuais são de adição de um IECA ao trata-

mento com diurético tiazídico, fundamentalmente, pelo caráter nefroprotetor do primeiro [71].

O estudo de três braços ONTARGET (*Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial*), com mais de 25 mil pacientes com DCV ou DM, mas sem ICC, comparou telmisartana 80 mg e telmisartana mais ramipril 10 mg a ramipril isoladamente. O desfecho primário foi mortalidade cardiovascular e incidência de eventos maiores. Não houve diferença entre os braços de tratamento para o desfecho principal e o grupo que recebeu terapia combinada apresentou, em relação ao grupo ramipril isolado, maiores taxas de hipotensão (risco relativo (RR) 2,8), síncope (RR 2,0), diarreia (RR 3,3), perda de função renal (1,6) e descontinuação do tratamento (RR 1,2). A conclusão dos autores é sensata: terapia combinada não agrega benefício e ainda aumenta risco de efeitos adversos importantes [72].

2.6. Atenção primária no SUS

No Brasil, a atenção primária do SUS é regida, principalmente, pelos princípios da universalidade, integralidade e descentralização [73]. Os centros de atenção primária devem, portanto, garantir acesso ao SUS a toda população adscrita e ser a principal porta de acesso ao sistema, coordenar o trânsito dos usuários entre os outros níveis de atenção à saúde (secundária e terciária) e ser administrados pelos municípios [73].

Programas para o fortalecimento da atenção primária têm sido implantados no país. A principal estratégia para a estruturação da atenção básica no SUS é o Programa Saúde da Família (PSF). Os postos do PSF são compostos por equipes de saúde integradas por pelo menos um médico, um enfermeiro, um auxiliar ou técnico de enfermagem, e seis agentes

comunitários de saúde, sendo que cada equipe é responsável pelo atendimento de 600 a 1000 famílias [73]. Este programa está em vigor em todo o território nacional desde 1998. Desde então, a atenção primária do SUS, como fonte usual de cuidados em saúde, passou de 42% para 57% dos brasileiros em 2008 [74]. O PSF, em 2010, contava com 236 mil agentes comunitários, 33 mil equipes de saúde, e alcançava 85% dos municípios do país, cobrindo 98 milhões de pessoas.

3. JUSTIFICATIVAS, OBJETIVOS E ASPECTOS ÉTICOS

3.1. Justificativas

Considerando-se que:

- HAS é uma das principais causas de morbidade e mortalidade no mundo e na população brasileira, apresentando, portanto, impacto considerável na utilização de recursos em saúde.
- Existem evidências inequívocas de que o tratamento da HAS resulta em redução de eventos clínicos, mortalidade cardiovascular e morte por qualquer causa.
- O manejo usual da HAS no âmbito da atenção primária brasileira nunca foi sistematicamente revisado e descrito.
- O SQ do tratamento da HAS no Brasil é comparador indispensável para futuras AES.
- Há escassez de ferramentas e, portanto, de dados de custo-efetividade do tratamento da HAS no Brasil.
- A prevalência nacional de HAS, baseada em estudos de base populacional, nunca foi estimada.
- Dados de prevalência de HAS são *sine qua non* para a estimação do ônus econômico da doença.
- Não há dados relativos ao ônus econômico do tratamento da HAS sob a perspectiva do SUS ou do paciente em âmbito nacional.
- A literatura em torno das AES é clara ao propor que dados de efetividade e custo são local-específicos.

Torna-se necessária a produção de instrumentos de pesquisa em ATS e a geração de dados nacionais de prevalência para viabilizar futuras AES que comparem estratégias de saúde

(diretrizes clínicas ou programas de saúde pública) ao SQ da prática clínica (manejo ambulatorial usual da HAS).

3.2. Objetivos

3.2.1. Objetivos gerais

- Estimar a prevalência nacional de HAS para futuras análises de ônus econômico da doença no Brasil.
- Contribuir para pesquisa nacional em ATS e AES com a formação de conhecimento e ferramentas pertinentes para tal.

3.2.2. Objetivos específicos

- Estimar a atual prevalência nacional de HAS em adultos e o comportamento desta durante as últimas três décadas através da revisão sistemática com meta-análise e meta-regressão de estudos de base-populacional representativos.
- Estimar a prevalência nacional de HAS, atual e nas últimas três décadas, em idosos através da revisão sistemática com meta-análise de estudos de base-populacional representativos.
- Descrever, através de revisão sistemática, a prática assistencial usual em relação ao diagnóstico, estratificação de risco e tratamento farmacológico da HAS a nível da atenção primária do SUS.

3.3. Aspectos éticos

Trata-se de trabalho baseado inteiramente em revisão da literatura e em dados secundários, portanto não há meios de ferir a saúde, integridade, autonomia ou privacidade de pacientes ou participantes.

4. Referências da Introdução e Revisão da Literatura

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5. ARTIGO 1

TRENDS IN PREVALENCE OF HYPERTENSION IN BRAZIL: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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TRENDS IN PREVALENCE OF HYPERTENSION IN BRAZIL: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Running title

Trends in prevalence of hypertension in Brazil

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The authors declare no conflicts of interest.

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Abstract

Background

The prevalence of hypertension in emerging nations was scarcely described to date. In Brazil, many population-based surveys evaluated the prevalence in cities throughout the country. However, there is no population-based nationwide study of prevalence of hypertension. In this study, we estimated the prevalence of hypertension for the country and analyzed the trends for the last three decades.

Methods

Cross-sectional and cohort studies conducted from 1980 to 2010 were independently identified by two reviewers, without language restriction, in the PubMed, Embase, LILACS, and Scielo electronic databases. Unpublished studies were identified in the Brazilian electronic database of theses and in annals of Cardiology congresses and meetings. In total, 40 studies were selected, comprising 122,018 individuals.

Results

Summary estimates of prevalence by the former WHO criteria (BP ≥ 160/95 mmHg) in the 1980's and 1990's were 23.6% (95% CI 17.3–31.4%) and 19.6% (16.4–23.3%) respectively. The prevalence of hypertension by the JNC criteria (BP ≥ 140/90 mmHg) in the 1980's, 1990's and 2000's were 36.1% (95% CI 28.7–44.2%), 32.9% (29.9–36.0%), and 28.7% (26.2 – 31.4%), respectively (P <0.001). In the 2000's, the pooled prevalence estimates of self-reported hypertension on telephone inquiries was 20.6% (19.0–22.4%), and of self-reported hypertension in home surveys was 25.2% (23.3–27.2%).

Conclusions

The prevalence of hypertension in Brazil seems to have diminished 6% in the last three decades, but it still is approximately 30%. Nationwide surveys by self-reporting by telephone interviews underestimate the real prevalence. Rates of blood pressure control decreased in the same period, corresponding currently to only one quarter of individuals with hypertension.

Key words

Hypertension, Meta-analysis, Systematic review, Epidemiology, Prevalence

Introduction

Hypertension has become a growing public health concern, particularly in developing countries, with an estimated prevalence of 37.3%, in comparison with 22.9% in industrialized nations.[1] Projections are that by the year of 2025, 75.0% (or 1.17 billion people) of the people with hypertension in the world will be living in emerging nations [1].

Although hypertension has been recognized as a major risk factor for cardiovascular morbidity and mortality worldwide, there are lacking nationwide prevalence data in most emerging countries [2,3]. Such information is needed in order to determine the economic burden of hypertension, as well as to optimize health resources allocation toward improvement on its detection, treatment and control. In Brazil, many population-based surveys, representative of cities and of one state, have been done in the last three decades, but there is no estimate of prevalence for the whole country or of trends in this period. Hence, our study aimed to estimate the prevalence trends of hypertension in the adult Brazilian population through a systematic review with meta-analysis of population-based studies.

Methods

Study designs and eligibility criteria

The eligibility criteria included population-based cross-sectional or cohort studies among participants aged 18 years or older, from 1980 to 2010. Studies with pregnant women were not included.

Studies with duplicate data were excluded. Population-based studies that addressed only specific socioeconomic strata (such as low-income individuals, or certain industry workers) were not considered representative of its geographical (city, State, or region) pop-

ulation and, therefore, deemed ineligible. Studies that assessed only secondary hypertension, or used samples originated from sources other than the general geographical population (i.e. not population-based) were also excluded.

Information sources

The search of the published literature was conducted in the electronic databases of PubMed, Embase, LILACS (Latin American and Caribbean Health Sciences Literature), and Scielo (Scientific Electronic Library Online) using MeSH terms and Entrees for PubMed e Embase, and DeCS (Health Sciences Descriptors) for the other two databases. Data that were not formally published were additionally searched in PhD theses and Master's dissertations registered in the electronic database of the Coordination for the Improvement of Higher Education Personnel (CAPES), Ministry of Education, Brazil. Annals of national and regional scientific sessions of Cardiology in Brazil were searched to identify studies presented only in these meetings. Full-text version of all potentially relevant articles, theses, or dissertation were downloaded from electronic databases or requested directly to the authors via e-mail.

Searching

All searches were carried out independently by two reviewers. Search strategies were tested with the key words "hypertension", "prevalence", "statistics", and "Brazil", using the Boolean operator "OR", which retrieved tens of thousands of records. A second attempt was carried out in the same databases using the operator "AND". The following search strategies were used on PubMed: ("Hypertension"[Majr] AND "Prevalence") AND "Brazil" limited to all adults (≥19 years-old), and ("Hypertension/epidemiology"[Majr] OR

"Hypertension/statistics and numerical data"[Majr]) AND "Brazil" limited to all adults (≥18 years-old). Only searches on PubMed and Embase were filtered for studies conducted in adults. No language restriction was applied. Independent manual search on reference lists of retrieved articles was also undertaken

Study selection and data collection

The first screening was based on a double-screening of titles and abstracts. Results which met explicit exclusion criteria were excluded. In the second step, the remaining manuscripts were assessed for full-text reading. In case of disagreement among reviewers, a third reviewer assessed the study and a decision for inclusion was reached by consensus. Data were entered in a pre-tested Microsoft Office Excel™ spreadsheet that was designed based on the Strengthening the Reporting of Observational Studies in Epidemiology Statement (STROBE) checklist [4]. Items 4, 5, 6a, 7–10, 12c–e, 13a, 14b, 16a, and 17 of the STROBE checklist were taken into account for the development of the data extraction spreadsheet.

Hypertension prevalence was the main summary measure used in this systematic review, which was extracted from studies using different definitions, that comprised four diagnostic criteria: blood pressure (BP) ≥ 140/90 mmHg or use of BP lowering medication (BPLM) (hereafter the JNC criteria - according to the Fourth to Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure); BP ≥ 160/95 mmHg or use of BPLM (henceforward former World Health Organization (WHO) criteria, employed in older studies); self-reported hypertension through home visits, and self-reported hypertension through telephone inquiries [6,7]. Many studies with measured

blood pressure presented estimates for the former WHO and JNC criteria, but older studies presented only for the former WHO criteria. Hypertension control rate was defined as the proportion of subjects with hypertension using BPLM and normal BP over the total number of subjects with hypertension on treatment.

Assessment of study quality and risk of bias

All studies were assessed for selection and measurement biases as well as bias in the data analysis based on guidelines of the MOOSE checklist [5]. Selection biases were characterized by refusals to participate in the study of 20% or higher, description of a non-random sampling, the use of other than a random process for participants recruitment, and data collection made through telephone interviews, since it covers participants of higher socio-economic level. Measurement biases were defined considering the type of device used for blood pressure measurement, the discard of the first measurement, except for studies that used self-reported hypertension or the report of lacking impact in the analysis. Bias in the analysis was considered possible if the design effect was not taken into account in calculating the prevalence of hypertension. All biases were dealt with sensitivity analyses, defined *a priori*, using the abovementioned factors stratified for diagnostic criteria and decade (e.g. oscillometric *vs.* all devices, according to JNC criteria in the 2000's; studies adjusted to design effect *vs.* all studies, according to the former WHO criteria in the 1980's; etc.). Also, a sensitivity analyses comparing the overall prevalence of hypertension, according to the JNC criteria in the 2000's, versus the pooled prevalence without studies carried out exclusively in rural populations or studies that did not investigated elderly individuals was performed.

Data analysis

All point estimates of analyses and their 95% confidence interval (95% CI) were calculated using random effects models according to decade, sex (when possible), and hypertension definition. The random effects model, wherein the study weight is inversely proportional to the sum of within and between studies variance (τ^2). Hence the variance of one study gets diluted in the variance between studies, consequently, studies weights are more evenly distributed across studies. In other words, the impact of the sample size of a given study on the study weight is considerably diminished, and so is the influence of individual studies weights to the model as a whole. Nevertheless, the analyses using fix effect models were also tested, resulting in identical point estimates, but with narrower confidence intervals (data not shown).

Subgroup analyses included overall prevalence of hypertension according to the JNC criteria by decade, analyses by macro-region and design effect correction in the 2000's, and control rates from 1980 to 2010 by decade. Heterogeneity and consistency were evaluated through Cochran's *Q* and the I^2 statistics, respectively. Analyses were performed using the second version of the Comprehensive Meta-Analysis™ software. Forest plots were constructed using an electronic spreadsheet developed by Neyeloff et al [8].

Chi-square (χ^2) was used to assess difference in prevalence rates among two distinct decades. Chi for trend (χ^2 for trend) was used to evaluate prevalence and control rate across the three decades. Meta-regression – regressing the year of data collection and local human development index (HDI) on the logit prevalence rate – was employed to assess the prevalence variation throughout the studied period, using the method of moments for the estimation of τ^2.

The Institution Review Board, which is accredited by the US Office of Human Research Protections, approved the research protocol.

Results

Synthesis of data

Through the searches, 761 articles were found in the electronic databases (51 being theses/dissertations published in the CAPES's database), one study published by some of the authors was further analyzed to provide data, and other six articles retrieved by manual search – totalizing 600 initial records after removal of duplicates [9]. Manual search of the Annals of Cardiology meetings identified only studies already found in other sources. The first screening excluded 444 records and the second screening, another 108. By consensus with the third reviewer another eight studies were excluded, leaving 40 studies with 122018 individuals for the analysis. Agreement among reviewers for individual selection of studies was 78%, and after consensus meetings it reached 100%. Flowchart of studies selection is presented in Figure 1. The list of studies included and excluded in the meta-analysis, and the reasons for exclusion, are presented in the supplemental table.

Prevalence rates and their 95% CI by decade, diagnostic criteria, and method of assessment (measured or self-reported) are presented in Table 3. Summary estimates according to the former WHO criteria (BP ≥ 160/95 mmHg or BPLM) in the 1980's and 1990's were 23.6% (95% CI 17.3–31.4%) and 19.6% (16.4–23.3%), respectively. In the 2000's, the pooled prevalence estimates of self-reported hypertension on telephone inquiries was 20.6% (19.0–22.4%), and of self-reported hypertension in home surveys was 25.2% (23.3–27.2%).

Prevalence of hypertension by the former WHO criteria in older studies was obviously lower than the prevalence by the JNC criteria. Self-reported hypertension, either at home or by telephone interview (mostly previous doctor's diagnoses), yielded lower prevalence rates as well. Prevalence rates were roughly similar among men and women and did not change substantially in studies with adjustment for the design effect or using different blood pressure devices. Heterogeneity was present in all the pooled estimates shown in Table 3 ($P<0.001$ and $I^2>90.0\%$ for every analyses).

Prevalence rates according to the JNC criteria in individual studies, summary estimates by decade, and overall pooled rate are presented in Figure 2. The prevalence decreased by decades: 36.1% (28.7–44.2) in the 1980's, 32.9% (29.9–36.0) in the 1990's, and 28.7 (26.2–31.4) in the 2000's (P for trend <0.001). The estimated prevalence for the past three decades (according to the JNC criteria) was 31.0%, with 95% CI from 29.1 to 32.9%. With the exception of the North macro-region, which had estimates of prevalence exclusively from the Alto Xingu Indian population, the prevalence was similar among the various Brazilian macro-regions (Figure 3).

In the 2000's, pooled prevalence rate for studies adjusted for the design effect did not differ from all studies (adjusted and unadjusted) according to the JNC criteria (χ^2 P=0.07) and telephone inquiries (P=0.51). The meta-regression of year of data collection over logit prevalence confirmed a trend toward decreasing in prevalence from 1987 to 2007, with a slope of -0.018 (P=0.02). Furthermore, a τ^2=0.05 was found, which means that differences in the year of data collection explain 90.2% of the between-studies variance (Figure 4).

