REVIEW ARTICLE

Quaternary prevention and its implications for the clinical practice: a systematic review

Milena Seoane Colmenero Muniz[1], Sylmara Esther Negrini Ferrari[1], Iury Nascimento Duarte[2], Luciane Loures dos Santos[1], Janise Braga Barros Ferreira[1]

ABSTRACT

The growing production regarding iatrogenesis justifies the discussion about the incorporation of quaternary prevention in the daily medical practice. This study identified and systematized the production of knowledge about quaternary prevention and its implications for the clinical practice. This is a systematic descriptive review supported by the guiding question: What evidence has been produced regarding quaternary prevention and its impact on the clinical practice? A bibliographic survey was carried out between August and September 2020 using the descriptor "quaternary prevention" in English, Portuguese and Spanish. The analysis of 30 articles produced evidence on potentially harmful medical interventions that would justify the adoption of quaternary prevention. The study invites the medical community to reflect on the incorporation of quaternary prevention, aiming for a less iatrogenic care practice, valuing person-centered medicine and the attributes of primary health care.

Keywords: Quaternary prevention, Iatrogenic disease, Primary health care, Systematic review.

INTRODUCTION

The concept of health established by the World Health Organization (WHO) is complete physical, mental and social well-being and not merely the absence of disease or infirmity[1]. This definition motivates discussions in the global scientific scenario regarding the relevance of the treatments proposed to confront the morbidity and mortality of a population. The principle of non-maleficence, described by Hippocrates, in his work Epidemics by Hippocrate, contrasts with the medicalizing and interventionist character of medical practices in recent decades[2]. This condition can generate complications for people's lives and is known as iatrogenesis, classified into three subtypes: clinical, social and cultural[3]. Clinical iatrogenesis is directly caused by healthcare. Social iatrogenesis reflects the effect of medicalization on society that becomes increasingly dependent on procedures and medicines, attributing to individuals the role of mere "patients". Finally, cultural iatrogenesis is understood the loss of a people's identity, their way of life, and their traditional ways of dealing with illness and death[3].

The concept of Quaternary Prevention (P4) proposed in the 1990s by family physician Marc Jamoulle and made official in 2003 by the World Organization of National Colleges (WONCA) is based on the detection of individuals who are at risk of overtreatment, and proposes alternatives that are ethical, acceptable and supported by scientific evidence[4,5].

To give an idea of the scale of this problem, in the United States of America the incidence of iatrogenic events has reached the level of the third highest cause of death[6]. Accordingly, structuring projects aimed at medical education, reinforcing the principles of evidence-based medicine and its supporting factors, professional experience, the values and wishes of the patient associated with the available scientific evidence, has become a public health issue[6].

Therefore, the aims of this study were to identify and systematize the production of knowledge on quaternary prevention and its implications for the clinical practice.

METHODOLOGY

This is a descriptive systematic review[7,8,9] using the PICO strategy, with "P" being the population (general population), "I" the phenomenon

[1] Universidade de São Paulo. Faculdade de Medicina de Ribeirão Preto, Ribeirão Preto, (SP), Brazil.
[2] Secretaria Municipal de Saúde de Araraquara, Araraquara, (SP), Brazil.

https://doi.org/10.11606/issn.2176-7262.rmrp.2022.188477

of interest (quaternary prevention), "C" comparison (no comparison) and "O" outcome (implication for the clinical practice), to elaborate the guiding question: "What is the scientific evidence produced on P4 and its implications for the clinical practice?"

The bibliographic survey was carried out by consulting the electronic databases LILACS, PubMed, Scopus and Embase, using the descriptor/term "quaternary prevention". As inclusion criteria, articles were selected that were published from January 2000 to August 2020, in English, Portuguese and Spanish, and that allowed access to the full text. The following exclusion criteria were adopted: theses, dissertations and editorial notes. Those articles that only discussed the concept of P4 were also excluded.

Using the Rayyan[10] software, the bank of articles was created and, after elimination of duplications, the evaluation was carried out independently by three reviewers. First, the titles and abstracts were read, performing the exclusions according to the adopted criteria. The three reviewers discussed and consensually resolved any disagreements regarding the blind evaluation. Subsequently, the reviewers proceeded to read the selected articles in full, forming the final sample of the review. The descriptive analysis of the selected studies included, firstly, the extraction of data: article title, authors, type of study, year and country. In classifying the level of evidence of the selected articles, the Strength of Recommendation Taxonomy (SORT) was adopted: Level A. Consistent, good-quality, patient-oriented evidence; Level B. Inconsistent or limited-quality patient-oriented evidence. Level C. Consensus, disease-oriented evidence, usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening[11]. At the second moment, the systematization and interpretation of the evidence related to P4 and its implications for the clinical practice were carried out. The PRISMA recommendation (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) was used in the preparation of the article[12].

RESULTS

The search strategy identified 238 articles, with 56 being in more than one database, 78 in LILACS, 82 in Scopus, 21 in Embase and 57 in PubMed (Figure 1). After reading the titles and abstracts, 94 manuscripts were selected for full reading, after which 30 articles were selected to compose the final sample (Figure 1).

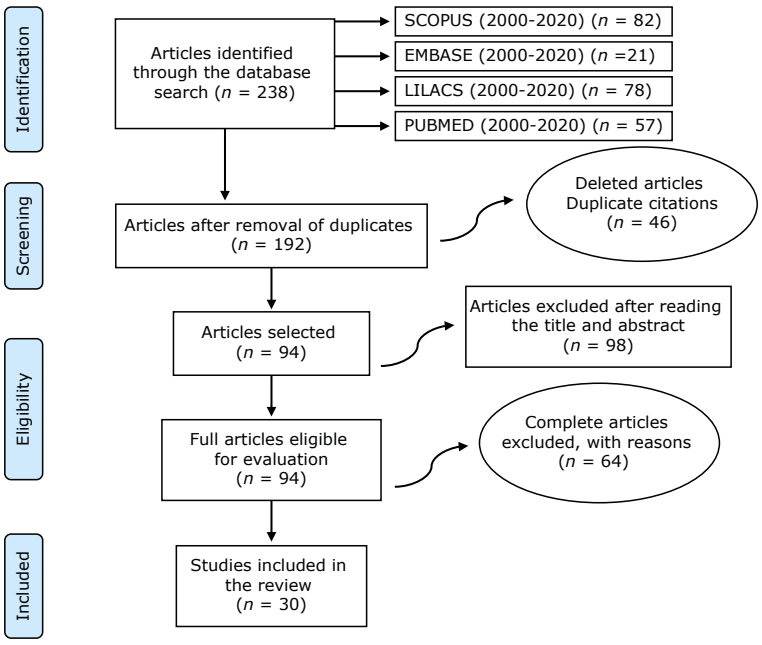

Figure 1: Flowchart of the article selection process based on the PRISMA model[12]

