



ORIGINAL ARTICLE

Comprehensive management of risk factors in peripheral vascular disease. Expert consensus[☆]



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KEYWORDS

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Abstract

Introduction: There is currently a degree of divergence among the main clinical practice guidelines on the management of risk factors for peripheral arterial disease (PAD). This project aims to gain understanding of the management of PAD risk factors in clinical practice and to reach a multidisciplinary consensus on the strategies to be followed in order to optimize its identification, treatment, and follow-up.

Methodology: A multidisciplinary consensus following the Delphi methodology.

Results: Professionals (n = 130) with extensive experience in PAD participated in this consultation. The results suggest that in order to optimize the control of risk factors, efforts should be aimed at: (1) promoting the involvement and awareness of all specialists in the identification of and screening for the disease; (2) guaranteeing the possibility of evaluating the ankle-brachial index (ABI) in all the medical specialties involved; (3) promoting strategies for patients to quit smoking through the use of drugs, programs, or referrals to specialized units;

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(4) promoting an appropriate Mediterranean-based diet and the prescription of daily exercise; (5) raising awareness of the importance of ensuring LDL cholesterol values below 70 mg/dL, especially in symptomatic but also in asymptomatic patients (<55 mg/dL following the publication of the ESC/EAS guide); (6) recommending the use of antiplatelet therapy in asymptomatic patients with diabetes mellitus (DM) and/or a pathological ABI; and (7) protocolizing the annual evaluation of ABI in high-risk patients.

Conclusion: This document presents the 22 agreed-upon strategies which are intended to help professionals optimize multidisciplinary management of PAD risk factors.

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PALABRAS CLAVE

Enfermedad arterial periférica;
Factores de riesgo;
Consenso;
Delphi;
Multidisciplinar;
Práctica clínica

Manejo integral de los factores de riesgo en enfermedad arterial periférica. Consenso de expertos

Resumen

Antecedentes y objetivo: Actualmente, existe cierta divergencia entre las principales guías de práctica clínica sobre el manejo de los factores de riesgo de la enfermedad arterial periférica (EAP). El objetivo de este proyecto es conocer el manejo de los factores de riesgo de la EAP en la práctica clínica y alcanzar un consenso multidisciplinar sobre las estrategias que se tienen que seguir para optimizar su identificación, tratamiento y seguimiento.

Metodología: Consenso multidisciplinar mediante metodología Delphi.

Resultados: En la consulta participaron 130 profesionales con amplia experiencia en EAP. Los resultados sugieren que para optimizar el control de los factores de riesgo los esfuerzos deben dirigirse a: 1) promover la involucramiento y concienciación de todas las especialidades en la identificación y el cribado de la enfermedad; 2) garantizar la posibilidad de realizar el índice tobillo-brazo (ITB) en todas las especialidades implicadas; 3) fomentar estrategias de deshabituación del tabaquismo mediante el uso de fármacos, programas o derivaciones a unidades especializadas; 4) promover el seguimiento de una alimentación adecuada basada en la dieta mediterránea y la prescripción de ejercicio diario; 5) concienciar sobre la importancia de alcanzar unos valores de colesterol unido a lipoproteínas de baja densidad (cLDL) inferiores a 70 mg/dL especialmente en pacientes sintomáticos, pero también en asintomáticos (< 55 mg/dL tras la publicación de la guía ESC/EAS); 6) recomendar el uso de antiagregantes plaquetarios en pacientes asintomáticos con diabetes mellitus (DM) y/o ITB patológico, y 7) protocolizar la reevaluación del ITB anualmente en pacientes de alto riesgo.

Conclusión: Las 22 estrategias consensadas en el presente documento pretenden ayudar a los profesionales a optimizar el manejo multidisciplinar de los factores de riesgo de la EAP.

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Introduction

Peripheral artery disease (PAD) is a chronic, essentially arteriosclerotic illness that mainly affects the lower limbs, conditioning blood flow to them¹. It tends to appear in people older than 50 years and its prevalence increases with age². Due to population aging and the increase in the incidence of risk factors, its prevalence has risen in recent years³.