Meta-regression of year of data collection over logit prevalence according to sex showed a non-significant slope of -0.012 (P=0.42) for women, and a significant slope of -0.035 (P=0.02) for men (τ^2=0.11; explained between-studies variance of 79.2%) (data not

shown). Meta-regression of HDI on logit prevalence (according to 2000 HDI for each city) retrieved a non-significant slope of 1.070 (P=0.42) (data not shown).

Additionally, control rates were properly reported in 10 studies and pooled rates, according to the JNC criteria, were 33.8% (26.0–42.6%), 28.1% (23.7–32.7%), and 24.1% (10.1–47.3%) in the 1980's, 1990's and the 2000's, respectively (χ^2 for trend p<0.001).

Assessing bias

All studies were cross-sectional, and there was moderate (59.0%) overlap of records across different databases. Five studies (12.5%) were from the 1980's, 11 (27.5%) from the 1990's and 24 (57.5% to 60.0%) from 2000's. Sample sizes varied substantially with a median of 1268 (IQR 838.5). Most studies that measured blood pressure employed aneroid or mercury manometers (18 studies), and eight used oscillometric manometers. Almost all studies were from urban populations (37 studies), and mostly were done in the South and Southeast macro-regions of Brazil. Table 1 presents the overall characteristics of the 40 studies. In regard to methodological features of the studies, 33 used multistage cluster sampling, six used simple random sampling, and the study by Gimeno et al. evaluated 90% of the adults of Alto Xingu's native Brazilian [10]. Most studies (n=25; 62.5%) did not have selection bias with potential to compromise their internal validity. Fourteen (35.0%) studies had sampling or sample size calculation poorly described. Only one study had high rate of missing data. In 10 studies the first measurement was discarded. Twelve (30.0%) studies, mostly done in the 2000's, presented data adjusted for design effect. Table 2 presents data on potential selection and measurement biases, as well as bias in the analysis.

Sensitivity analyses were carried out excluding studies conducted in rural areas (n=3), studies that did not investigate elderly individuals (n=2), studies that employed oscillometric wrist manometer (n=1), and one with a small sample size [11-16]. The overall prevalence for the decade did not alter significantly (30.8%; 95%CI: 27.8–34.0%). All other sensitivity analyses defined *a priori* (see Assessment of study quality and risk of bias) showed similar results with no statistically significant differences (data not shown).

Interpretation and discussion

In this comprehensive systematic review with meta-analysis of cross-sectional surveys done in Brazil in the last three decades, including more than 120 thousand individuals, it was possible to compute precise estimates of prevalence by decade, by criteria of definition of hypertension, by methods of diagnosing hypertension, and by gender. Overall, the prevalence was similar to described in developed countries, particularly of hypertension diagnosed by blood pressure measurement and based on the contemporaneous universal criteria for diagnosis of hypertension, and without any substantial differences by gender [1,17]. An apparent trend to lowering in prevalence by decade was evident. The proportion of one-third of hypertensive individuals with controlled blood pressure is also within the range of rates of control described worldwide [18].

Our study could circumvent many limitations of individuals studies selected for the meta-analysis of Danaei et al, such as regional inequities [19]. Furthermore, Danaei et al employed mean systolic blood pressure to describe trends of risk, an approach that does not take into account the real number of subjects at risk. The potential reasons for bias in

the whole estimates are the overrepresentation of studies done in metropolitan populations, particularly from the South and Southeast macro-regions of the country. Nonetheless, 84.4% of the Brazilian population lives nowadays in cities [20]. The absence of representative data from the North macro-region was partially overcome by the inclusion of a study of native Brazilians. On the other hand, the North macro-region, although has the largest area, has the lowest density in the country, comprising 50% of Brazil's land territory, but only 5% of the country's population [20]. A few studies enrolled subjects below the age range, but the analysis with and without those studies did not change substantially the overall estimates.

Prevalence rates based on direct measurement of blood pressure were higher than those based on self-report hypertension [21-23]. The lower prevalence in telephone surveys may additionally be secondary to the differential distribution of telephones by social classes, leading to an underrepresentation of individuals from lower classes, who had higher prevalence of hypertension [22,24,25].

Most studies did not take into account the distortions caused by multistage and weighting sampling. The lack of adjustment for design effect can compromise accuracy of prevalence confidence intervals for individual studies and, consequently, making the results of older surveys less reliable than those done in the last decade [26,27]. Nevertheless, the comparison between studies with and without adjustment for sampling design showed that the former provided reliable estimates.

The average absolute reduction in prevalence of 3.7% per decade is consistent with recent meta-analysis that found a mean 1.8 and 3.5 mmHg decrease per decade in systolic blood pressure for males, and females, respectively, from 1980 to 2008 [7]. Also, meta-regression showed a slight, but steady relative reduction in prevalence of 1.8% per year

from 1987 to 2007. This trend reproduces the estimates observed in industrialized nations, confirming that the epidemiological transition already finished in Brazil in regard to hypertension. Significant reduction in prevalence among men and non-significant reduction in women might suggest that the overall prevalence decrease had a greater impact in men.

The trend toward reduction of the control rate was contrary to expectations. Increase in detection of hypertension and of the access to BPLM in the Brazilian Health System (universal coverage and free of charge), in the 1990's. Hence, the number of subjects on treatment for hypertension might have augmented proportionally more than the number of subjects with controlled hypertension in the last two decades. It might give the false impression that fewer subjects are keeping their blood pressure below 140/90 mmHg. Nonetheless, the pooled estimate of control rate is consistent with the literature [28].

Despite the heterogeneity of studies, lack of adjustment for effect design in many studies, and underrepresentation of the population from the North macro-region, the estimates are reliable and within the range of prevalence described for industrialized nations. The trend for lowering in the prevalence rates by decade follows the pattern of industrialized countries as well. The proportion of individuals with controlled hypertension, of about one-third of individuals, is similar to the described in other countries, and it requires innovative and effective means to improve the rates of control.

This pooled analysis of prevalence of hypertension is an attempt to fill the lack of national data. However, the estimates of prevalence of hypertension not adequately represent the Brazilian Indians, the rural population, and those living in the vicinity of the Amazon rainforest. This study presents data for the most populated areas of Brazil, as can be seen in the Brazil map (Appendix). Therefore, the results are not a substitute for a national preva-

lence study. However, until this study be conducted, these analyzes are the best estimates available that can serve as a reference for public health policy [29].

Conclusions

As such, this meta-analysis was an alternative way to establishing the hypertension prevalence in Brazil, which is necessary to assess the hypertension burden and to implement cost-effective interventions. Nonetheless, a nationwide prevalence study is still needed to confirm the estimates and determine more accurate rates for specific populations.

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Tabela 1

Table 1. Source, year, sample size and methodological aspects of the 40 studies included in meta-analysis (in alphabetical order of first author).

First author	Source or database	Year of data collection	N	Age criterion for study entry (years)	City, State, or region	Devices used and hypertension assessment method	BP cut-off value for hypertension (SBP/DBP in mm Hg)
Costa VG	LILACS	1982	1200	18–80	Uberlândia	Device not described	160/95
de Lolio CA	PubMed & LILACS	1987	1199	15–74	Araraquara	Aneroid	140/90 & 160/95
Martins IS	Embase, LILACS, PubMed & Scielo	1987	1041	≥20	Cotia	Mercury & SRH	140/90 & 160/95
Ayres JE	PuMed	1988	1944	≥15	Piracicaba	Device not described	160/95
Fuchs FD	Embase, PubMed & LILACS	1989	1091	≥18	Porto Alegre	Aneroid, BPLM & SRH	140/90 & 160/95
Bloch KV	Embase, PubMed & LILACS	1991	1268	≥20	Rio de Janeiro city	Mercury & BPLM	160/95
Piccini RX	Embase, LILACS, PubMed &Scielo	1992	1657	20–69	Pelotas	Aneroid, BPLM & SRH	160/95
Trindade IS	Embase, LILACS, PubMed & Scielo	1995	206	≥18	Passo Fundo	Aneroid, BPLM & SRH	160/95
Fuchs SC‡	Embase, PubMed & LILACS	1996	1174	≥18	Porto Alegre	Aneroid & SRH	140/90
Barreto SM	Embase, LILACS, PubMed & Scielo	1997	820	18–59	Bambuí	Mercury & SRH	140/90
de Oliveira RZ	Embase & LILACS	1998	411	20–69	Cianorte	Mercury, BPLM & SRH	140/90 & 160/95
Freitas OC	Embase, LILACS, PubMed & Scielo	1998	688	≥18	Catanduva	Aneroid	140/90
da Costa JSD	LILACS & CAPES-TD	1999	1968	20–69	Pelotas	Aneroid & BPLM	160/95
Gus I	LILACS & Scielo	1999	1063	≥20	Rio Grande do Sul (state)	No description & SRH	140/90 & 160/95
Lessa I	Embase, LILACS, PubMed & Scielo	1999	1439	≥20	Salvador	Oscillometric & BPLM	140/90
First author	Source or database	Year of data collection	N	Age criterion for study entry (years)	City, State, or region	Devices used and hypertension assessment method	BP cut-off value for hypertension (SBP/DBP in mm Hg)
Mill JG	Article references & CAPES-TD	1999	1656	25–64	Vitória	Mercury & BPLM	140/90
Gimeno SGA	Embase	2000	201	≥20	Alto Xingu	Aneroid & Mercury	140/90
de Souza LJ	LILACS	2001	1039	≥18	Campos dos Goytacazes	Aneroid &, BPLM SRH	140/90
INCA**	Article reference	2002	17059	≥25	18 Capitals	SRH	Not applicable
Jardim PCBV	Embase, LILACS, PubMed & Scielo	2002	1739	≥18	Goiânia	Oscillometric & BPLM	140/90
Barbosa JB	Embase, LILACS, PubMed & Scielo	2003	835	≥18	São Luís	Aneroid & BPLM	140/90
Capilheira MF	LILACS	2003	3100	≥20	Pelotas	SRH	Not applicable
Cassanelli T	CAPES-TD	2003	1699	18–74	Cuiabá	Device not described & BPLM	140/90
de Souza JJG	LILACS & CAPES-TD	2003	1667	≥20	São Paulo city	SRH	Not applicable
Hartmann M	PubMed, LILACS, Scielo & CAPES-TD	2003	1020	20–60	São Leopoldo	Aneroid & BPLM	140/90
Matos AC	LILACS	2003	126	≥19	Cavunge	Aneroid & BPLM	140/90
Monteiro CA*	Article references	2003	2122	≥18	São Paulo city	SRH	Not applicable
Carvalhaes MABL*	LILACS	2004	1410	≥18	Botucatu	SRH	Not applicable
Cesarino CB	LILACS & Scielo	2004	1717	≥18	São José do Rio Preto	Device not described & BPLM	140/90
de Castro RA	Embase, LILACS, PubMed & Scielo	2004	285	≥18	Formiga	Oscillometric	140/90

Table 1. Cont.

First author	Source or database	Year of data collection	N	Age criterion for study entry (years)	City, State, or region	Devices used and hypertension assessment method	BP cut-off value for hypertension (SBP/DBP in mm Hg)
First author	Source or database	Year of data collection	N	Age criterion for study entry (years)	City, State, or region	Devices used and hypertension assessment method	BP cut-off value for hypertension (SBP/DBP in mm Hg)
Borges HP*	Embase, LILACS & Scielo	2005	2352	≥18	Belém	SRH	Not applicable
Fuchs SC[†]	Article reference	2005	1007	≥18	Porto Alegre	Oscillometric, BPLM & SRH	140/90
Peixoto MRG*	LILACS	2005	2002	≥18	Goiânia	SRH	Not applicable
SOFT study	Directly from the author	2005	1858	18–90	Porto Alegre	Oscillometric & BPLM	140/90
Ferreira SRHG*	Pubmed	2006	54369	≥18	Brasília & state capitals	SRH	Not applicable
Nunes Filho JR	LILACS	2006	353	20–59	Luzerna	Aneroid, BPLM & SRH	140/90
Rosário TM	LILACS, Scielo & CAPES-TD	2006	1003	18–90	Nobres	Oscillometric	140/90
Braga Junior FD	CAPES-TD	2007	1298	20–59	Cuiabá	Device not described	140/90
Chrestani MAD	LILACS, Scielo & CAPES-TD	2007	2910	≥20	Pelotas	Wrist Oscillometric, BPLM & SRH	140/90
Longo GZ	Scielo	2007	2022	20–59	Lages	Oscillometric & BPLM	140/90

doi:10.1371/journal.pone.0048255.t001

Continuação da Tabela 1.

Tabela 2

Table 2. Meta-analysis of observational studies: prevalence rate of hypertension by decade and adjustment to the design effect, including 12 2018 individuals.

Decade	Hypertension criteria (number of studies/number of adjusted studies)	Prevalence rate (95% CI)				Adjusted *vs.* unadjusted*
		Males	Females	Overall (all studies)	Overall (adjusted studies)	
1980's	WHO (n = 5/1)	21.6 (14.9–30.2)	18.0 (11.3–27.4)	23.6 (17.3–31.4)	31.3 (28.6–34.2)	<0.001
	JNC (n = 3/2)	45.1 (40.0–50.4)	34.6 (23.7–47.5)	36.1 (28.7–44.2)	36.7 (24.4–51.0)	0.57
1990's	WHO (n = 6/0)	20.3 (17.0–24.1)	20.02 (14.4–27.6)	19.6 (16.4–23.3)	–	–
	JNC (n = 8/0)	29.7 (22.5–38.2)	27.2 (19.9–36.1)	32.9 (29.9–36.0)	–	–
2000's	Self-report in home visit (n = 4/2)	15.8 (11.7–21.0)	23.4 (16.6–31.9)	25.2 (23.3–27.2)	20.0 (14.4–27.1)	<0.001
	Self-report through telephone inquiry (n = 5/4)	18.6 (17.4–19.9)	23.2 (21.1–25.4)	20.6 (19.0–22.4)	21.4 (20.3–22.6)	0.51
	JNC (n = 14/4)	27.3 (22.5–32.8)	27.7 (23.7–32.0)	28.7 (26.2–31.4)	30.7 (26.6–35.1)	0.07
Decade	**Hypertension criteria (number of studies)**	**χ^2 (P value)**				
1980's *vs.* 1990's	WHO (n = 11)	0.33	0.10	<0.001		
1980's *vs.* 1990's	JNC (n = 11)	<0.001	<0.001	0.02		
1980's *vs.* 2000's	JNC (n = 17)	<0.001	0.006	<0.001		
1980's to 2000's	JNC (n = 25)	<0.001**	<0.001**	<0.001**		

WHO = World Health Organization diagnostic criteria; JNC = Joint National Committee diagnostic criteria; 95% CI = 95% confidence interval.
*P value for χ^2.
**P value for χ for trend.
doi:10.1371/journal.pone.0048255.t002