The 30 selected articles presented the following distribution according to publication language: 17 (56.7%) in English, nine (30.0%) in Spanish and four (13.3%) in Portuguese. Regarding the country of origin of the study, two[19,34] were from the United States, two[22,37] from India, two[26,42] from Uruguay, three[21,32,33] from Portugal, four[24,28,29,41] from Brazil, nine[13,14,15,16,17,18,27,33,40] from Spain and the other eight[20,23,25,30,35,36,38,39] from eight different countries. The first six articles[13,14,15,16,17,18] of the review were of Spanish origin. Regarding the level of evidence of the selected articles: 26 were descriptive studies (level 3), two were case reports (level 3) and two were analytical (level 2)[11]. Table 1 summarizes the data extracted from the selected articles: title, author, type of study, year, country of origin and publication.

Table 1
Information regarding the selected studies

Title	Authors	Type of study	Year	Country of origin	Country of publication
Genética y prevención cuaternaria.El ejemplo de la hemocromatosis	[13] Gérvas J, Fernández MP.	Descriptive	2003	Spain	Spain
Moderación en la actividad médica preventiva y curativa. Cuatro ejemplos de necesidad de prevención cuaternaria en España	[14]Gérvas J.	Descriptive	2006	Spain	Spain
Uso y abuso del poder médico para definir enfermedad y factor de riesgo, en relación con la prevención cuaternaria	[15] Gérvas J, Fernández MP.	Descriptive	2006	Spain	Spain
Iatrogenia y prevención cuaternaria en salud mental	[16]Alberto Ortiz Lobo; Vicente Ibáñez Rojo;	Descriptive	2011	Spain	Spain
El enigma de la prevención cuaternaria en atención primaria.Cuándo hacer y cuándo no hacer (a propósito de 2 casos)	[17] Cucalón JM, Guiu M.	Case study	2012	Spain	Spain
Prevención cuaternaria em ancianos	[18] Gérvas J.	Descriptive	2012	Spain	Spain
American Society of Clinical Oncology Provisional Clinical Opinion: The Integration of Palliative Care Into Standard Oncology Care	[19] Smith TJ et al.	Descriptive	2012	USA	USA
The four steps in the prevention of human papillomavirus-associated neoplasia: considerations for preventive measures, screening, disease impact, and potential overtreatments in HPV-related pathology	[20]Liverani CA.	Descriptive	2013	Italy	Switzerland
Rastreamento do câncer de mama: as três luzes do semáforo	[21]Santos JA.	Descriptive	2013	Portugal	Brazil
Quaternary prevention and diabetes	[22] Kalra S, Sreedevi A, Unnikrishnan, AG	Descriptive	2014	India	Pakistan
Quaternary prevention as a basis for rational approach to the patient in family practice.	[23] Baricević IZ, Botica MV, Pavlic-Renar, I	Descriptive	2014	Croatia	Croatia
Cuidado (!) na prevenção do câncer: ética, *danos e equívocos*	[24] Tesser CD.	Descriptive	2014	Brazil	Brazil
Multimorbidity and quaternary prevention	[25] Mangin, Dee; Heath, Iona;	Descriptive	2015	England	Brazil

(Continuação)

Tabela 1

(continuação)

Title	Authors	Type of study	Year	Country of origin	Country of publication
¿ Overscreening o prevención a escala humana? Tamizaje excessivo	[26] Báez MP.	Descriptive	2015	Uruguay	Brazil
Prescrição prudente e desprescrição de fármacos como ferramentas para a prevenção quaternária	[27] Santana MCG, Gavilán-Moral E, Villafaina-Barroso A, Gracia LJ.	Descriptive	2015	Spain	Brazil
Prevenção quaternária: as bases para sua operacionalização na relação médico-paciente	[28] Norman AH, Tesser CD	Descriptive	2015	Brazil	Brazil
Violência obstétrica e prevenção quaternária: o que é e o que fazer	[29] Tesser CD, Knobel R, Andrezzo H, Faria HFA, Diniz SG.	Descriptive	2015	Brazil	Brazil
Surgical pathology in cancer diagnosis: implications for quaternary prevention	[30] Yver M.	Descriptive	2015	France	Brazil
Breast and testicular self-examinations in cancer screening: a matter of quaternary prevention?	[31] Santos JA;	Descriptive	2015	Portugal	Brazil
Migraine treatment: a chain of adverse effects	[32] Veloso, T. S.; Cambão, M. S.;	Case study	2015	Portugal	Switzerland
Sobre la prevención cuaternaria en niños escolares	[33] Cruz-Tabuenca H.	Descriptive	2015	Spain	Spain
Overtesting and the downstream consequences of overtreatment: implications of "preventing overdiagnosis" for emergency medicine	[34] Carpenter, Christopher R.; Raja, Ali S.; Brown, Michael D.;	Analytical	2015	USA	USA
Attention-deficit hyperactivity disorder: preventing overdiagnosis and overtreatment	[35] St-Onge JC.	Descriptive	2015	Canada	Brazil
Impact of quaternary prevention as a brief intervention in medical students' clinical decisions: experience from Vietnam	[36] Tran THV, Vo TL.	Descriptive	2015	Vietnam	Brazil
Prevention of lipohypertrophy	[37] Kalra S, Kumar A, Gupta, Y.	Descriptive	2016	India	Pakistan
Primary care physicians' action plans for responding to results of screening tests based on the concept of quaternary prevention	[38] Bae J-M, Jamoulle M.	Analytical	2016	Korea	Korea
Medical overuse and quaternary prevention primary care–A qualitative study with general practitioners	[39] Alber K, Kuehlein T, Schedlbauer A, Schaffer S.	Descriptive	2017	Germany	UK
Impact of overdiagnosis and overtreatment on the patient, the health system and society	[40] Coll-Benejam T, Bravo-Toledo R, Marcos-Calvo MP, Astier-Peña MP	Descriptive	2018	Spain	Spain
A not-so-blue November: debating screening of prostate cancer and men's health	[41] Modesto AADA, Lima RLB, D'Angelis AC, Augusto DK.	Descriptive	2018	Brazil	Brazil
*Vacunación contra el virus del papiloma humano a la luz de la prevención cuaternari*a	[42] Báez MP, Jamoulle M	Descriptive	2019	Uruguay	Brazil