5.2. Figuras do artigo 1

Figura 1

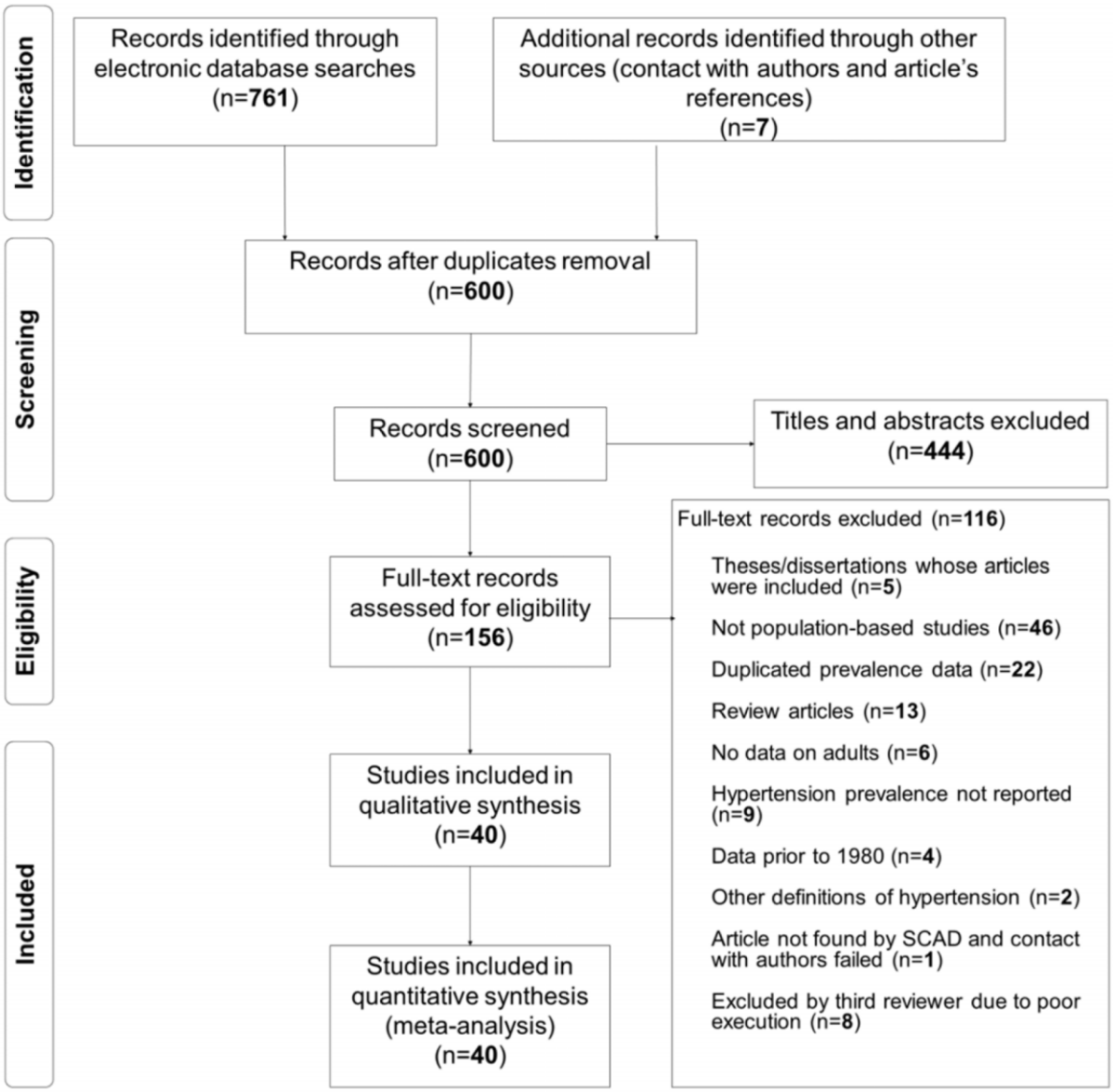


Figure 1. Flowchart of records retrieved, screened and included in the systematic review.
doi:10.1371/journal.pone.0048255.g001

Figura 2

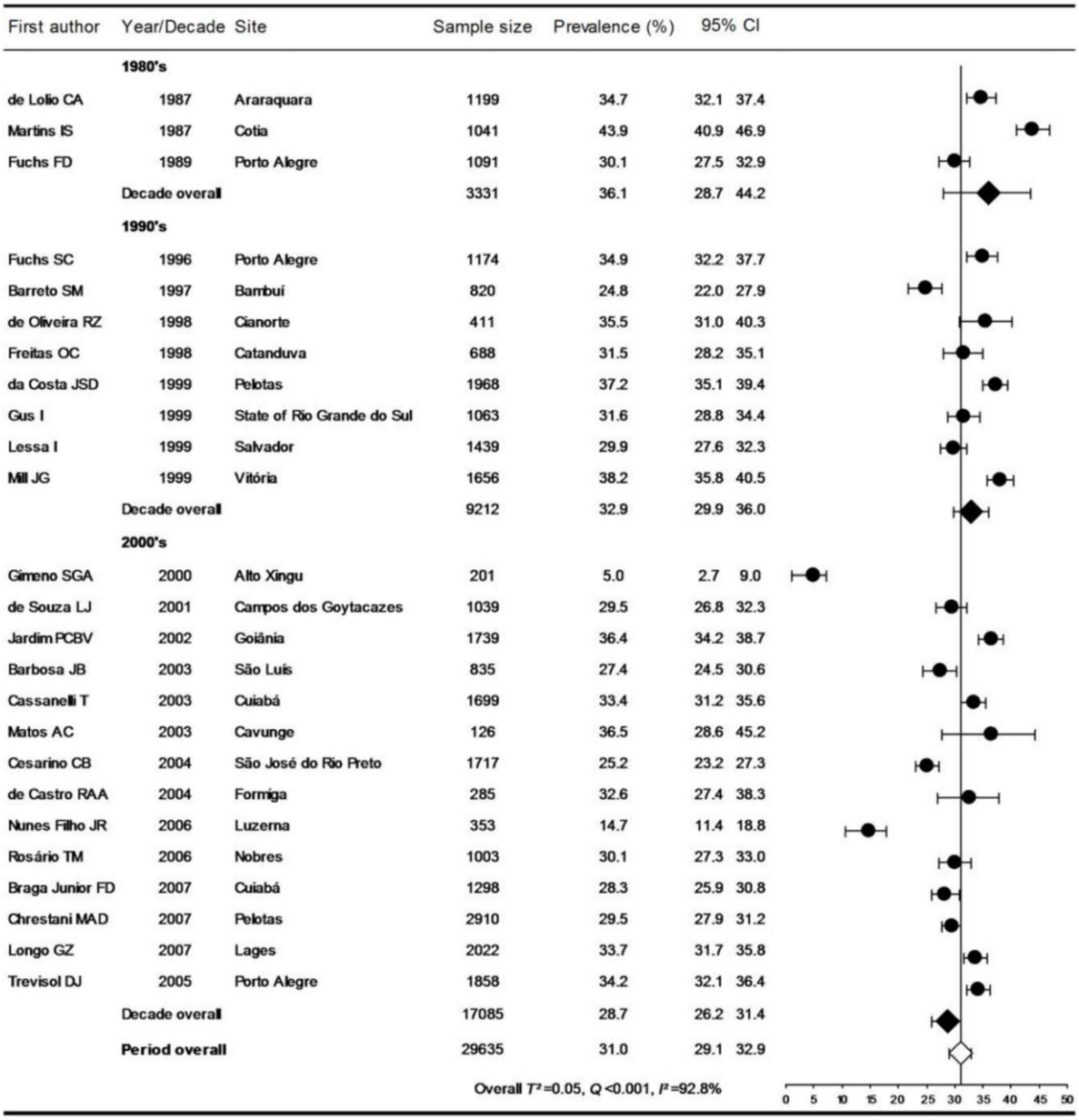


Figure 2. Prevalence of hypertension, according to the JNC criteria, by decade.
doi:10.1371/journal.pone.0048255.g002

Figura 3

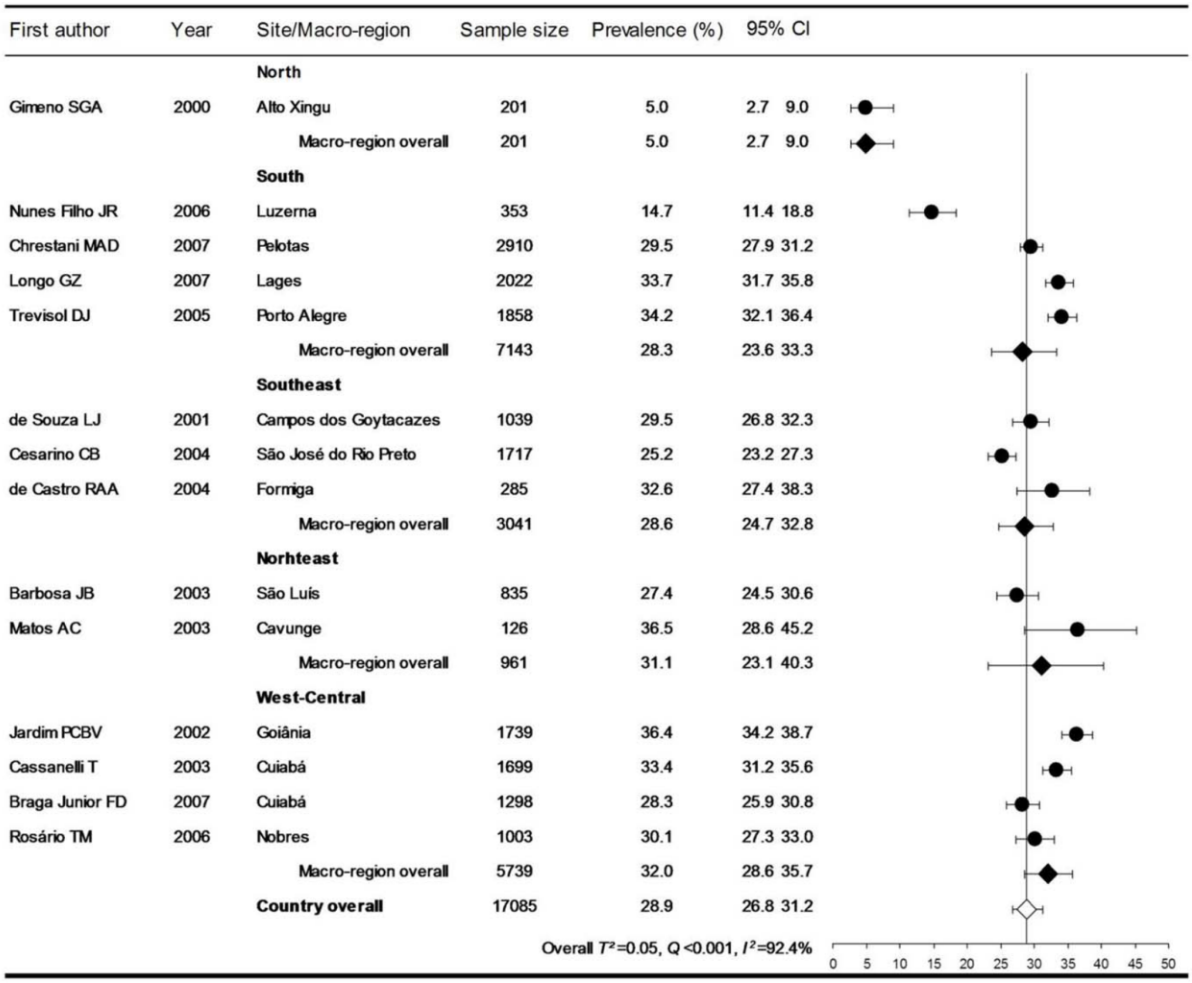
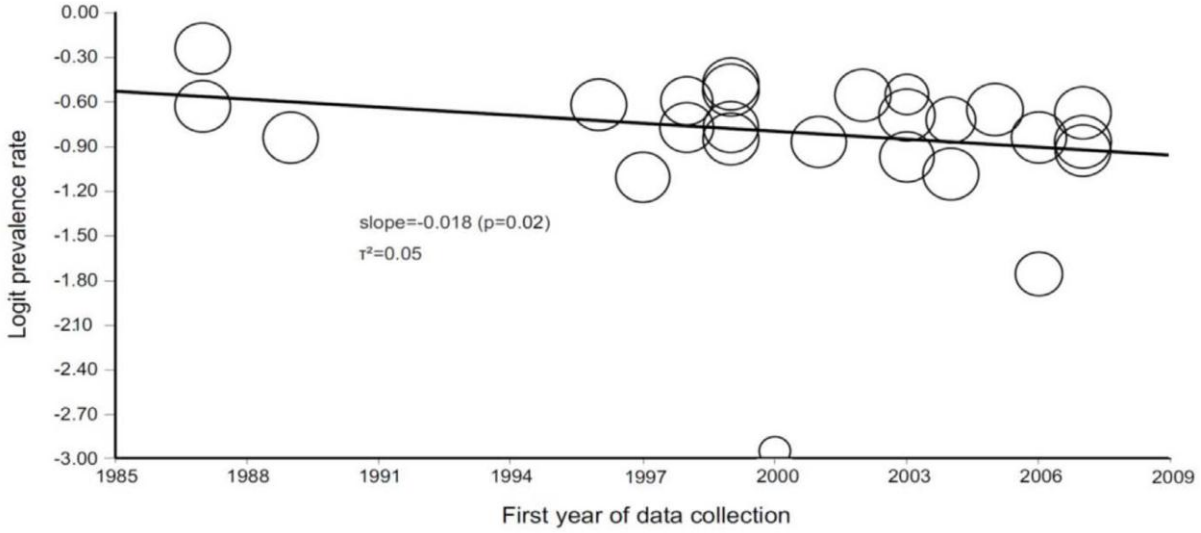


Figure 3. Prevalence of hypertension, according to the JNC criteria, by Brazilian macro-region in the 2000's.
doi:10.1371/journal.pone.0048255.g003

Figura 4



Circles are individual studies; diameters of the circles are proportional to studies' weight for the analysis.

Figure 4. Regression of first year of data collection on logit prevalence rate according to the JNC criteria.
doi:10.1371/journal.pone.0048255.g004

Figura 5

Stars are cities comprehended in the meta-analysis.

Adapted from:
Instituto Brasileiro de Geografia e Estatística. Mapas Escolares: Brasil Regiões. Accessed on September 3. Available fron
http://www.ibge.gov.br/ibgeteen/mapas/imagens/brasil_regioes_gde.gif

Figure 5. Map of Brazil according to its five macro-regions with the cities comprehended in the meta-analysis.
doi:10.1371/journal.pone.0048255.g005

5.3. Suplementos do artigo 1

Tabela suplementar 1

Table S1. List of studies selected for the systematic review and the reasons for exclusion of studies

First Author	Year of publication	Eligibility
Achutti A	1994	Excluded - Data prior to 1980
Ala L	2004	Excluded - Not population-based: restricted to certain socio-economic stratum
Alves LM	2007	Excluded - Not population-based: restricted to outpatient clinics
Ayres JE	1991	Included
Ayres JE	1990	Excluded - Review article
Barbieri MA	2006	Excluded - Other definition of hypertension
Barbosa JB	2008	Included
Barbosa PJB	2006	Excluded - Duplicate data
Barreto ML	1980	Excluded - Data prior to 1980
Barreto SM	2001	Included
Barreto SM	2003	Excluded - Duplicate data
Barros FC	1999	Excluded - No data on adults
Barros MBA	2006	Excluded - Review article
Bloch KV	1994	Included
Bloch KV	2003	Excluded - Duplicate data
Borges HP	2008	Included
Braga Junior FD	2007	Included
Bulbol WS	1981	Excluded - Other definition of hypertension
Bustos P	2007	Excluded - Duplicate data
Cabral PC	1983	Excluded - Not population-based: restricted to outpatient clinics
Capilheira MF	2004	Excluded - No report on hypertension prevalence
Capilheira MF	2008	Included
Caranti DA	2008	Excluded - No data on adults
Cardoso AM	2001	Excluded - Sampling inadequately described
Carneiro G	2003	Excluded - Not population-based: prevalence among the obese
Carvalhaes MABL	2008	Included
Carvalho JJ	1983	Excluded - Data prior to 1980
Cassanelli T	2005	Included
Cercato C	2004	Excluded - Not population-based: restricted to outpatient clinics
Cesarino CB	2008	Included
Chrestani MAD	2009	Included
Coimbra Jr CE	2001	Excluded - Full-article unavailable
Cordeiro	1998	Excluded - Not population-based: restricted to certain working class
Costa EA	1990	Excluded - Data prior to 1980
Costa VG	1984	Included
Curzio EMFO	2003	Excluded - Not population-based: restricted to outpatient clinics
da Costa AS	1986	Excluded - Other definition of hypertension
da Costa JSD	2007	Excluded - Duplicate data
da Costa JSD	2002	Included
de Aquino EMMLL	2001	Excluded - Not population-based: restricted to certain work-

		ing class
de Castro RAA	2007	Included
de Lólio CA	1989	Excluded - Thesis/dissertation whose article was included
de Lolio CA	1990	Included
de Lolio CA	1990	Excluded - Review article
de Lolio CA	1993	Excluded - Duplicate data
de Oliveira NMCM	2005	Excluded - Not population-based: restricted to certain socio-economic stratum
de Oliveira RZ	2003	Included
de Sousa LB	2006	Excluded - Not population-based: restricted to outpatient clinics
de Souza ARA	2007	Excluded - Not population-based: non-probabilistic sampling
de Souza JJG	2006	Included
de Souza LJ	2003	Included
Dressler WW	1991	Excluded - Full-article unavailable
Duda NT	1994	Excluded - Review article
Duncan BB	1993	Excluded - Not population-based: non-probabilistic sampling
Dutra CLC	2004	Excluded - No data on adults
Feijão AM	2005	Excluded - Not population-based: restricted to certain socio-economic stratum
Ferreira SRG	2009	Included
Florencio TT	2004	Excluded - Not population-based: restricted to certain socio-economic stratum
Formigli VLA	1998	Excluded - Not population-based: non-probabilistic sampling
Franco GPP	2009	Excluded - No report on hypertension prevalence
Freitas OC	2001	Included
Fuchs FD	1997	Excluded - Not population-based: restricted to outpatient clinics
Fuchs FD	1994	Excluded - Review article
Fuchs FD	1995	Excluded - Not population-based: restricted to outpatient clinics
Fuchs FD	1994	Included
Fuchs SC	2008	Included
Fuchs SC	2001	Included
Fuzikawa AK	2008	Excluded - No data on adults
Gigante DP	2009	Excluded - Duplicate data
Gimeno SGA	2007	Included
Gomes BMR	2007	Excluded - Not population-based: data restricted to students
Guimarães AC	2002	Excluded - Review article
Gus I	2002	Included
Gus I	2004	Excluded - Duplicate data
Gus M	2004	Excluded - Duplicate data
Gus M	1998	Excluded - Duplicate data
Hartmann M	2007	Included
Hasselmann MH	2008	Excluded - Not population-based: restricted to certain working class
IBGE*	2003	Excluded - No report on hypertension prevalence
INCA**	2004	Included
James SA	1991	Excluded - Review article
Jardim PCBV	2007	Included
Klein CH	1985	Excluded - Data prior to 1980
Klein CH	1995	Excluded - No report on hypertension prevalence
Klein CH	1995	Excluded - Duplicate data
Lessa I	1981	Excluded - Not population-based: data restricted to students
Lessa I	2004	Excluded - No report on hypertension prevalence
Lessa I	2006	Included
Lima-Costa MF	2004	Excluded - Duplicate data

Longo GZ	2009	Included
Lubianca Neto JF	1997	Excluded - Not population-based: restricted to outpatient clinics
Magalhães MOC	2008	Excluded - No data on adults
Makdisse M	2008	Excluded - Definition of hypertension not reported
Manfroi WC	2002	Excluded - Not population-based: patients with acute myocardial infarction
Marcopito LF	2005	Excluded - Sampling inadequately described
Marquezine GF	2008	Excluded - Duplicate data
Martins IS	1997	Included
Martins IS	1989	Excluded - No report on hypertension prevalence
Masson CR	2004	Excluded - Thesis/dissertation whose article was included
Matos AC	2003	Included
Mesquita CMB	2008	Excluded - Thesis/dissertation whose article was included
Mill JG	2004	Included
Molina MCB	2003	Excluded - Duplicate data
Monteiro CA	2005	Included
Moreira LB	1998	Excluded - Duplicate data
Muccini AR	1993	Excluded - Not population-based: subjects accessed in a Health Fair of the city
Nakazone MA	2007	Excluded - Not population-based: patients with hypertension and CVD risk factors of a private clinic
Neves EB	2008	Excluded - Not population-based: male members of the Brazilian Army Post-Graduation School for Officers
Nissinen A	1988	Excluded - Review article
Nunes Filho JR	2007	Included
Olinto MTA	2004	Excluded - Duplicate data
Oliveira EP	2006	Excluded - Other definition of hypertension
Passos VMA	2006	Excluded - Review article
Peixoto MRG	2008	Included
Pereira JC	2009	Excluded - Excluded - Duplicate data
Pereira MR	2007	Excluded - Not population-based: subject selected from a list of electric power connections
Pereira RA	1999	Excluded - No report on hypertension prevalence
Piccini RX	1994	Included
Pimenta AM	2005	Excluded - Thesis/dissertation whose article was included
Pimenta AM	2008	Excluded - Duplicate data
Polidoro AA	2008	Excluded - Not population-based: non-probabilistic sampling of undergraduate students from Maringá University
Pousada JMDC	2006	Excluded - Not population-based: Spaniards and their descendants presently living in Salvador and registered with the Spanish Consulate or at the Spanish Hospital as members of Spanish community in Salvador, Brazil
Rego RA	1990	Excluded - Not population-based: non-probabilistic sampling of 8 sectors of the city, being two of low socioeconomic status
Reichert FF	2009	Excluded - Duplicate data
Ribeiro AB	1986	Excluded - Review article
Ribeiro MD	1982	Excluded - Not population-based: workers from labor force of the Metropolitan region of São Paulo
Ribeiro RQC	2003	Excluded - Not population-based: school-based sampling of subjects aged 6 to 18 years.
Rodrigues SL	2006	Excluded - Duplicate data
Rosário TM	2009	Included
Rosenbaum P	2005	Excluded - Not population-based: Japanese-Brazilian population over 30 years of age invited to participate.

Rosini N	2006	Excluded - Not population-based: a population sample of hypertensive smokers diagnosed and enrolled at the *Hiperdia* Program of the Ministry of Health
Sabry MOD	2002	Excluded - Not population-based: employees of a university in the city of Fortaleza, in state of Ceará, Fortaleza, Brazil.
Salaroli LB	2007	Excluded - No report on hypertension prevalence
Sarno F	2007	Excluded - Not population-based: a sample of employees from a private general hospital
Sawaya AL	2005	Excluded - Review article
Schmidt MI	2009	Excluded - Duplicate data
Schwingel A	2007	Excluded - Not population-based: subjects from an urban areas in Japan and Brazil
Sichieri R	2001	Excluded - Full-article unavailable
Sichieri R	2000	Excluded - refusal to participate ≥25%
Silva GEC	2004	Excluded - Not population-based:
Silva MAD	1998	Excluded - Not population-based: patients were selected in 20 medical centers in Brazil
Simony RF	2007	Excluded - Not population-based: subjects from the first and second-generation Japanese-Brazilians
Siqueira AFA	2007	Excluded - Not population-based: non-mixed population of subjects from the first and second-generation Japanese-Brazilians living in Bauru
SOFT***	2007	Included
Sparrenberger	2008	Excluded – Duplicate data
Stamm AMNF	2007	Excluded - Not population-based: hypertensive patients undergoing treatment at the Internal Medicine and Cardiology Outpatient Clinics at a University Hospital in the Southern Region of Brazil.
Teichmann LM	2005	Excluded - No report on hypertension prevalence
Teodósio MR	2004	Excluded - Not population-based: mothers of students enrolled at schools of Jaboatão dos Guararapes, Pernambuco, Brasil
Trindade IS	1998	Included
van Eyken EBBDO	2009	Excluded - Not population-based: men 20 to 49 years of age, from a list of residents within this age range of Family Medicine Service
Velasquez-Melendez G	2007	Excluded - Not population-based: five settlements, each located between 1 and 5 km from Virgem das Graças, a rural village in the municipality of Ponto dos Volantes, situated in a semiarid region of the Jequitinhonha Valley in the state of Minas Gerais, Brazil. It was a convenient sampling.
Velásquez-Meléndez G	2002	Excluded - Not population-based: Participants were female volunteers in apparent good general health, with no chronic or acute metabolic or infectious complaints, who were treated at the various departments of the Health Center, with the objective of obtaining a wide range of age and BMI values.
Wiehe M	2004	Excluded - Thesis/dissertation whose article was included
Wiehe M	2006	Excluded - Duplicate data
Yunis C	1998	Excluded - Review article
Zaitune MPA	2006	Excluded - No data on adults

* The Brazilian Institute for Geography and Statistics
** The Brazilian National Cancer Institute
*** The Syndrome of Obesity and Cardiovascular Risk Factors Study

Tabela suplementar 2

Table S2. Spreadsheet for extraction of data of studies selected for the systematic review. The spreadsheet may be useful to those who are going to conduct a systematic review. (*Para o arquivo completo em XLS acesse o* site *supracitado*)

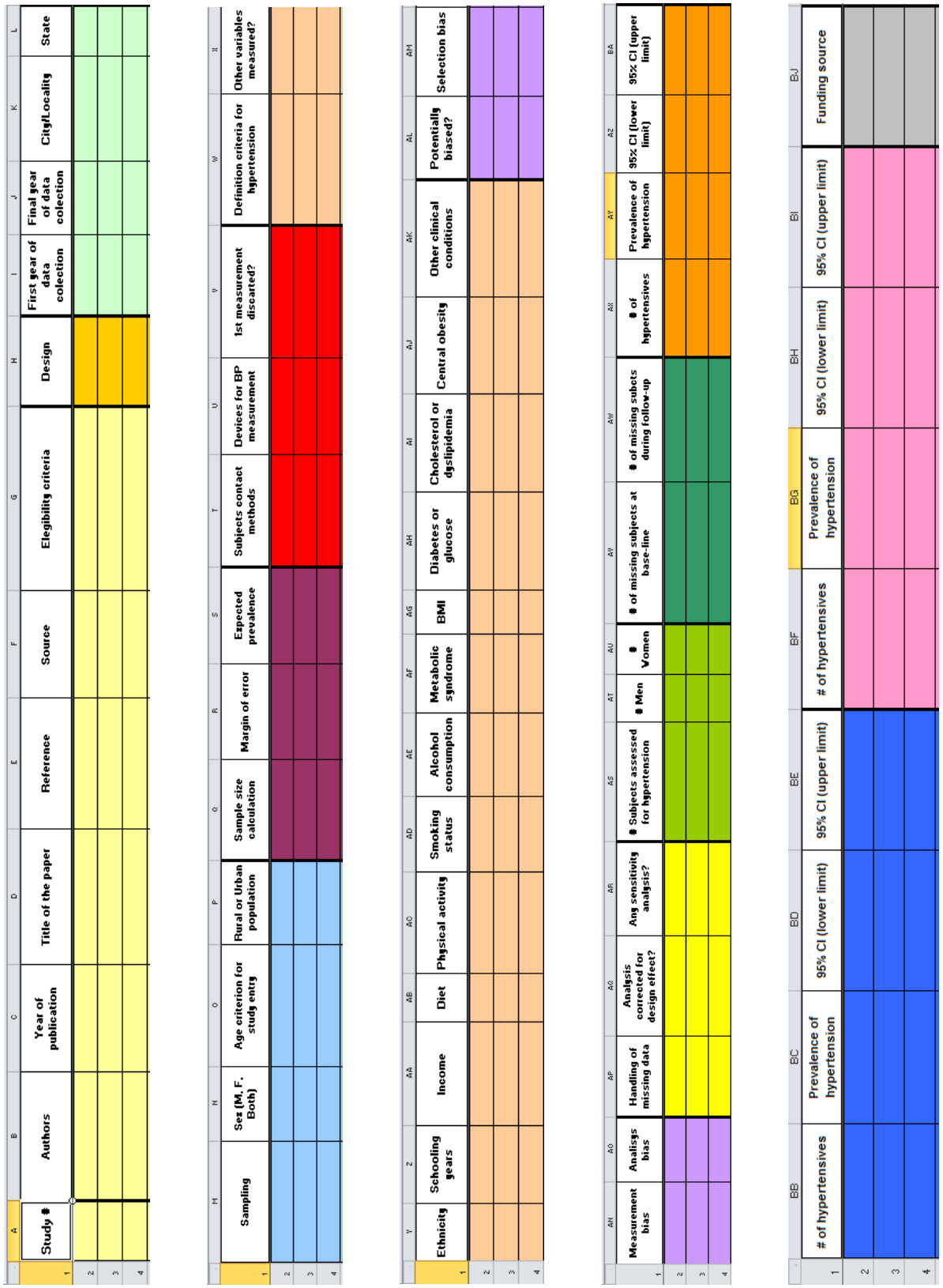


Tabela suplementar 3

Table S3. Review protocol of the Systematic Review.

1. Search strategy:

a) Key words: “hypertension”, “prevalence”, “statistics”, and “Brazil”

b) PubMed search: ("Hypertension"[Majr] AND "Prevalence") AND "Brazil" limited to all adults (≥19 years-old), and ("Hypertension/epidemiology"[Majr] OR "Hypertension/statistics and numerical data"[Majr]) AND "Brazil" limited to all adults (≥18 years-old).

c) Embase search: 'hypertension'/exp/mj AND 'prevalence'/de AND 'brazil'/exp AND ([article]/lim OR [article in press]/lim) AND [adult]/lim AND [humans]/lim

d) Screened: titles and abstracts

e) Excluded: secondary hypertension and non-probabilistic sampling*

*A probability sampling should describe: eligible population, sampling procedure, studied population (refusal or loose rate)

f) Assessed: full-text reading

g) Compared the lists of selected papers by the reviewers.

h) Disagreement among reviewers: called a third reviewer and decision for inclusion reached by consensus.

2.Data extraction:

a) Spreadsheet designed based on the Strengthening the Reporting of Observational Studies in Epidemiology Statement (STROBE) checklist: items 4, 5, 6a, 7–10, 12c–e, 13a, 14b, 16a, and 17 (see supplementary file).

Table S4. PRISMA 2009 Checklist.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

6. ARTIGO 2

PREVALENCE OF HYPERTENSION AMONG ELDERLY IN URBAN BRAZIL: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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(fator de impacto 3,2)

PREVALENCE OF HYPERTENSION AMONG ELDERLY IN URBAN BRAZIL: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Running title

Prevalence of hypertension among elderly

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Abstract

Background

The prevalence of hypertension among the elderly has been assessed in several circumscribed studies scattered across Brazil, and there is no representative data of the whole country. In this meta-analysis with systematic review we provide a summary estimate for urban Brazil and present the trend of prevalence between 1980 and 2010.

Methods

Population-based prevalence studies carried out between 1980 and 2010 were identified by two independent reviewers, with no language restrictions, in electronic databases. For PubMed searches we used the following Mesh Terms: "Aged"[Majr] AND "Hypertension" AND "Prevalence" AND "Brazil". Elderly individuals were defined as being ≥60 or ≥65 years-old, depending on the study's age cutoff. Hypertension was defined as the use of antihypertensive medication or by seated blood pressure ≥140/90 mmHg – according to the Joint National Committee (JNC) criteria. The prevalence of self-reported hypertension, assessed by household surveys and through telephone inquiries, was also evaluated. Prevalence estimates were calculated using random effects model.

Results

After the screening process, we selected 16 studies for the meta-analysis comprising 13,978 individuals. The prevalence of hypertension for the period from 1980 to 2010, according to the JNC criteria, was 68.0% (95% CI 65.1%–69.4%). In the 2000's, prevalence following the same criteria was 68.9% (95% CI 64.1%–73.3%), whereas self-reported preva-

lence through household surveys was 49.0% (95% CI 46.8%–51.2%) and through telephone surveys was 53.8% (95% CI 44.8%–62.6%).

Conclusions

Prevalence of hypertension is high among the elderly and there is considerable underestimation of disease prevalence through self-reported estimates.

Key words

Hypertension; Meta-analysis; Systematic review; Epidemiology; Prevalence; Brazil

Introduction

Hypertension is a major risk factor for cardiovascular disease (CVD), particularly in the elderly.[1] Despite the fast rising of the elderly (≥60 year-old) population in Brazil in the past decade (from 6.7%, in 2000, to 10.8%, in 2010), there is no estimate of the prevalence of hypertension for the whole country among this age group.[2,3] The importance to have better data about the prevalence of hypertension in the elderly and very elderly is emphasized by the high efficacy of the antihypertensive treatment to prolong life expectancy and to prevent the incidence of major cardiovascular outcomes of elderly and very-elderly patients with hypertension.[4,5] Nationwide estimates of prevalence of hypertension can provide information necessary to plan the allocation of resources for health care. This study aimed to present a summary estimate of the prevalence of hypertension from population-based studies and the trend between 1980 and 2010, obtained through a systematic review and meta-analysis, for the urban elderly population of Brazil.

Methods

Eligibility criteria

The eligibility criteria included population-based studies, either cross-sectional or cohort studies, conducted between 1980 and 2010 that reported the overall prevalence rate of hypertension or the prevalence stratified by age. Duplicate studies with overlapping data were excluded. Population-based studies that addressed specific socioeconomic strata (such as low-income individuals, or industry workers) were not considered representative of its geographical (city, State, or region) population and, therefore, deemed ineligible. Studies

with the former World Health Organization definition of hypertension (blood pressure (BP) ≥160/95 mmHg) were not included.