Source: Produced by the authors, 2020.

The analysis of the evidence highlighted articles produced in the areas of children's, women's, men's, and older adult's health, urgency and emergency care, mental health, screening, drug deprescription and palliative care. Furthermore, in the results, questions emerged regarding the systematization of medical practice based on P4, the development of a critical view of unnecessary interventions in health institutions and the importance of including P4 medical training to assist in clinical decisions. Table 2 summarizes the main findings of the studies in relation to P4 in terms of the area of application and its implications for clinical practice.

Table 2

Areas of application of P4 and its implications for the clinical practice.

Title	Area of application	Implications for the practice
[38]Primary care physicians' action plans for responding to results of screening tests based on the concept of quaternary prevention	The application of the P4 concept helping family and community physicians to gain better insights into screening tests aimed at preventing chronic non-communicable diseases.	The authors suggest that screening tests for chronic noncommunicable diseases should be customized according to individual characteristics, rather than being performed based on general guidelines.
[28]*Prevenção quaternária: as bases para sua operacionalização na relação médico-paciente*.	P4 implies the strengthening and critical review of the clinical reasoning of family physicians.	The article provides a conceptual framework for operationally discussing P4 arising from doctor-patient relationship, which is relevant to service practices and teaching environments such as family and community medicine residency programs.
[34]Overtesting and the downstream consequences of overtreatment: implications of "preventing overdiagnosis" for emergency medicine	The concept of P4 discussed in relation to its implementation, in urgent/emergency care.	The authors describe and assess the barriers and opportunities to reduce overtesting and interventions in urgent and emergency care units.
[33]*Sobre la prevención cuaternaria en niños escolares*	Discussion about P4 in a specific orthopedic context, with a significant prevalence in the population of schoolchildren.	The article discusses the diagnosis of scoliosis that is often performed in schoolchildren and the real need for investigation with complementary exams and questions about treatment, with the patient being asymptomatic.
[14]*Moderación en la actividad médica preventiva y curativa. Cuatro ejemplos de necesidad de prevención cuaternaria en España*	The P4 concept applied in more prevalent health situations	The paper discusses clinical activity as an intervention, which should be of low intensity and high quality, without compromising patient safety.
[18]*Prevención cuaternaria em ancianos*	P4 applied in the older adult population.	The article discusses the context of morbidity and death in the health care of the older adult, the need to avoid screening without scientific basis and to propose alternatives for rehabilitation, which maintain as much of an active life as possible.
[20]The four steps in the prevention of human papillomavirus-associated neoplasia: considerations for preventive measures, screening, disease impact, and potential overtreatments in HPV-related pathology	P4 analyzed in the context of HPV infection and the four steps for its prevention.	The article states that the widespread use of the HPV test, outside the published guidelines, raises the possibility that healthy patients will be assigned the sick label, leading to wasted time and generating unnecessary expenses, both for patients and for health services. The social repercussions of this fact are also discussed.
[25]Multimorbidity and quaternary prevention	P4 and patient-centered medical care.	The manuscript discusses the importance of considering the patient's experience with the disease and the medical approach, suggesting public policies directed toward this problem.
[26]*¿ Overscreening o prevención a escala humana? Tamizaje excessivo*	Analysis of P4 in the scenario of the abusive, excessive or unnecessary application of screening methods	The authors reorient the approach to prevention, redirecting the disease prevention model to the individual and organizing the medical practice considering the P4 concept.

(Continuação)

Tabela 2

(continuação)

Title	Area of application	Implications for the practice
[27]*Prescrição prudente e desprescrição de fármacos como ferramentas para a prevenção quaternária*	Conscious prescribing and deprescribing of drugs as P4 tools	The manuscript presents conscious deprescribing and prescribing as fundamental tools to avoid overmedicalization of the population.
[21]*Rastreamento do câncer de mama: as três luzes do semáforo*	P4 analysis related to breast cancer screening	The article suggests that reading the scientific evidence implies the need to turn on the yellow light (balance between risk/benefit) for breast cancer screening, in order to combat overdiagnosis and overtreatment.
[31]Breast and testicular self-examinations in cancer screening: a matter of quaternary prevention?	Analysis of P4 related to breast and testicular self-examination in screening for neoplasms	The manuscript argues that breast and testicular self-examination are practices without proven benefits.
[35]Attention-deficit hyperactivity disorder: preventing overdiagnosis and overtreatment	Analysis of P4 in the scenario of Attention Deficit Hyperactivity Disorder (ADHD)	The article highlights the existence of clear evidence regarding the overdiagnosis of ADHD. It also notes that the drugs are effective only in the short term and can lead to adverse effects.
[15]*Uso y abuso del poder médico para definir enfermedad y factor de riesgo, en relación con la prevención cuaternaria*	P4 as a basic activity of Medicine and Public Health.	The article indicates the need to develop studies around P4, as well as the establishment of warning systems related to patient safety.
[28]*Prevenção quaternária: as bases para sua operacionalização na relação médico-paciente*	The systematization of medical care with a focus on P4.	The article advocates that P4 strengthens the reconstruction of the critical and epistemological capacity of family physicians, which positively impacts the medical practice.
[24]*Cuidado (!) na prevenção do câncer:* ética*, danos e equívocos*	Analysis of P4 in the context of social medicalization that advances towards a supposed prevention	The study makes a comparison between P4 protocols, and facilitating and hindering factors, in Brazil and Uruguay, problematizing social medicalization. The author addresses this issue from the breast cancer screening protocols in these countries.
[29]*Violência obstétrica e prevenção quaternária: o que é e o que fazer*	Analysis of obstetric violence and how P4 can intervene in this condition	The authors discuss P4 in relation to obstetric violence in Brazil. They reflect that P4, in this scenario, requires the support of pregnant and postpartum women for the participatory elaboration of birth plans and for the humanization needs to be fulfilled in prenatal and delivery care.
[32]Migraine treatment: a chain of adverse effects	Analysis of P4 related to migraine and the adverse effects of its treatments	The manuscript describes the importance of P4 in the management of migraine. It shows the low efficacy of the use of some drugs and what options would be most indicated for the treatment of this condition.
[40]Impact of overdiagnosis and overtreatment on the patient, the health system and society	Conceptualization of overdiagnosis and overtreatment, discussing the applicability of the concepts in institutional health environments.	The authors propose the development of a critical view of the work process, highlighting the cultural issues of Primary Prevention and P4.
[41]A not-so-blue November: debating screening of prostate cancer and men's health	Analysis of P4 in the context of population screening for prostate cancer	The authors discuss prostate cancer screening, based on programmatic activities such as the "Blue November" Campaign, questioning its effectiveness.
[19]American Society of Clinical Oncology provisional clinical opinion: The integration of palliative care into standard oncology care	Palliative care approach and P4	The authors discuss excesses in the treatment of patients with incurable diseases and present tools for less iatrogenic care.

(Continuação)

Tabela 2

(continuação)

Title	Area of application	Implications for the practice
[30]Surgical pathology in cancer diagnosis: implications for quaternary prevention	Analysis of the role of surgical pathology in the diagnosis of neoplasms considering P4	The article suggests that more independent studies are needed to emphasize and more accurately determine the role of surgical pathology and the use of some of its techniques, in order to avoid overdiagnosis and overtreatment in cancer cases.
[17]*El enigma de la prevención cuaternaria en atención primaria. Cuándo hacer y cuándo no hacer (a propósito de 2 casos)*	Clinical practice in PHC and P4	The manuscript reflects on common interventions in the clinical practice, through two case reports of patients with several comorbidities, exposed to polypharmacy and its potential harm.
[13]*Genética y prevención cuaternaria. El ejemplo de la hemocromatosis*	Discussion about genetic screening and P4	The author discusses the genetic screening of hemochromatosis and the prevalence of the disease in the population, in addition to the iatrogenesis related to the screening, due to the low phenotypic expression of the disease.
[16]*Iatrogenia y prevención cuaternaria en salud mental*	P4 and iatrogenesis in the field of mental health.	The article exposes the importance of weighing up the positive and negative aspects of treatments, taking into account symptoms and the context in which the patient is inserted, avoiding excessive pharmacological and psychotherapeutic interventions.
[36]Impact of quaternary prevention as a brief intervention in medical students' clinical decisions: experience from Vietnam	Evaluation of the decision process of medical students after an intervention regarding P4	A total of 115 fifth-year medical students participated in the 'Screening and Prevention for the Individual and Family' course module. The introduction of this discussion into medical education has been shown to help change clinical decisions, highlighting the adoption of patient-centered care, with the aim of avoiding inappropriate medical interventions.
[39]Medical overuse and quaternary prevention in primary care–A qualitative study with general practitioners	Study of the relevant aspects that lead to excessive medical intervention and the importance of P4	The study describes family and community physicians as professionals who are often located at the starting point of the diagnosis and treatment process. The potential of these professionals in the performance of P4 is highlighted.
[37]Prevention of lipohypertrophy	The approach to lipohypertrophy with preventive actions, including P4	The author describes, from the perspective of lipohypertrophy, how one can act at each level of prevention, including P4.
[22]Quaternary prevention and diabetes	The approach to diabetes mellitus considering levels of prevention.	The study describes P4 as a necessary attitude for the management of diabetic patients, seeking to avoid over-medicalization.
[42]Vacunación contra el virus del papiloma humano a la luz de la prevención cuaternaria	Discussion of the relevance of mass vaccination against HPV, considering P4.	The article reinforces the need for the dissemination of knowledge, in a wide network of information, so that family and community physicians can discuss with their patients, individually, the conduct most indicated for each case.

Source: Produced by the authors, 2020.

DISCUSSION

In the sample studied, the concept of P4 developed by Jamoulle was referenced in six articles[15,18,24,33,38,41], two[14,26] used the principle of non-maleficence described by Hippocrates to discuss P4 and the other 22 articles did not explicitly presented a concept for P4.

Jamoulle's conceptualization of P4 remained dormant until the early 2000s, when it began to be discussed by family physicians in various parts of the world. This was especially the case

for the Spanish physician Juan Gérvas, author of four[13,14,15,18] of the six articles identified in this review, prior to 2012, highlighting the need to avoid unnecessary and harmful medical interventions as a central action of family doctors. In the other countries, there was an increase in publications on P4, starting in 2012 and, particularly, in 2015, when 40% of all publications found were published, with Brazil responsible for the publication of 75% of these articles. This expansion of the discussion on P4 relates to the international WONCA events in 2010 and 2013, which brought the concept to light in the discussion, publishing documents in more than six languages, crossing borders and reaching new territories[5].