Information sources

The search of published studies was conducted from November 2009 to December 2010. The following electronic databases were used: PubMed, Embase, LILACS (Latin American and Caribbean Health Sciences Literature), and Scielo (Scientific Electronic Library Online) using MeSH terms and Emtrees for the first two, and DeCS (Health Sciences Descriptors) for other two databases. The search included the examination of the references of manuscripts and from the Brazilian Guidelines on Arterial Hypertension as well.

Data that were not formally published were additionally searched in PhD theses and master's dissertations registered in the electronic database of the Coordination for the Improvement of Higher Education Personnel (CAPES), Ministry of Education, Brazil. Annals of national and regional scientific sessions of Cardiology in Brazil were searched to identify studies presented only in these meetings. Full-text version of all potentially relevant articles or theses/dissertations were downloaded from electronic databases or requested directly to the authors.

Search

Search strategies were tested with the key words "hypertension", "prevalence", "statistics", and "Brazil", using the Boolean operator "OR", which retrieved tens of thousands of records. A second attempt was carried out in the same databases using the operator "AND". The following search strategies were used on PubMed: ("Hypertension"[Majr]

AND "Prevalence") AND "Brazil" limited to all adults (≥19 years-old), and ("Hypertension/epidemiology"[Majr] OR "Hypertension/statistics and numerical data"[Majr]) AND "Brazil" limited to all adults (≥19 years-old). Only searches on PubMed and Embase were filtered for adults of all ages. No language restriction was applied.

Study selection, data collection process, and data items

The first screening was based on a double-screening of titles and abstracts. Results which had explicit exclusion criteria such as the assessment of secondary hypertension or use of a non-probabilistic sampling were excluded. In the second step, the remaining manuscripts were assessed for full-text reading. In case of disagreement among reviewers, a third reviewer assessed the study and a decision for inclusion was reached by consensus. Data were entered in a pre-tested Microsoft Office Excel™ spreadsheet that was designed based on the Strengthening the Reporting of Observational Studies in Epidemiology Statement (STROBE) checklist.[6] Items 4, 5, 6a, 7–10, 12c–e, 13a, 14b, 16a, and 17 of the STROBE checklist were taken into account for the development of the data extraction spreadsheet.

Risk of bias within and across studies

All studies were assessed for selection and measurement bias as well as bias in the data analysis. Selection biases were characterized by a refusal rate 20% or higher among studies' participants, recruitment of participants and data collection conducted by other than home or telephone interviews, and sampling methods that were not population-based. Measurement biases were accounted considering type of device used for BP measurement, except for studies that used self-reported hypertension. Bias in the analysis was considered

possible if the design effect (i.e. the ratio between the variance calculated taking into account the complex sample design and the variance using a simple random sample) was not accounted for in calculating the prevalence of hypertension. The risk of publication bias across studies was explored by a funnel plot with prevalence rate as a function of sample size according to the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) criteria.[7]

Summary measures

Hypertension prevalence across studies comprised three diagnostic criteria: blood pressure (BP) ≥140/90 mmHg or use of BP lowering medication (BPLM) (hereafter the JNC criteria - according to the Fourth to Seventh reports of the JNC); self-reported hypertension through home visits, and self-reported hypertension through telephone inquiries.[8,9]

Synthesis of results and statistical analysis

The pooled point prevalence estimates and all subgroup analyses and their 95% confidence interval (95% CI) were calculated through random effects model according to decade, sex, and hypertension definition. Subgroup analyses included prevalence of hypertension according to the JNC criteria by decade and design effect adjustment. Heterogeneity and consistency were evaluated through Cochran's Q (*Q*) and the I^2 statistics, respectively. Chi-square (χ^2) was used to assess difference in prevalence rates among two distinct decades and to compare prevalence rates between different diagnostic criteria. Chi-square for trend (χ^2 for trend) was used to evaluate prevalence rates across the three decades. The entire analysis was performed using the second version of the Comprehensive Meta-

Analysis™ software (Biostat Inc., Englewood, NJ, USA, for more information, see: http://www.meta-analysis.com), and forest plots were constructed.[10]

Results

Study selection

Through the searches, 763 records were found in the electronic databases (51 being theses/dissertations found through the CAPES's database) and other six article references retrieved by manual search – totalizing 602 initial records after duplicates removal. Manual search of the annals of scientific sessions of Cardiology did not identify a report that had not already found in other sources. The first screening excluded 444 results and the second screening, another 142, leaving 16 final records with 13978 elderly individuals for analysis. One study from our group, conducted in 2005 and published in 2011, was reanalysed with the purpose of adding data from the 2000's.[11] Figure 1 depicts flow-chart of the identified records throughout the systematic review.

Study characteristics and risk of bias within and across studies

All studies had cross-sectional design and there was substantial (68.8%) overlapping of records across different databases. In addition, there was considerable scarcity of studies done in the 1980's, and only one fulfilled the eligibility criteria (6.3%) for that decade. Conversely, in the 1990's and the 2000's five (31.3%) and 11 (68.8%) studies, respectively were included. Moreover, the sample sizes varied considerably among studies with a median of 215 (inter-quartile range 693), as well as the devices used for BP measurements, five studies reported the use of aneroid or mercury manometers and six used oscillometric monitors.

Finally, all studies analyzed urban populations (one assessed both rural and urban, but prevalence rates did not differ) mostly from the south and southeast regions of Brazil.

The description of the studies regarding methodological features and the definition of hypertension are shown in Table 2. Seventeen studies used multistage cluster sampling and one used random sampling. Additionally, six (37.5%) studies used design effect adjustment for the statistical analysis, being five from the 2000's and only one from the 1980's.

A funnel plot is shown in Figure 2 in which studies' prevalence rates are a function of their sample size, according to the JNC criteria as of 1980, scattered around the pooled prevalence estimate, depicted as a red line. Seven out of 10 studies laid within five percentage points from the pooled estimate in an anarchical distribution, making publication bias unlikely.

Synthesis of results

Pooled prevalence estimates for 13,978 elderly individuals were described according to hypertension criteria and by study decade in Table 3. As noted, the JNC criteria were assessed throughout the three decades, although there was only one study from the 1980's. Self-reported hypertension through household visits and telephone inquiries has been seen only since 2000.

Figure 3 shows that the prevalence of hypertension, according to the JNC criteria, was roughly stable among the three decades: 64.5% (95% CI 57.6–70.8%) in the 1980's, 68.0% (63.5–72.1%) in the next decade, and 68.9% (64.1–73.3%) in the 2000's. The pooled prevalence for the whole period was 68.0% (65.1–70.8%).

During the 2000's, the pooled prevalence for self-reported hypertension in the household surveys was 49.0% (46.8–51.2%) and 53.8% (44.8–62.6%) for self-reported hypertension. There were statistically significant differences between pooled prevalence rates according to the measured and self-report by the JNC criteria, with the underestimation of hypertension on household and telephone interviews of 19.8% and 15.1%, respectively. There were no differences on rates between overall and design effect-adjusted pooled prevalence within diagnostic criteria, except for self-reported hypertension through telephone, with a 4.0% absolute difference.

Discussion

In this systematic review we described estimates of the prevalence of hypertension among elderly individuals in urban Brazil and the trends of prevalence for the past three decades. Our results present a comprehensive view about the burden of hypertension in the country, especially for the urban population of the south and southeast regions, demonstrating that around two thirds of elderly Brazilians have hypertension and that there was substantial underestimation by self-report surveys. There was no substantial variation in the prevalence in the last decades – although 12, out of the 16, studies came from the same decade –, indicating that public and individual interventions aiming to prevent hypertension failed to lower the prevalence of hypertension in this age group.

Our prevalence estimates of 68.0% were not different from those reported for this age stratum in other countries. In the United States, the prevalence between 1999 and 2004 was 78.0% for elderly women and 64.0% for elderly men.[12] In Japan (60%) and Taiwan (48.0% for males and 60.0% for females) the prevalence tended to be lower, but in and

South Korea the prevalence rate for elderly men and women was 68.7%, similar to our findings.[13-15] Similarly, in Portugal, the country of origin of most Brazilian Caucasians ancestors, the reported prevalence rates for men and women in 2003, according to the JNC criteria, were 79.0% and 78.7%, respectively.[16]

As expected, substantial absolute difference in the prevalence of hypertension by direct measurement and self-reported methods of evaluation was found.[17–19] The non-universal access to landlines might explain the difference seen on telephone interviews, as the poorest, and most affected, segments of the population were underrepresented in those studies.[8,20] In addition, memory bias is another potential problem that may explain such discrepancy.[18] Even so, the elderly population is growing with increased life expectancy, in parallel with the burden of cardiovascular disease. The results based on studies that measured the blood pressure of the participants showed that the prevalence of hypertension remained stable along the three decades. It is of note, however, this is just a rough estimate of stability, since in the decade of 1980 there is only one study, in comparison with three in the 1990's and 12 in the last decade.

The major limitation of our study was the absence of studies representative of some regions of the country. Moreover, the studies were conducted mainly in metropolitan regions, not investigating the people from smaller cities and rural regions. The skewed distribution of studies might have biased the overall estimate. Nonetheless, nowadays, 84.4% of the Brazilian citizens live in urban regions.[8] In addition, most studies did not take into account the distortions caused by multistage and weighting sampling. The lack of adjustment for design effect can compromise the confidence intervals, but the weighting affects accuracy of individual studies – and, consequently, the pooled prevalence estimates – making the results of older studies less reliable than those done in the last decade.[21-23] Nevertheless,

the comparison between studies with and without adjustment for sampling design showed that the former provided reliable estimates for the JNC and self-report through home visit criteria. Despite the heterogeneity of studies, lack of adjustment for design effect in many studies, and underrepresentation of rural populations, the estimates are reliable and within the range of prevalence described for industrialized nations.[12-16] Another potential problem is the impossibility to address masked and white coat hypertension in our study. A recent population-based study conducted among elderly aged 75 years or older showed that the rate of masked hypertension can be as high as 41%.[24]

In conclusion, the prevalence of hypertension among elderly Brazilians remained stable in the last three decades, affecting two out of three elderly individuals. Self-reported assessment of hypertension, either by home visits or telephone interview deemed to be an unreliable and inaccurate method for the elderly population in our country. Nationwide well designed population-based studies are warranted to provide more precise and representative prevalence estimates, but the current evidence is sufficient to compel for urgent measures to tackle the burden of hypertension among the elderly in Brazil.

Disclosure

The authors declare no conflicts of interest.

Funding

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(IATS), and the Fund for Research and Events (FIPE) of the Hospital de Clínicas de Porto Alegre, RS, Brazil. The funding agencies had no participation in the planning, execution, or in the analyses of this study.

Author Contributions

SF and RP: conceived the study hypothesis; RP: designed the analysis plan; FF and LBM: contributed to the data interpretation and preparation of the manuscript. All authors approved the final version of the manuscript.

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6.1. Tabelas do artigo 2

Tabela 1

Table 1. Source, year, sample size and methodological aspects of the 16 studies included in meta-analysis (in chronological order)

First author	Source or database	Data collection	N	Elderly defined as	City, state, or locality	Devices used and hypertension assessment method	BP cut-off value for hypertension (SBP/DBP in mmHg)
Fuchs FD	Embase, PubMed, and LILACS	1989	201	≥68 years	Porto Alegre	Aneroid & BPLM	140/90 & 160/95
de Oliveira RZ	Embase and LILACS	1998	43	≥60 years	Cianorte	Mercury & BPLM	140/90 & 160/95
da Costa JSD	LILACS & CAPES-TD	1999	229	≥60 years	Pelotas	Aneroid & BPLM	140/90 & 160/95
Lessa I	Embase, LILACS, PubMed, and Scielo	1999	179	≥60 years	Salvador	Oscillometric & BPLM	140/90
INCA*	Article reference	2002	2833	≥60 years	18 Capitals	SRH-HI	Not applicable
Jardim PCBV	Embase, LILACS, PubMed, and Scielo	2002	260	≥60 years	Goiânia	Oscillometric & BPLM	140/90
Barbosa JB	Embase, LILACS, PubMed, and Scielo	2003	123	≥60 years	São Luís	Aneroid & BPLM	140/90
de Souza JJG	LILACS and CAPES-TD	2003	872	≥60 years	São Paulo City	SRH-HI	Not applicable
Giacomin KC	Pubmed	2003	1786	≥70 years	Belo Horizonte	SRH-HI	Not applicable
de Castro RA	Embase, LILACS, PubMed, and Scielo	2004	36	≥65 years	Formiga	Oscillometric	140/90
Borges HP	Embase, LILACS, and Scielo	2005	200	≥65 years	Belém	SRH-HI	Not applicable
Peixoto MRG	LILACS	2005	190	≥65 years	Goiânia	SRH-HI	Not applicable
Trevisol	Reanalysis of data	2005	599	≥60 years	Porto Alegre	Oscillometric	140/90

First author	Source or database	Data collection	N	Elderly defined as	City, state, or locality	Devices used and hypertension assessment method	BP cut-off value for hypertension (SBP/DBP in mmHg)
Ferreira SRG	Pubmed	2006	5654	≥65 years	Brasília e 26 capitals	SRH-HI	Not applicable
Rosário TM	LILACS, Scielo, and CAPES-TD	2006	180	≥60 years	Nobres	Oscillometric	140/90
Chrestani MAD	LILACS, Scielo, and CAPES-TD	2007	593	≥60 years	Pelotas	Oscillometric & BPLM	140/90

N = study sample size; CAPES-TD = CAPES Electronic Theses Database; SRH-HI= self-reported hypertension in home interview; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; BPLM = use of blood pressure lowering medication; INCA = National Cancer Institute.

* Self-reported hypertension assessed through survey in the Federal District and in state capitals: Aracaju, Belém, Belo Horizonte, Campo Grande, Curitiba, Florianópolis, Fortaleza, João Pessoa, Manaus, Natal, Palmas, Porto Alegre, Recife, Rio de Janeiro, São Luís, São Paulo and Vitoria.

Table 2. Clustered definition of hypertension, sampling and critical appraisal of the 16 studies included in the meta-analysis (in chronological order)

Decade	Data collection	First author	Definition of hypertension	Sampling	Design effect adjustment	Potential selection bias in the study
1980's	1989	Fuchs FD	JNC	Multistage	Yes	No
1990's	1998	de Oliveira RZ	JNC	Multistage	No	
	1999	Lessa I	JNC	Multistage	No	
		da Costa JSD	JNC	Multistage	No	
2000's	2002	INCA	SRH-HI	Multistage	No	
		Jardim PCBV	JNC	Multistage	No	
		Barbosa JB	JNC	Multistage	No	
	2003	de Souza JJG	SRH-HI	Multistage	Yes	
		Giacomin KC	SRH-HI	Multistage	No	
	2004	de Castro RA	JNC	Simple random	Not applicable	
		Borges HP	SRH-TI	Multistage	No	Telephone recruitment & sampling poorly described
	2005	Trevisol	JNC	Multistage	Yes	
		Peixoto MRG	SRH-TI	Multistage	Yes	Telephone recruitment & 27% missing data
	2006	Ferreira SRG	SRH-TI	Multistage	Yes	Telephone recruitment
		Rosário TM	JNC	Multistage	Yes	
	2007	Chrestani MAD	JNC	Multistage	No	

JNC = Joint National Committee criteria; INCA = National Cancer Institute.

SRH-HI: self-reported hypertension in home interview

SRH-TI: self-reported hypertension in telephone interview

Table 3. Meta-analysis of observational studies: overall, and adjusted for design effect, prevalence rates by decade

Decade	Hypertension criteria	N of studies (N studies adjusted to design effect)	Overall			Adjusted studies prevalence (95% CI)	Overall *vs.* Adjusted*	JNC *vs.* other criteria*	
			Prevalence [% (95% CI)]	*Q* (P)	I^2 (%)			Overall	Adjusted
1980's	JNC	1 (1)	64.5 (57.6–70.8)	1	0	64.5 (57.6–70.8)	1	–	–
1990's	JNC	3	68.0 (63.5–72.1)	0.42	0	–	–	–	–
2000's	SRH-HI	3 (1)	49.0 (46.8–51.2)	0.01	47.4	46.8 (43.5–50.1)	0.14	<0.001	<0.001
	SRH-TI	3 (2)	53.8 (44.8–62.6)	0.02	73.8	57.8 (56.5–59.1)	0.01	<0.001	<0.001
	JNC	6 (2)	68.9 (64.1–73.3)	0.01	66.4	69.1 (61.4–75.9)	0.33	–	–

Decade	Hypertension criteria (N of studies)	Comparison between and across decades*	
		Overall	Adjusted
1980's vs. 1990's	JNC (4)	0.40	–
1980's vs. 2000's	JNC (7)	0.40	0.18
1980 through 2010	JNC (10)	0.56 **	–

JNC: Joint National Committee
SRH-HI: Self-reported hypertension in household interview
SRH-TI: Self-reported hypertension in telephone interview
N = number; 95% CI = 95% confidence interval.
* Comparison between proportions (χ^2 P value).
** Comparison between proportions (χ^2 for trend P values).