In this review, the implications of P4 for the clinical practice were discussed in different situations, including: the critical review of clinical reasoning and the practice of the family doctor; clinical activity and patient safety; the exercise of P4 in urgent and emergency services; consideration of the patient's illness experience in the clinical practice; reorientation of the application of screening methods; the conscious prescription and deprescription of drugs; the analysis of social medicalization and morbidity conditions in population groups and in specific health conditions, including: child orthopedics, older adults, HPV approach, ADHD, obstetric violence, and migraine in children.

Due to the potential severity of the diagnoses and the need for quick decision-making, American authors, when evaluating urgent/emergency services, understood that the chances of iatrogenic behaviors occurring in these spaces were greater, which would justify the discussion about P4. Considering that spending on unnecessary treatment in the United States ranged between US$158 and US$226 billion in 2011, and that the mean cost of emergency care in that country increased from US$560 in 2003 to US$1,354 in 2011, the authors highlighted the relevance of acting from the perspective of P4, not only to reduce iatrogenic events, but also to reduce inefficiency in the health systems[34].

Overtreatment can occur when a correct and timely diagnosis is made, however, a treatment is initiated in which the harm outweighs the benefit to the patient. Accordingly, a reflection on the effects of overdiagnosis and overtreatment for patients is proposed, for the health system and for society in general. Furthermore, action proposals based on P4 are emphasized, highlighting the importance of Primary Health Care (PHC) as an essential scenario to reduce iatrogenic practices[40]. It should be noted that this prominent role of PHC in relation to P4 is due to the structuring characteristics of its work process, based on attributes that include integrality, longitudinality, the establishment of interpersonal bonds, the encouragement of people's autonomy in the development of the care, interprofessional work, knowledge of the territory, and cultural competence[43,44]. In Brazil, the Family Health Strategy, is suggested as the preferred model for the organization of PHC in the National Health System (*Sistema* Único *de Saúde* - SUS), which brings together a multidisciplinary team closely linked to the territory, emphasizing the activities carried out by the community health agent. It is believed that this care model can greatly contribute to the operationalization of P4, mainly due to its proximity to the community, which allows for a more in-depth knowledge of the health needs.

The issue addressed in one article produced in Brazil was the probable damage caused to society by the media, when transmitting to citizens the fear related to a neglected diagnosis and its consequences. The authors commented that the fascination with hard technologies and governmental programmatic actions reinforced the interventionist view and, consequently, increased the probability of the occurrence of iatrogenic action[25].

A study carried out with schoolchildren in Spain showed that radiography requests for school-age children, due to the presence of asymptomatic scoliosis, were not risk-free, as it is known that X-rays replace calcium ions with cesium (radioactive), increasing the incidence of bone tumors. The authors questioned the real need to investigate these cases with complementary exams, in addition to addressing questions about treatment when the patient is asymptomatic, which could produce more harm than benefit[33].

The article from Italy indicated that something similar happened with low-grade lesions,

in the cytology of women infected with the human papillomavirus (HPV). In the treatment of many HPV lesions, active management strategies are employed for low-risk cytological abnormalities. Risks associated with pregnancy after cervical surgery, possible complications related to the interventions and increased costs were examples of harmful consequences of overtreatment, without any evidence of benefit for women individually[20].

A study carried out in Spain analyzed how the prescription of statins, antidepressants of the selective serotonin reuptake inhibitor class and proton pump inhibitors increased in recent years in PHC, without a decrease in morbidity and mortality[14]. The medicalization of risk factors is an issue that goes beyond the statistical association of an increased probability of the occurrence of the disease and generates an association of causality, fear and inappropriate use of medications[43]. There was consensus among different authors when they analyzed the medicalization of risk factors, placing P4 as an essential activity in Medicine and Public Health. They also highlighted the need to develop more comprehensive studies on the practice of P4, extrapolating those that emphasize the establishment of patient safety warning systems[15,45].

Similarly, Brazilian authors discussed that medicalization can lead to polypharmacy, that is, patients who use five or more medications. The researchers recommended reconsidering the prescription from the anamnesis, from the physical examination to the diagnosis, in order to assess the real indication of drug use[27]. They also highlighted the need for physicians to exercise conscious deprescription and prescription, recognizing these as fundamental tools to avoid overmedicalization of the population[27].

The theoretical and practical aspects of the medical consultation associated with ethical professional performance were also explored, in order to preserve patient safety and facilitate the joint construction of behaviors. The management of patients' expectations, ideas and perceptions about the illness, differentiating present suffering from future suffering and the use of the permitted delay were characterized as favorable aspects for the exercise of P4[28].

Studies from Belgium and Spain presented the discussion about the greater exposure of family physicians to non-communicable chronic diseases, which are generally controllable and not curable, resulting from the epidemiological and demographic transition observed since the 1970s. This reality allows the family doctor to exercise P4 more routinely due to the uniqueness of the organization of the PHC medical practice, where there is the possibility of personalizing the use of screening tests for chronic non-communicable diseases, seeking individual characteristics, instead of being based only on general guidelines[38]. Furthermore, the scenario of morbidity and death was problematized, specifically, in health care for older adults[18].

A Brazilian study, when discussing screening tests, that is, those performed in an asymptomatic population, aiming for the early diagnosis of certain diseases, reaffirmed the possibility of their results being true or false. However, if the patient clearly comprehends these conditions, the probability of the emergence of a problem between the doctor and the patient is reduced when the test results are communicated[26]. This implies recognizing that a good doctor-patient relationship represents fertile ground for the development of P4, especially in controversial situations in the medical practice.

A clear example of controversial screening is that related to prostate cancer. In the European Randomized Study of Screening for Prostate Cancer, 182,160 men were randomized in nine countries, based on the variables age group, Prostate-Specific Antigen (PSA) cut-off point to indicate biopsy, and screening frequency. The frequency of testing to detect signs of disease ranged from 2 to 7 years, PSA levels from 2.5 to 10 ng/ml, and age from 55 to 69 years. After 13 years of follow-up, only an absolute reduction of 0.11 deaths from prostate cancer was observed for every 1,000 men undergoing early detection procedures[41]. These data reinforce the P4 measure of not recommending prostate cancer screening.