6.2. Figuras do artigo 2

Figura 1

Figure 1. Flow chart of records retrieved, screened, and included in the systematic review.

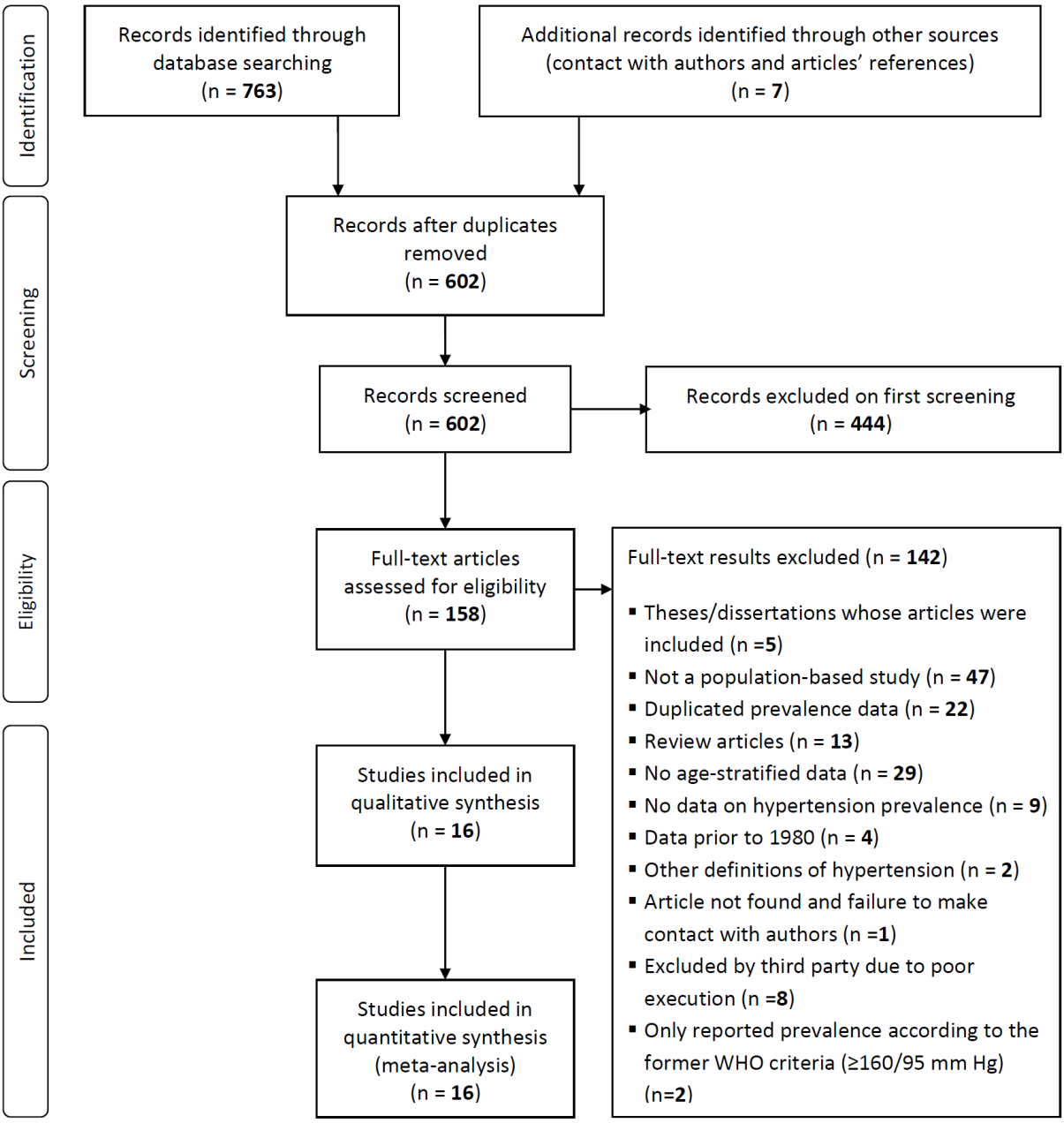


Figura 2

Figure 2. Funnel plot showing studies' sample size as a function of their respective prevalence rates, according to the JNC criteria, with pooled hypertension prevalence, from 1980 to 2010, depicted as a vertical line.

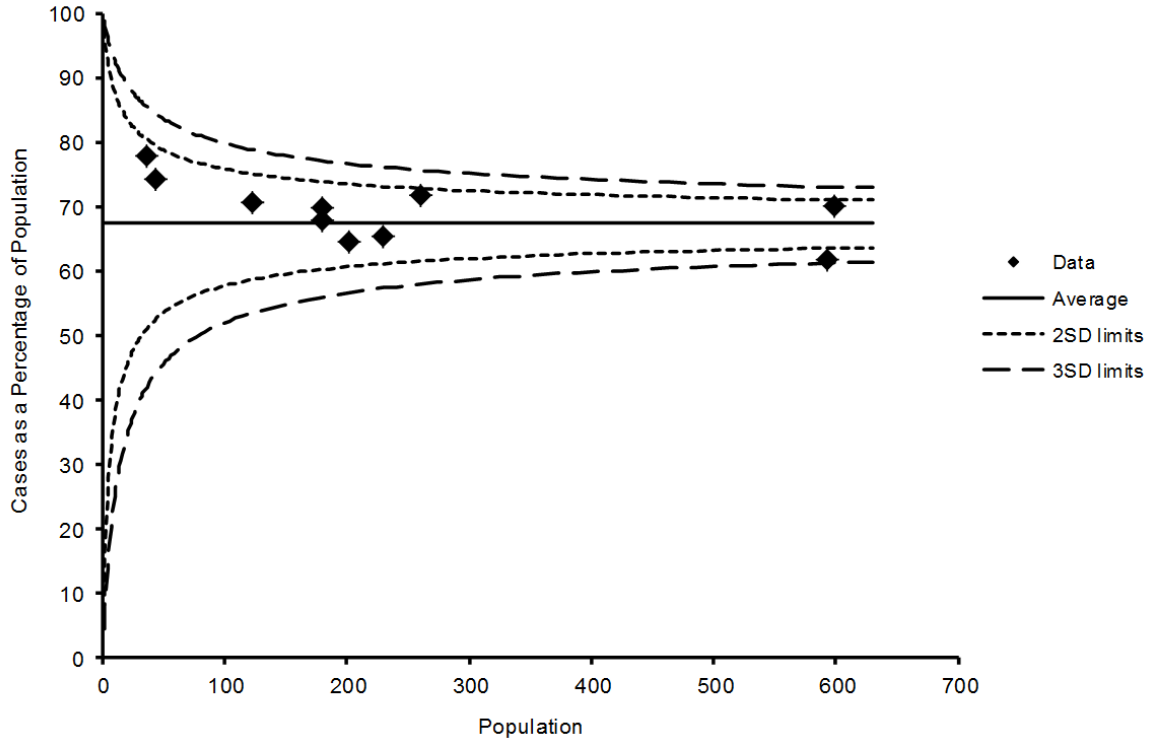
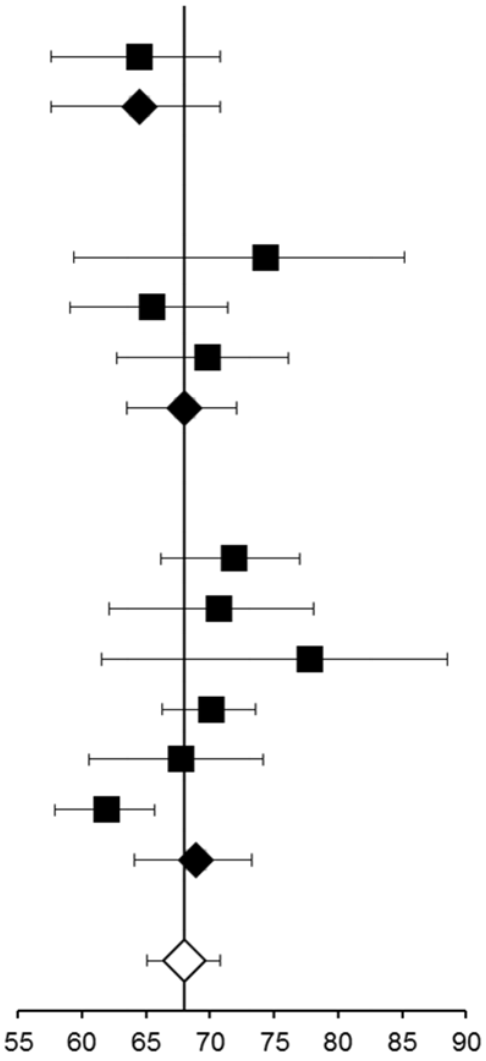


Figure 3. Pooled prevalence of hypertension according to the JNC criteria by decade.

First author	Decade/year	N	Prevalence (%)	CI 95%	
	1980				
Fuchs FD	1989	201	64.5	57.6	70.8
Decade overall		201	64.5	57.6	70.8
	1990				
de Oliveira RD	1998	43	74.4	59.4	85.2
da Costa JSD	1999	229	65.5	59.1	71.4
Lessa I	1999	179	69.8	62.7	76.1
Decade overall		451	68.0	63.5	72.1
	2000				
Jardim PCBV	2002	260	71.9	66.2	77.0
Barbosa JB	2003	123	70.7	62.1	78.1
de Castro RAA	2004	36	77.8	61.5	88.5
Trevisol DJ	2005	599	70.1	66.3	73.6
Rosário TM	2006	180	67.8	60.6	74.2
Chrestani MAD	2007	593	61.9	57.9	65.7
Decade overall		1791	68.9	64.1	73.3
Period overall		2443	68.0	65.1	70.8

N = sample size; 95% CI = 95% confidence interval



7. ARTIGO 3

HYPERTENSION MANAGEMENT IN BRAZIL: USUAL PRACTICE IN PRIMARY CARE – A SYSTEMATIC REVIEW WITH META-ANALYSIS

HYPERTENSION MANAGEMENT IN BRAZIL: USUAL PRACTICE IN PRIMARY CARE – A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Abstract

Background

For many years, several Brazilian medical societies have suggested their own clinical guidelines to be incorporated by the Brazilian public healthcare system without contemplating the already established health care scenario. However, understanding how a disease is customarily managed is crucial for health economical evaluations, since usual clinical practice (the *status quo*) is an always valuable baseline comparator for such assessments. Evermore relevant diseases like hypertension should have their typical management taken into consideration for cost-effectiveness analysis, and before the incorporation of a new health technology or treatment guideline into the healthcare system. Thus, we aim to give an accurate description on Brazil's usual clinical practice toward hypertension management in primary care.

Methods

A systematic review of population-based and outpatient-based cross-sectional or cohort studies carried out since 2000 was undertaken using the PubMed, Embase, and Brazilian Virtual Health Library databases. Target population was composed by adults from the general population or treated in primary care facilities affiliated to the Brazilian public healthcare system. Variables of interest were: frequency of medical appointments and type of healthcare service used; number and frequency of diagnostic tests; number and type of blood pressure lowering medication in use; and clinical characteristics.

Results

Hypertensive individuals had in average 2.6 medical appointments per year and half stated using the Brazilian public healthcare services most of the time. Three quarters were using al least one blood pressure medication and a third of individuals were in use of two drugs. Thiazide type diuretics (18.2%) and angiotensin-converting enzyme inhibitors (16.2%) were the most often used medications in single-drug therapy and combined with each other (14.9%). Approximately a third of hypertensives were tested for total serum cholesterol, triglycerides, fasting plasma glucose, and serum creatinine in the last 12 months. Current smokers accounted for 21.7% of subjects with hypertension and 13.5% of hypertensives were also diabetics.

Conclusions

More information on hypertension management inside the Brazilian primary care setting is still needed. Nonetheless, our assessment achieved its goals of describing relevant aspects of usual primary care in Brazil. Future economical evaluations are needed to assess forthcoming clinical guidelines' cost-effectiveness over the *status quo*.

Key words

Hypertension, primary care, usual clinical practice, Brazilian Healthcare System, *Sistema Único de Saúde*, systematic review, and meta-analysis.

Introduction

Measurement of costs and determination of the health outcomes can generate estimates to compare and choose between screening, diagnostic or therapeutic strategies to be incorporated into a healthcare system. The purpose is to achieve maximum health gains with the available resources, thereby respecting the expectations of the population covered by the Brazilian public healthcare system – the Unified Health System (*Sistema Único de Saúde* (SUS)) –, and considering the limitations of those resources.[1] Bearing this concept in mind, health economic evaluations (HEE) rises as useful tools for health policy makers when they have to ponder resource allocation between two or more health strategies, or even the assimilation of an entirely new health technology. HEE are particularly valuable when considering the incorporation of health strategies to prevent and control non-communicable diseases, which impose a great burden in Brazil.

Among these diseases is hypertension (HT), with estimated prevalence of 28.7% (95% confidence interval (95% CI) 26.2–31.4%).[2] Hypertension is a well-known risk factor for cardiovascular disease (CVD), responsible for significant morbidity and mortality, a subject already extensively studied. [3,4] For many years, strategies for detection and treatment of HT are recommended, in de United States, by the reports of the Joint National Committee, on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC), and in Brazil, by the Brazilian Hypertension Guidelines (DBH), currently in its seventh and sixth edition, respectively.[5,6] However, approaches supported by the DBH towards diagnosis, risk stratification, and treatment of HT have never had their cost-effectiveness properly assessed.

A suitable HEE on that matter would include a comparison between the DHB strategy and usual practice (*status quo*) in the context of outpatient care targeting primary CVD pre-

vention. The *status quo* may serve as the baseline for comparisons whenever a new health strategy is being proposed for consideration.[7] Nevertheless, one might argue that such evaluation has never been done simply because the *status quo* has never been adequately described, it varies according time and place, or even that there is not only one *status quo*. Hence, our study aims to describe the usual practice, in the SUS primary care setting, toward diagnosis, risk stratification, and pharmacological treatment of HT.

Methods

Design and data sources

To assure data's comprehensiveness and maximize our findings' generalization capacity, a systematic review of the pertinent literature followed by meta-analyses of collected data was carried along with re-analyses of three available datasets.[8–10] Studies selected from a previously undertaken systematic review and meta-analysis on prevalence of HT in Brazil were also used as data source.[2]

Two of the datasets are from population-based cross-sectional studies, which were also included in the previous systematic review, conducted among representative samples of two cities: one undertaken in Porto Alegre, and the other in Pelotas.[11,12] The third dataset was originated from a nationwide cross-sectional study conducted among industry workers (SESI study) – previously carried out by one of the authors and not included in the aforesaid systematic review – that provided relevant laboratory measuremtents.[13,14]

Searches for the review were carried out on PubMed, Embase, and the Brazilian Virtual Health Library (BVS) with no language restriction. Data from the Registration and Moni-

toring of Hypertensive and Diabetic Patients Program (HIPERDIA) – a nationwide register of hypertensive and diabetic patients treated in SUS' primary care facilities – were extracted from database (DATASUS) website.[15] Searches were conducted on April 2012.

Target population and variables of interest

Our target population was composed by Brazilian adults (≥18 years) with usual blood pressure (BP) ≥140/90 mmHg or in use of BP lowering medication (BPLM) either from the general population or from those treated in SUS's primary care facilities. In order to gather relevant information on patient management and to assure comparability with the 6th edition of the DBH, the following variables were searched for data extraction: frequency of medical appointments and type of healthcare service (e.g. SUS's, private, or health plan physician) used most of the time; number and frequency of diagnostic tests comprised in the DBH (e.g. ECG, fasting plasma glucose, and radiography); number and type of BPLM (at least the pharmacological class of the antihypertensive); clinical characteristics such as mean systolic BP (SBP), mean serum total cholesterol and high-density lipoprotein (HDL) cholesterol, and prevalence of other relevant morbidities used in the estimation of patients' CVD risk (i.e. *diabetes mellitus* (DM) and smoking status).[16] Smoking and diabetes prevalence rates among hypertensive individuals registered in HIPERDIA from May 2002 to April 2012 were also assessed.