The US Preventive Health Task Force analyzed seven clinical, randomized, controlled trials (total of 600,000 women) comparing the mortality rate of a group of women aged 39 to 74 years undergoing screening mammography, with the

rate of a group of women not submitted to the examination, after 13 years. The relative risk was 0.85 (0.75-0.96) for women aged between 39 and 49 years, 0.86 (0.75-0.99) for women aged between 50 and 59 years and of 0.68 (0.54-0.87) for those aged between 60 and 69 years. As a result of this study, the institution recommended screening for breast cancer with biannual mammography (level of evidence B) for women aged between 50 and 69 years[41]. Mammography leads to a higher rate of detection of slowly growing cancers, especially carcinoma in situ. It is noted that this screening method presents an estimated percentage of detection of this type of cancer between 19% and 30%. From this perspective, researchers from The Nordic Cochrane Center warned about the adoption of this type of conduct when they estimated that regular screening, for 10 years, of 2 thousand women, ten healthy women would receive the diagnosis of breast cancer that would never compromise quality of life, however, it could lead to invasive interventions and psychological impairment[21].

In a Brazilian study, the author, when discussing the indication of breast cancer screening, urged family doctors and health authorities to review the protocol that can cause harm to women. The urgency of disseminating evidence-based information was also highlighted, with the production of understandable guidelines that contribute to the sharing of decisions between physicians and their patients[24].

The Portuguese study compiled considerations regarding breast and testicular self-examination in cancer screening, recording the absence of evidence that self-examination would reduce the population's morbidity and mortality[31].

A Canadian study estimated that one in five children was diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) in Kentucky, USA. In the previous two decades, the incidence of ADHD has increased, especially in the US, with a tenfold increase in medication use. The anti-ADHD drug market grew from US$15 million in the mid-1990s to US$9 billion in 2012. The consequence of these diagnoses was the emergence of polymedicated individuals, with potentially disastrous results. In 2010, a survey of 325 participants indicated that 48% of patients diagnosed with ADHD reported at least one side effect with the use of the medications recommended to treat this disease, such as appetite change, insomnia and mood swings. In addition, anti-ADHD drugs proved to be ineffective in the long term, and their use was associated with serious adverse events[35].

A similar situation was observed in the treatment of migraine in children, in the 2015 Portuguese study Migraine treatment: a chain of adverse effects. It was found that the large-scale use of acetaminophen, a drug with low migraine abortive power, in migraine attacks, exposed patients to the adverse effects of this drug, confirming the importance of P4 in the management of migraine in children[32].

It is important to highlight the Brazilian study that analyzed the exercise of P4 related to obstetric violence, defined as any form of damage caused by professional obstetric care. Obstetric violence affected 25% of women who needed this care, highlighting the high number of cesarean sections (55.6% of all births in Brazil) and unnecessary interventions (venoclysis, routine oxytocin and episiotomy)[29]. According to a document published by the WHO, the desirable cesarean rate is around 10%[46]. Therefore, the authors provoked reflection on the power of the exercise of P4 in the obstetric scenario, however, warned that this practice requires the support of pregnant women in the participatory elaboration of birth plans, considering humanized care practices for prenatal care and delivery[29].

The analysis of the palliative care approach highlighted the excesses in the treatment of patients with incurable diseases and presented tools for less iatrogenic care, indicating the practice of P4 for this population. The WHO recommends an integrated approach to palliative care in the treatment of cancer patients, characterized by psychosocial support, symptom management and a care plan[19].

One Brazilian study reinforced the dialogue between the family physician and the pathologist, as a way of exercising P4, so that changes in pathological anatomy exams derived from various techniques are not evaluated in a way that is disconnected from the patient's clinical condition, as this could lead to an increase in unne-

cessary care[30]. The study encouraged the family doctor to discuss cancer cases with the pathologist, from the perspective of the P4 concept, so that overdiagnosis and surgical overtreatment are avoided[30].

The main findings of one Brazilian study indicated that the adequate use of the available health resources, with clear indications based on scientific evidence, is necessary for the maintenance of the services, favoring the quality of care offered and reinforcing the importance of a robust and transparent doctor-patient relationship, as a basis for the exercise of P4[28].

The report of two clinical cases described interventions performed on older adult patients, with multimorbidities and using several medications, who suffered from additional diseases secondary to the adopted therapies. The need to balance the positive and negative factors to define the conduct to be taken was emphasized, especially with the older adult population[17].

Spanish authors exposed the difficulty in carrying out P4 based on genetic factors, as discoveries in the field of genetics often provide a false impression of control over diseases. The study emphasized that identifying the genotype does not always determine the pathological phenotype[13].

The compilation highlighted in another Spanish article warned of the production of care related to mental disorders and its possible iatrogenic effects, describing situations where pharmacological and psychotherapeutic intervention proved to be more harmful than beneficial, ratifying P4 as an essential factor for integrative mental health care[16].

The study produced in Vietnam evaluated the decision making of Vietnamese students after a brief intervention related to P4. The fifth-year medical students were submitted to three clinical situations before and after the intervention. The analysis of the actions proposed by the students showed a change of thinking, mainly related to primary and quaternary prevention, with a reduction in the proposal of unnecessary actions[36]. This evidence enables the discussion on the inclusion of P4 as a strategic element of medical education, as its adoption requires the development of specific skills and abilities to promote profound changes in health care, such as communication skills and the fundamental elements of person-centered care[47]. Therefore, it is necessary to contemplate changes in the curricular organization that stimulate the reflective and proactive attitude of students through the incorporation of varied pedagogical concepts that cover the complexity of the teaching-learning process[47].

The aim of the study from Germany was to gain a deep understanding of the most important factors that lead to excessive behavior in the medical practice. A group of family physicians from Bavaria responded to a semi-structured interview and, after analyzing the responses, the results showed difficulty in patient management, as they had free access to secondary care, leading to specialized medical treatment, without a precise indication. Furthermore, the research participants perceived poor acceptance by the community of the fact that PHC is the gateway to the health system. The changes proposed included investments in medical education, the development of a reliable doctor-patient relationship, the improvement of PHC structures and the involvement of patients and society in the definition of clinical conduct, from the perspective of the interviewees[39].

The Indian study focusing on lipodystrophy described actions related to the levels of primary, secondary, tertiary and quaternary prevention. It also emphasized that the diagnosis is essentially clinical, and the request for exams (such as ultrasound) and the excessive prescription of injectable medications should be avoided, reaffirming the use of P4 as an instrument for the reduction of actions that cause harm to patients with this condition[37].

Despite the fact that the present article was prepared from the guiding question of individual clinical practice and, in particular, of medical practice, it is important to note that P4 also acts on health activities, from the perspective of constructing good health practices to confront cultural, technical and institutional trends that may harm people and the community[47]. Therefore, it is a practice to be exercised by all members of the health teams, including managers, in order to protect the population from unnecessary and iatrogenic interventions[47].

CONCLUSION

The analyzed evidence recommends the strengthening of the doctor-patient relationship for the construction of less iatrogenic care and addresses actions in the areas of child, women and older adult health care, as well as in specific diseases such as hemochromatosis and migraine. Likewise, the analyzed studies ratified the complexity of the health-disease process and the fact that its analysis only from the perspective of the biomedical model hinders the exercise of P4, as it minimizes the importance of social determinants of health and cultural factors in the production of illness.

A limitation of this study is the performance of a single evidence search strategy based on the research question, due to the reduced number of articles published on the subject. The fact that the study did not include the total period of the Covid-19 pandemic may also be a limitation, considering that there were important changes in the health work process, with consequences in the follow-up of patients and in the exercise of prevention measures.

However, the results of the study provoke reflection on the incorporation of a less iatrogenic medical practice, valuing medicine centered on the person and on the attributes of PHC. The results reaffirm that clinical procedures must be increasingly individualized, considering not only protocols and guidelines, but also the combination of patient expectations and the natural history of the disease. It became clear that a robust doctor-patient relationship and the longitudinality of care constitute facilitating conditions for the exercise of less interventionist clinical practices, reducing ineffective interventions that generate risk and high cost for the health system. It is believed that the main contribution of this study, by presenting a synthesis of the evidence of P4 directed toward the clinical practice, is to alert the scientific community to the importance of the medical practice and, particularly, to encourage the family and community physician to strengthen their operationalization, which will have an impact on direct care gains for the patient and for the management of the health systems.

REFERENCES

1. WORLD HEALTH ORGANIZATION. Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 1946, June, no. 2, p. 100.
2. Gillon R. " Primum non nocere" and the principle of non-maleficence. British medical journal (Clinical research ed.). 1985; 291(6488)130.
3. Illich I, Cavalcanti JK. A expropriação da saúde: nêmesis da medicina. 1975.
4. Bentzen N. Wonca Dictionary of General. Family Practice, 2004.
5. Jamoulle M. Prevenção quaternária: primeiro não causar dano. Revista Brasileira de Medicina de Família e Comunidade. 2015; 10(35): 1-3.
6. Guyatt G, Cairns J, Churchill, Cook D, Haynes B, Hirsh J et al. Evidence-based medicine: a new approach to teaching the practice of medicine. Jama, 1992; 268 (17): 2420-2425.
7. Sampaio RF. Estudos de revisão sistemática: um guia para síntese criteriosa da evidência científica. Rev. bras. fisioter., 2007; 11(1): 83-89.
8. Berwanger O, Suzumura EA, Buehler AM, Oliveira JB. Como avaliar criticamente revisões sistemáticas e meta-análises. Rev Bras Ter Intensiva, 2007; 19(4): 475-80.
9. Guanilo MCDLTU, Takahashi RF, Bertolozzi MR. Revisão sistemática: noções gerais. Revista da Escola de Enfermagem da USP. 2011; 45(5): 1260-1266.
10. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. Systematic reviews, 2016; 5(1): 1-10.
11. Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. The Journal of the American Board of Family Practice, 2004; 17(1): 59-67.
12. Galvao TF, Pansani, TSA, Harrad D. Principais itens para relatar Revisões sistemáticas e Meta-análises: A recomendação PRISMA. Epidemiol. Serv. Saúde, 2015; 24(2): 335-342.
13. Gervás J, Fernández MP. Genética y prevención cuaternaria. El ejemplo de la hemocromatosis. Atención Primaria. 2003; 32(3):158-162.
14. Gervás J. Moderación en la actividad médica preventiva y curativa. Cuatro ejemplos de necesidad de prevención cuaternaria en España. Gac Sanit. 2006; 20 (Suppl 1):127-34.
15. Gervás J, Fernández MP. Limits to the power of medicine to define disease and risk factor, and quarternary prevention. Gac Sanit. 2006; 20 (Suppl 3):66-71.

16. Ortiz LA, Ibáñez RV. Iatrogenia y prevención cuaternaria en salud mental. Revista española de salud pública. 2011; 85: 513-525.

17. Cucalón JM, Guiu M. El enigma de la prevención cuaternaria en atención primaria. Cuándo hacer y cuándo no hacer (a propósito de 2 casos). SEMERGEN-Medicina de Familia; 2012; 39(6):313-315.

18. Gervás J. Prevención cuaternaria en ancianos. Revista Española de Geriatría y Gerontología; 2012; 47(6): 266-9.

19. Smith TJ, Temin S. Alesi ER, Abernethy AP, Balboni TA, Basch EM et al. American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. Journal of clinical oncology. 2012; 30(8): 880-887.

20. Liverani CA. The four steps in the prevention of human papillomavirus-associated neoplasia: considerations for preventive measures, screening, disease impact, and potential overtreatments in HPV-related pathology. Arch Gynecol Obstet. 2013;288(5):979-88.

21. Santos J. Rastreamento do câncer de mama: as três luzes do semáforo. Revista Brasileira de Medicina de Família e Comunidade. 2013; 8(26): 11-15.

22. Kalra S, Sreedevi A, Unnikrishnan, AG. Quaternary prevention and diabetes. Journal of the Pakistan Medical Association. 2014; 64(11) :1324-26.