Eligibility criteria for the review and screening process

Studies conducted in Brazil, since 2000, including patients with HT treated in any primary care facility affiliated to the SUS or population-based studies which reported data on adults with HT were considered eligible for data extraction. Inpatients were out of the scope of this analysis, thus studies carried out on this population were excluded. Outpatient studies that did not assess any of the abovementioned variables were also excluded.

The search results retrieved were handled in a double-screening fashion: first their titles and abstracts were scrutinized, then, those deemed eligible had their full-texts examined. Duplicated results were excluded.

Search strategies

The following search strategies were employed: on BVS using Health Science Descriptors (DeCS): "Hipertensão" AND "Atenção Primária à Saúde" AND "Brasil"; on Embase using Emtrees: 'brazil'/exp AND 'hypertension'/exp AND 'primary health care'/exp; and on Pubmed using MeSH Terms: (("Hypertension"[Mesh]) AND "Primary Health Care"[Mesh]) AND "Brazil"[Mesh].

Data analysis

Continuous data were treated as means and standard deviations (SD). Binary data were treated as proportions using point estimates and 95% confidence interval (95% CI). Meta-analyses were performed whenever our data allowed pooling means or proportions. Random effects model was mostly used, however, fixed effect model was employed when

non-significant (P value ≥0.05) heterogeneity was observed, as measured by Cochran's Q. The I^2 statistic was employed as a measure of inconsistency. Because this study is entirely descriptive, we did not formulate nor test any hypothesis.

Results

Figure 1 depicts the flow of search results in this review. The BVS search retrieved 31 results, PubMed 18 results, and Embase another 31 results. Embase and BVS retrieved identical results which encompassed all of the 18 articles found in PubMed. After first screening and removal of overlapping result across databases, 19 articles were deemed eligible.

Four studies reported data on at least one of the stipulated variables of interest and were included in the meta-analysis. Another four studies included in the previous systematic review were considered eligible and, hence, were added to the meta-analysis along with the three aforementioned datasets, rendering a total of 11 studies.

Table 1 shows the five studies and the HIPERDIA registry, which provided data on clinical characteristics of individuals with HT according to sex. Higher prevalence of DM was seen among patients registered in HIPERDIA, especially when compared to the participants of the SESI study. Smoking prevalence rates were more evenly distributed across the SESI study, HIPERDIA registry, and the population-based studies, with a higher prevalence of current smokers in men in comparison to women.

Table 2 describes information from seven studies which provided data on pharmacotherapy, diagnostic tests, and medical appointments. Less than half of the hypertensive subjects were using a single BPLM, and the most common class of BPLM was thiazide diuret-

ics, followed by angiotensin-converting enzyme inhibitors. Data on diagnostic tests came from one study, and estimates on most used type of medical services came from another study. Approximately a third of individuals with known HT were screened to other morbidities by fasting plasma glucose, serum triglycerides, total cholesterol, and creatinine level in the previous 12 months. On average, an adult with HT had 2.6 medical appointments per year, and more than half of subjects who sought medical appointments used mostly those provided by the SUS. Figures 2, 3, and 4 are forest plots illustrating contents from Table 2.

Discussion

Our systematic review examined every pertinent available database that might have some information on the management of HT among the Brazilian adult population. Unfortunately, there is a scarcity of reports on this subject. Most of the 19 articles selected after the first screening did not report any quantitative data found relevant to this review. Some of them only qualitatively described the implementation of different local Health Secretariats' treatment guidelines or discoursed over the importance of such.[17-19] One article assessed physicians compliance to a municipal HT treatment guideline and detected nonconformity rates of 56.8%, 63.8%, and 54.0% regarding HT staging, cardiovascular risk classification, and choice of treatment, respectively.[20]

The paucity of publications contrasts with the huge amount of relevant data on patient management generated every day, since Brazil has one of the largest healthcare systems, which provides free and universal coverage to an enormous population.[21] Additionally, there were more than 40.4 million medical appointments recorded in the HIPERDIA registry from August 2011 to July 2012.[15] But one must be careful when interpreting administra-

tive databases since, even though they have great amounts of data, they are not completely reliable.[22,23]

Although there are several population-based studies that evaluated the prevalence of HT all over the country, only four studies provided information on how participants with hypertension were treated. The vast majority of these field studies restricted their assessment to measuring the prevalence of HT and other diseases among the general population, reporting little or no information with regard to individuals with HT (e.g. mean age of participants with HT).

In addition, there are controversies among population-based information and the government sources. For instance, approximately half of the participants with HT detected in the population-based study carried in the city of Pelotas reported have been using SUS' services most frequently. It contrasts with official data claiming that three quarters of the country's population depends exclusively on SUS for health care.[24] This may be explained by biases in both sources of information; the use of SUS services could not reach the 75% rate of use for all health conditions or recall bias for the medical appointments made in the previous month by participants of the population-based study. Nonetheless, the review data derives from a single city therefore is hardly representative of the entire country.

Pharmacotherapy, conversely, was more often reported in studies, and we believe it to be more representative of the reality of those who seek medical assistance through the SUS. Blood pressure control rates among individuals with HT are not shown, but previously conducted systematic review identified a pooled control estimate of 24.1% (10.1–47.3%).[2]

Finally, this review attempted to summarize the *status quo* of HT management in Brazil in order to construct a useful research tool for future HEE. More information on hypertension management inside the Brazilian primary care setting is still needed. However, we believe that, even though there are limitations to this work, our assessment achieved its goals of describing relevant aspects of usual primary care. We also trust that usual medical practice should be better understood before suggesting improvements over it or the incorporation of a nationwide clinical guideline. Perhaps, forthcoming guidelines would be more easily incorporated by the SUS health services and accepted by clinicians if one could establish cost-effectiveness dominance over the *status quo*.

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7.1. Tabelas do artigo 3

Tabela 1

Table 1. Clinical characteristics of individuals with hypertension from the SESI study, the HIPERDIA registry, and from meta-analyses of four population-based studies

Studies and clinical characteristics of participants	Mean (±SD) / Prevalence (95% CI)	
	Men	Women
SESI study: no. of participants	1034	114
Age (years)	40.57 (11.75)	41.50 (9.20)
Systolic blood pressure (mmHg)	152.54 (15.91)	150.36 (21.65)
Total cholesterol (mg/dL)	188.82 (39.96)	195.99 (39.19)
HDL cholesterol (mg/dL)	49.30 (20.94)	56.76 (12.69)
Current smokers	18.30 (15.94–20.66)	15.50 (8.86 –22.14)
Diabetes mellitus	5.6 (4.20–7.00)	3.5 (0.13–6.87)
HPERDIA registry: no. of participants	2.5 million	4.8 million
Current smokers	21.42 (20.39–22.5)	15.58 (14.71–16.49)
Diabetes mellitus	21.87 (19.84–24.04)	24.87 (22.85–27.00)
Current smokers with DM	6.31 (5.84–6.81)	5.62 (5.22–6.04)
Population-based studies: no. of participants	5064	8126
Current smokers	21.69 (17.17–27.01)‡	14.76 (10.12–21.03)*
*Diabetes mellitus***	13.46 (12.53–14.44)†	13.29 (8.25–20.71)#

‡ Q p<0.01; I^2=90.0%
* Data from 7867 women. Q p<0.01; I^2=94.1%
† Fixed effect model analysis. Q p=0.24; I^2=27.4%
** Data from 4912 men and 7867 women.
# Q p<0.01; I^2=87.3%

Tabela 2

Table 2. Frequencies of blood pressure lowering medication use, diagnostic tests, and medical appointments

	Prevalence (95% CI)/mean (±SD)		
	Status quo	Q P-value	I^2
Blood pressure lowering medication (%)			
In use of one BPLM	42.7 (28.6–58.1)	<0.01	99.0
In use of two BPLM	33.0 (23.7–43.9)	<0.01	92.4
Type of BPLM			
Thiazide diuretics			
Single-drug or combined therapy	46.1 (33.2–59.6)	<0.01	97.5
Single-drug therapy	18.2 (7.4–38.4)	<0.01	96.6
Combined with ACEI	14.9 (11.1–19.8)	<0.01	84.6
Combined with BB	9.4 (5.7–15.2)	<0.01	86.5
Combined with CCB‡	5.0 (2.4–7.6)	–	–
Angiotensin-converting enzyme inhibitors			
Single-drug or combined therapy	45.0 (29.3–61.8)	<0.01	97.0
Single-drug therapy	16.2 (11.6–22.1)	<0.01	85.0
Combined with BB†	3.4 (2.5–4.7)	0.07	62.1
Combined with CCB‡	4.00 (2.1–5.9)	–	–
Beta-blockers			
Single-drug or combined therapy	21.2 (17.3–25.8)	<0.01	84.3
Single-drug therapy†	10.0 (8.1–12.3)	0.17	46.2
Combined with CCB‡	2.3 (0.5–4.1)	–	–
Calcium channel blockers			
Single-drug or combined therapy	12.1 (8.3–17.5)	<0.01	83.0
Single-drug therapy‡	3.9 (1.6–6.2)	–	–
Angiotensin receptor blockers			
Single-drug or combined therapy †	2.3 (1.4–3.6)	0.06	71.2
Diagnostic tests and procedures (%) among hypertensive subjects			
Previous month			
Electrocardiography‡	6.30 (3.9–8.8)	–	–
Any radiography‡	9.70 (6.8–12.7)	–	–
Any urine test‡	8.40 (5.6–11.2)	–	–
Any blood test‡	12.60 (9.3–16.)	–	–

Direct ophthalmoscopy‡*	35.0 (30.2–39.8)	–	–
Previous 12 months			
Serum potassium‡	19.5 (13.9–25.2)	–	–
Serum creatinine‡	31.0 (24.4–29.6)	–	–
Total serum cholesterol‡	35.5 (28.7–42.3)	–	–
Serum LDL or HDL cholesterol‡	25.0 (18.3–31.2)	–	–
Serum triglycerides‡	34.0 (27.3–40.8)	–	–
Fasting plasma glucose‡	36.5 (29.6–43.4)	–	–
Urine analysis‡	25.0 (18.8–31.2)	–	–
Medical appointments (%) among hypertensive subjects			
Annual mean	2.62 (2.37)	0.51	0
Mostly using Brazilian Healthcare System‡	51.2 (46.1–56.2)	–	–
Mostly using private physicians ‡	20.9 (16.8–25.1)	–	–
Mostly using health plan physician‡	13.0 (9.6–16.4)	–	–
Mostly using emergency services‡	1.9 (0.5–3.2)	–	–
Others‡	13.0 (9.6–16.4)	–	–

† Fixed effect analysis
‡ Based on one study
* Since the diagnosis of hypertension
LDL: low-density lipoprotein; HDL: high-density lipoprotein

7.2. Figuras do artigo 3

Figura 1

Figure 1. Flow chart of records retrieved, screened, and included in the systematic review.

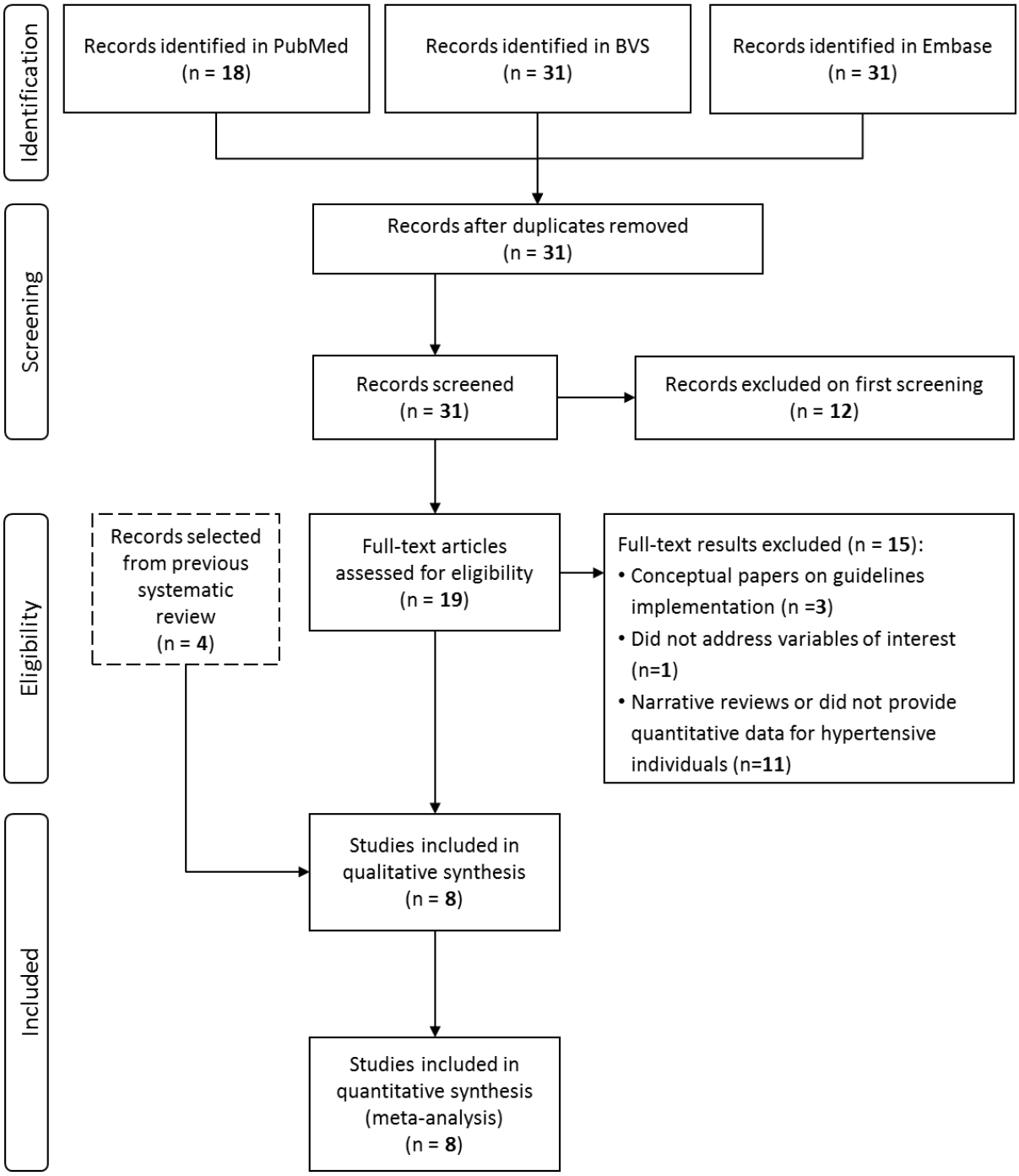
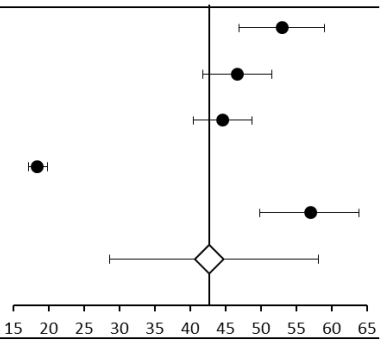


Figura 2

Figure 2. Meta-analysis of proportion of use of one BPLM (in chronological order according to the initial data collection year of studies).

First author	Year	City	Sample size	%	95% CI
da Costa JD	2000	Pelotas	262	53.0	46.9 — 59.0
de Souza JJG	2003	São Paulo	392	46.7	41.8 — 51.6
Moreira GC	2004	São José do Rio Preto	549	44.6	40.5 — 48.8
Lima SM	2005	Rio de Janeiro	3133	18.4	17.1 — 19.8
Maluf I	2006	Curitiba	189	57.0	49.8 — 63.9
Summary			**4525**	**42.7**	**28.6 — 58.1**

Summary T^2=0.82, Q<0.01, I^2=99.0%



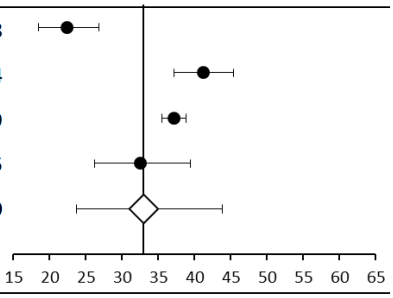
BPLM: blood pressure lowering medication; 95% CI: 95% confidence interval

Figura 3

Figure 3. Meta-analysis of proportion of use of two BPLM (in chronological order according to the initial data collection year of studies).