23. Baricević IZ, Botica MV, Pavlic-Renar I. Quaternary prevention as a basis for rational approach to the patient in family practice. Liječnicki Vjesnik. 2014; 136(5-6):152-155.

24. Tesser CD. Cuidado(!) na prevenção do câncer: ética, danos e equívocos. Revista Brasileira de Medicina de Família e Comunidade. 2014; 9(31): 180-182.

25. Mangin D, Heath I. Multimorbidity and quaternary prevention (P4). Revista Brasileira de Medicina de Família e Comunidade. 2015;10(35):1-5.

26. Báez MP. Sobrerastreamento ou prevenção em uma escala humana? Excesso de rastreamento. Revista Brasileira de Medicina de Família e Comunidade. 2015; 10(35): 1-7.

27. Santana MCG, Gavilán-Moral E, Villafaina-Barroso A, Gracia LJ. Prescripción prudente y deprescripción de fármacos como herramientas para la prevención cuaternaria. Revista Brasileira de Medicina de Família e Comunidade, 2015; 10(35): 1-8.

28. Norman AH, Tesser CD. Prevenção quaternária: as bases para sua operacionalização na relação médico-paciente. Revista Brasileira de Medicina de Família e Comunidade. 2015; 10(35): 1-10.

29. Tesser CD, Knobel R, Andrezzo H, Faria HFA, Diniz SG. Violência obstétrica e prevenção quaternária: o que é e o que fazer. Revista Brasileira de Medicina de Família e Comunidade. 2015; 10(35): 1-12.

30. Yver M. Surgical pathology in cancer diagnosis: implications for quaternary prevention. Revista Brasileira de Medicina de Família e Comunidade. 2015; 10(35): 1-7.

31. Santos JA. Breast and testicular self-examinations in cancer screening: a matter of quaternary prevention? Revista Brasileira de Medicina de Família e Comunidade. 2015; 10(36): 1-6.

32. Veloso TS, Cambão MS. Migraine treatment: a chain of adverse effects. Springerplus. 2015; 4(409):1-4.

33. Cruz-Tabuenca H. Sobre la prevención cuaternaria en niños escolares. Medicina Naturista. 2015;9(2): 119-23.

34. Carpenter CR, Raja AS, Brown MD. Overtesting and the downstream consequences of overtreatment: implications of "preventing overdiagnosis" for emergency medicine. Academic Emergency Medicine. 2015;22(12):1484-92.

35. ST-Onge JC. Attention-deficit hyperactivity disorder: preventing overdiagnosis and overtreatment. Revista Brasileira de Medicina de Família e Comunidade. 2015;10(35):1-8.

36. Tran THV, Vo TL. Impact of quaternary prevention as a brief intervention in medical students' clinical decisions: experience from Vietnam. Revista Brasileira de Medicina de Família e Comunidade. 2015; 10(35), 1-8.

37. Kalra S, Kumar A, Gupta, Y. Prevention of lipohypertrophy. J Pak Med Assoc. 2016; 66(7): 910-1.

38. Bae J-M, Jamoulle M. Primary care physicians' action plans for responding to results of screening tests based on the concept of quaternary prevention. Journal of Preventive Medicine and Public Health. 2016; 49(6): 343.

39. Alber K, Kuehlein T, Schedlbauer A, Schaffer S. Medical overuse and quaternary prevention in primary care – A qualitative study with general practitioners. BMC family practice. 2017; 18(1): 1-13.

40. Coll-Benejam T, Bravo-Toledo R, Marcos-Calvo MP, Astier-Peña MP. Impact of overdiagnosis and overtreatment on the patient, the health system and society. Aten Primaria. 2018;50 (Suppl 2): 86-95.

41. Modesto AADA, Lima RLB, D'Angelis AC, Augusto DK. A not-so-blue November: debating screening of prostate cancer and men's health. Interface-Comunicação, Saúde, Educação. 2018; 22(64), 251-262.

42. Báez MP, Jamoulle M. Vacunación contra el virus del papiloma humano a la luz de la prevención cuaternaria. Revista Brasileira de Medicina de Família e Comunidade. 2019; 14(41): 1-6.

43. Peduzzi M, Agreli HF. Teamwork and collaborative practice in Primary Health Care. Interface (Botucatu). 2018; 22(Supl. 2):1525-34

44. Oliveira MAC, Pereira IC. Atributos essenciais da Atenção Primária e a Estratégia Saúde da Família Rev Bras Enferm. 2013;66(esp):158-64.

45. Norman AH, Tesser CD. Prevenção quaternária na atenção primária à saúde: uma necessidade do Sistema Único de Saúde. Cad. Saúde Pública. 2009; 25(9): 2012-2020.

46. Organização Mundial da Saúde. Declaração da OMS sobre Taxas de Cesáreas. 2015 Available at: http://apps.who.

int/iris/bitstream/10665/161442/3/WHO_RHR_15.02_por.pdf

47. Depallens, MA et al. Prevenção quaternária, reforma curricular e educação médica. Interface - Comunicação, Saúde, Educação [online]. 2020, v. 24, suppl 1 [Accessed on April 20 2022] , e190584. Available at: <https://doi.org/10.1590/Interface.190584>. Epub 14 Set 2020. ISSN 1807-5762. https://doi.org/10.1590/Interface.190584.
48. Tesser CD. Por que é importante a prevenção quaternária na prevenção? Rev Saude Publica. 2017;51:116.

Authors' contributions

[1,2,3,4,5] Substantial contribution to study design or data interpretation; [1,5] Participation in the drafting of the preliminary version; [1,2,3,4,5] Participation in the review and approval of the final version; [1,2,3,4,5] Responsibility for the accuracy or completeness of all parts of the study.

Acknowledgment

To the librarian Márcia dos Santos for the assistance in accessing the databases.

Corresponding Author:
Janise Braga Barros Ferreira
janise@fmrp.usp.br

Editor:
Prof. Dr. Paulo Henrique Manso

Received: jul 14, 2021
Approved: aug 02, 2022