First author	Year	City	Sample size	%	95% CI
de Souza JJG	2003	São Paulo	392	22.4	18.5 — 26.8
Moreira GC	2004	São José do Rio Preto	549	41.2	37.2 — 45.4
Lima SM	2005	Rio de Janeiro	3133	37.2	35.5 — 38.9
Maluf I	2006	Curitiba	189	32.5	26.2 — 39.5
Summary			**4525**	**33.0**	**23.7 — 43.9**

Summary T^2=0.09, Q<0.01, I^2=92.4%

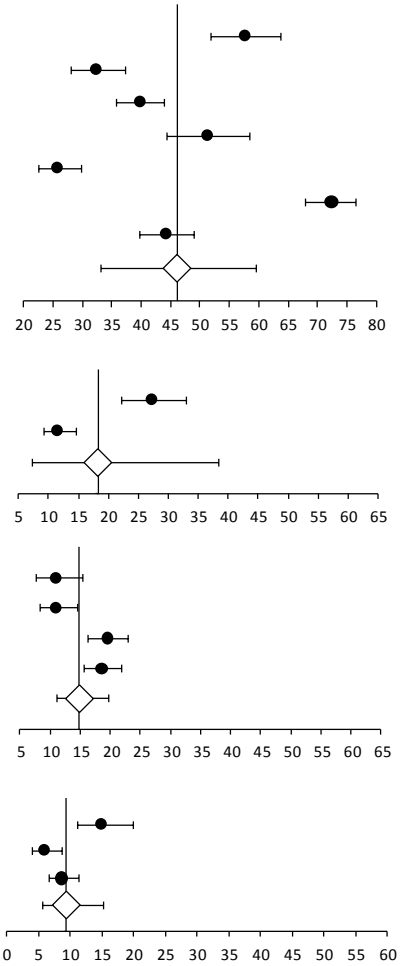


BPLM: blood pressure lowering medication; 95% CI: 95% confidence interval

Figura 4

Figure 4. Meta-analysis of proportion of thiazide-based therapy (in chronological order according to the initial data collection year of studies).

Type of therapy	First author	Year	Sample size	%	95% CI
Single-drug or combined					
	da Costa JD	2000	262	57.9	51.8 — 63.7
	de Souza JJG	2003	392	32.6	28.2 — 37.4
	Moreira GC	2004	549	39.9	35.8 — 44.0
	Maluf I	2006	189	51.5	44.4 — 58.5
	Santa Helena ET	2006	565	26.0	22.5 — 29.8
	Hoepfner C	2007	415	72.4	67.9 — 76.5
	Trevisol DJ	2007	426	44.4	39.7 — 49.1
	Summary		**2798**	**46.1**	**33.2 — 59.6**
			Summary τ^2=0.44, Q<0.01, I^2=97.5%		
Single-drug					
	da Costa JD	2000	262	27.4	22.3 — 33.1
	Moreira GC	2004	549	11.6	9.2 — 14.6
	Summary		**811**	**18.2**	**7.4 — 38.4**
			Summary τ^2=0.53, Q<0.01, I^2=96.6%		
Combined with ACEI					
	da Costa JD	2000	262	11.0	7.7 — 15.4
	de Souza JJG	2003	392	11.0	8.3 — 14.5
	Moreira GC	2004	549	19.5	16.4 — 23.0
	Santa Helena ET	2006	565	18.6	15.6 — 22.0
	Summary		**1768**	**14.9**	**11.07 — 19.7**
			Summary τ^2=0.10, Q<0.01, I^2=84.6%		
Combined with BB					
	da Costa JD	2000	262	15.0	11.2 — 19.9
	de Souza JJG	2003	392	6.0	4.0 — 8.8
	Moreira GC	2004	549	8.7	6.7 — 11.4
	Summary		**1203**	**9.4**	**5.7 — 15.2**
			Summary τ^2=0.20, Q<0.01, I^2=86.5%		



ACEI: angiotensin-converting enzyme inhibitors; BB: beta-blockers; 95% CI: 95% confidence interval.

8. Conclusões, Considerações Finais e Perspectivas Futuras

Ao longo do presente trabalho, abordamos temas centrais à compreensão da epidemiologia da HAS no Brasil: prevalência de doença e descrição da assistência usualmente prestada aos hipertensos na atenção primária. Nosso país carece dessas informações imprescindíveis para o planejamento e pesquisa em saúde pública no âmbito nacional. Tentamos, dessa forma, suprir tais necessidades através de três revisões sistemáticas.

Na primeira, investigamos a frequência de HAS e o comportamento de sua prevalência na população geral adulta ao longo das últimas três décadas. Nossos achados contrastam com o senso comum de que a prevalência da doença está aumentando, pois detectamos redução relativa de 1,8% entre 1987 e 2007. Por outro lado, vai ao encontro de publicações internacionais que demonstram a redução da média de PA na população mundial nos últimos 30 anos. Concluímos que, embora nossas estimativas sejam precisas e confiáveis, estudos de prevalência com amostra representativa do país deveriam ser realizados periodicamente a fim de confirmarmos essas tendências no Brasil, especialmente em função da escassez de dados provenientes da região Norte.

Na segunda revisão sistemática, estudamos segmento sub-representado no campo da pesquisa epidemiológica nacional: os idosos. Evidenciamos o peso da HAS sobre os idosos no país: dois terços dos nossos idosos são hipertensos. Também tornamos clara a subestimação da prevalência de HAS avaliada por inquérito telefônico e visita domiciliar sem aferição de PA nessa população. Assim, estudos de base populacional fazem-se ainda mais necessários para este conjunto da sociedade brasileira.

No terceiro estudo traçamos o panorama do manejo ambulatorial usual da HAS no Brasil. Contudo, não fomos capazes de dimensionar plenamente os cuidados habitualmente

dispensado aos hipertensos, pois o volume publicado de informações é insuficiente. Entretanto, encontramos meios de contornar esta aridez de dados através da agregação de estudos com delineamentos distintos e da utilização de diferentes bases e bancos de dados, e conseguimos estimar parâmetros e descrever aspectos relevantes do tratamento ambulatorial da HAS no país. Acreditamos que o entendimento deste cenário é crucial para a sugestão de novas políticas assistenciais em saúde pública assim como para o desenvolvimento de pesquisa em ATS e AES. Esperamos ter construído instrumento necessário para subvencionar mais trabalhos nessas áreas.

Por fim, aprofundaremos, futuramente, nossas investigações no intuito de estabelecer o ônus econômico da HAS no Brasil e a custo-efetividade de diferentes estratégias de tratamento, levando-se em conta o conhecimento edificado durante o doutoramento.

ANEXOS: PUBLICAÇÕES REALIZADAS DURANTE O DOUTORADO

ARTIGOS

Lukrafka JL, Fuchs SC, Moreira LB, Picon RV, Fischer GB, Fuchs FD. **Performance of the ISAAC questionnaire to establish the prevalence of asthma in adolescents: a population-based study.** J Asthma. 2010; 47:166-9.

Abstract

BACKGROUND:

The epidemiology of asthma has been investigated with questionnaires, such as the International Study of Asthma and Allergies in Childhood protocol.

AIM:

To investigate the performance of the questions of the International Study of Asthma and Allergies in Childhood questionnaire to diagnose asthma in adolescents.

METHODS:

This is a population-based cross-sectional study of adolescents in the Syndrome of Obesity and Risk Factors for Cardiovascular Disease study. The validity of the asthma symp-

toms of the International Study of Asthma and Allergies in Childhood protocol was assessed by calculating sensitivity, specificity, positive and negative posttest probabilities, and Youden's Index, taking as a gold standard the history of a medical diagnosis of asthma. Risk ratios (RRs) and 95% confidence intervals (CIs), adjusting for sex and age, were calculated using Cox regression model.

RESULTS:

In total, 575 adolescents were investigated. Overall, 28.7% reported a lifetime medical diagnosis of asthma, and 40.0% reported at least one episode of wheezing. Ever wheezing had the highest sensitivity (80.6%) for the diagnosis of asthma, compared with the other ISAAC questions. Adolescents who reported ever wheezing were about 8 times more likely (adjusted RR: 8.3; 95% CI: 4.9-14.2) to have ever had asthma, independent of age and sex. Symptoms within the last 12 months (wheezing, cough without cold or respiratory infection, sleep disturbed due to wheezing, wheezing due to exercise, speech limited due to wheezing) had specificity of 92.0% or higher. Dry cough at night without cold or respiratory infection was the strongest independent predictor of asthma (adjusted RR: 8.8; 95% CI: 6.1-12.7).

CONCLUSIONS:

Ever wheezing is the most sensitive indicator of the diagnosis of asthma but falsely identifies a portion of adolescents as asthmatic. Symptoms of asthma in the last 12 months, such as cough without cold or respiratory infection, are rarely positive in the absence of a lifetime asthma diagnosis. The combination of ever wheezing for screening and the pres-

ence of other symptoms within the past 12 months to confirm the diagnosis could be an effective strategy to identify the prevalence of asthma in communities.

Picon PD, Picon RV, Costa AF, Sander GB, Amaral KM, Aboy AL, Henriques AT. **Randomized clinical trial of a phytotherapic compound containing Pimpinella anisum, Foeniculum vulgare, Sambucus nigra, and Cassia augustifolia for chronic constipation.** BMC Complement Altern Med. 2010; 30; 10-7.

Abstract

BACKGROUND:

A phytotherapic compound containing Pimpinella anisum L., Foeniculum vulgare Miller, Sambucus nigra L., and Cassia augustifolia is largely used in Brazil for the treatment of constipation. However, the laxative efficacy of the compound has never been tested in a randomized clinical trial. The aim of this study was to evaluate the efficacy and safety of the product.

METHODS:

This randomized, crossover, placebo-controlled, single-blinded trial included 20 patients presenting with chronic constipation according to the criteria of the American Association of Gastroenterology. The order of treatments was counterbalanced across subjects: half of the subjects received the phytotherapic compound for a 5-day period, whereas the other half received placebo for the same period. Both treatment periods were separated by

a 9-day washout period followed by the reverse treatment for another 5-day period. The primary endpoint was colonic transit time (CTT), measured radiologically. Secondary endpoints included number of evacuations per day, perception of bowel function, adverse effects, and quality of life.

RESULTS:

Mean CTT assessed by X ray was 15.7 hours (95%CI 11.1-20.2) in the active treatment period and 42.3 hours (95%CI 33.5-51.1) during the placebo treatment ($p < 0.001$). Number of evacuations per day increased during the use of active tea; significant differences were observed as of the second day of treatment ($p < 0.001$). Patient perception of bowel function was improved ($p < 0.01$), but quality of life did not show significant differences among the study periods. Except for a small reduction in serum potassium levels during the active treatment, no significant differences were observed in terms of adverse effects throughout the study period.

CONCLUSIONS:

The findings of this randomized controlled trial allow to conclude that the phytotherapic compound assessed has laxative efficacy and is a safe alternative option for the treatment of constipation.

TRIAL REGISTRATION:

ClinicalTrial.gov NCT00872430.

Picon PD, Camozzato AL, Lapporte EA, Picon RV, Moser Filho H, Cerveira MO, Chaves ML. **Increasing rational use of cholinesterase inhibitors for Alzheimer's disease in Brazil: public health strategy combining guideline with peer-review of prescriptions**. Int J Technol Assess Health Care. 2010; 26:205-10.

Abstract

OBJECTIVES:

Since 2002, the treatment with cholinesterase inhibitors (CHEIs) for Alzheimer's disease (AD) has been paid for by the public health system of the Brazilian Ministry of Health for any patient that fulfills clinical criteria established by an evidence-based guideline developed and published by the Ministry. The aim of this study was to evaluate compliance of prescription patterns to the national guideline for use of CHEIs' in the southern Brazilian state of Rio Grande do Sul.

METHODS:

We created a regional expert-committee reference center to review all prescriptions of CHEIs and to send feedback to physicians whenever prescriptions without compliance to the guideline were noted. One thousand three hundred ninety-nine (1,399) CHEI prescriptions presented to the public health system from 2005 to 2007 were evaluated by an expert team of neurologists and psychiatrists. Clinical history, performance on mental status

screening by Mini Mental State Examination (MMSE), Clinical Dementia Rating scale (CDR), laboratory results, and neuroimaging findings were evaluated in relation to the adherence to the national guideline's recommendations. If the prescription was rejected because of lack of adherence to the criteria of the guideline, a written response was sent by the expert committee to physicians concerning the request.

RESULTS:

The majority of the requests (n = 1,044; 75 percent) did not meet the AD guideline's criteria, either for diagnosis or for treatment, and were not granted. A diagnostic mistake was evident in 64.3 percent of cases. Findings of vascular or Parkinson's dementia or severe AD were the main reasons for rejection. Rivastigmine was the most prescribed cholinesterase inhibitor, used in 86 percent of cases. Of note was the reduction in the number of CHEIs prescriptions in the years following this intervention.

CONCLUSIONS:

The public health strategy of using expert-review of prescriptions and their compliance to national guideline revealed a low rate of rational use of CHEIs for dementia. Such a strategy is relevant for protecting patients from unproven medical interventions and for reducing waste of resources.

RESUMOS EM ANAIS DE CONGRESSOS

- Picon RV; Fuchs FD; Riegel G; Moreira LB; Fuchs SC. Prevalence of hypertension among Brazilian elderly: a systematic review and meta-analysis. In: 9th HTAi Annual Meeting, 2012, Bilbao, Espanha. Gaceta Sanitaria, 2012. v. 26. p. 175-175.

- Picon RV; Fuchs SC. Cost-effectiveness analysis of the 7th report of the US Joint National Committee on Hypertension and the 6th Brazilian Guidelines for Systemic Hypertension recomendations' compared to the status quo on primary cardiovascular prevention: methods. In: 9th HTAi Annual Meeting, 2012, Bilbao, Espanha. Gaceta Sanitaria, 2012. v. 26. p. 207-208.

- Picon RV ; FUCHS, F. D. ; Riegel G ; MOREIRA, L. B. ; Fuchs, Sandra C. . Prevalência de Hipertensão Arterial Sistêmica no Brasil de 1980-2010: uma Revisão Sistemática com Meta-Análise. In: 66º Congresso Brasileiro de Cardiologia, 2011, Porto Alegre, RS. Arquivos Brasileiros de Cardiologia, 2011. v. 97. p. 8-8.

- Picon RV; Riegel G; Moreira LB; Fuchs FD; Fuchs FC. P2-245 Prevalence of hypertension in Brazil over the past 3 decades: a systematic review and meta-analysis. In: World Congress of Epidemiology, 2011, Edimburgo, Escócia. Journal of Epidemiology and Community Health, 2011. v. 65. p. A289-A289.

- Picon RV; Moreira LB; Fuchs, FD; Riegel G; Fuchs SC. Prevalência de hipertensão arterial sistêmica em indivíduos idosos no Brasil: comparação entre pressão medida e auto-referida. In: VIII Congresso Brasileiro de Epidemiologia, 2011, São Paulo, SP. Revista da ABRASCO, 2011.

- Fuchs SC; Picon RV; Riegel G; Moreira LB; Fuchs FD. Prevalence of hypertension in Brazil over the past three decades: a systematic review with meta-analysis. In: European Society of Cardiology Congress, 2011, Paris, França. European Heart Journal. Oxford, Grã-Bretanha: Oxford Journal, 2011. v. 32. p. 103-103

APRESENTAÇÃO ORAL EM CONGRESSO

- Picon RV; Fuchs FD; Riegel G; Moreira LB; Fuchs SC. Prevalência de Hipertensão Arterial Sistêmica no Brasil de 1980-2010: uma Revisão Sistemática com Meta-Análise. 2011. (Apresentação de Trabalho/Congresso).

CAPÍTULO DE LIVRO

- Picon PD; Picon RV . Uso Racional de Medicamentos: Aspectos Econômicos. In: Flávio Danni Fuchs; Lenita Wannmacher. (Org.). Farmacologia Clínica: Fundamentos da Terapêutica Racional. 4ed.Rio de Janeiro, RJ: Guanabara Koogan, 2010, v. 1, p. 54-60.