Though critical ischemia, its most severe form, can lead to limb amputation and the patient's death⁴, even its less severe or asymptomatic forms are associated with a high risk of cardiovascular morbidity and mortality, a reduction in mobility, and a decline in the patient's health-related quality of life^{3,4}. In fact, it is a disease with great prognostic significance in the event of a suspicion of arteriosclerotic disease in other territories⁵.

Taking into account that more than half of patients are asymptomatic⁶ and that preventative therapy reduces the risk of complications and death⁷, it is important to recognize subclinical forms in time and to control all risk factors of the disease. Some of these risk factors (age, sex, or family medical history) cannot be changed. However, there are others that can be modified (tobacco use, hypertension, hyperlipidemia, diabetes mellitus (DM), obesity, or poor dietary habits)⁸.

Though the main clinical practice guidelines emphasize the importance of a multidisciplinary approach in managing these risk factors^{9–12}, there are discrepancies among the guidelines on issues such as the population eligible for PAD screening. There is also a lack of specific recommendations related to risk factor management, such as tobacco use cessation, changes towards a healthy lifestyle, or hemoglobin A1c (HbA1c) therapeutic targets in patients with DM^{9–12}.

This work intends to explore the current situation and reach a multidisciplinary consensus using Delphi method, on strategies to be followed to optimize the identification, treatment, and follow-up of PAD risk factors in the Spanish healthcare setting.

Materials and methods

Study design

The project was led by a multidisciplinary scientific committee comprising eight representatives of the scientific societies which supported the project: the Spanish Society of Arteriosclerosis (SEA), the Spanish Society of Cardiology (SEC), the Spanish Diabetes Society (SED), the Spanish Society of Endocrinology and Nutrition (SEEN), the Spanish Society of Primary Care Physicians (SEMERGEN), the Spanish Society of Family and Community Medicine (semFYC), and the Spanish Society of Internal Medicine (SEMI).

To reach a consensus among the participants, two rounds of Delphi consultations were conducted. This formal, systemic method is used to reach consensus among experts in a specific area of knowledge or common practice. It is an iterative, anonymous process with controlled feedback that provides a statistical response from the group¹³.

The first round questionnaire was developed based on a literature review (MEDLINE/PubMed and gray literature) and a discussion group with the scientific committee. The first round questionnaire consisted of two sections: (1) context: open and closed questions (multiple choice or dichotomous response) on participants' sociodemographic and workplace characteristics and issues related to the perception of the therapeutic target for low-density lipoprotein cholesterol (cLDL)¹⁴ and (2) consensus: description of habitual clinical practice and definition of recommendable strategies for the identification and screening of patients with PAD, the control of risk factors (tobacco use, DM, cLDL, lifestyle, hypertension), and treatment and follow-up of patients with PAD.

The second round only included statements that did not reach consensus in the first round. Each panelist was shown their score and the score awarded by the majority of panelists in the first round.

The level of agreement with the statements presented was evaluated using a 7-point Likert scale (from "1 = completely disagree" to "7 = completely agree") and from three perspectives: habitual clinical practice, necessity, and feasibility of being implemented in the short- to medium-term (≤ 5 years). Consensus was defined as at least 75% of panelists coinciding on agreement (5–7) or disagreement (1–3).

Panel of experts

Each scientific society selected and invited participants according to their professional experience in managing PAD. A link to the online questionnaire was sent via email to a total of 250 experts. The consultation, which was not remunerated, was carried out between May and June 2019.

Data analysis

The percentages obtained for each response were calculated along with the means and standard deviations (SD) of the val-

Table 1 Panelists' sociodemographic characteristics.

	Total (n = 130)
Sociodemographic characteristics	
Age, years [mean (SD)]	50.0 (9.8)
Sex, male [% (n)]	63.1 (82)
Medical specialty [% (n)]	
<i>Angiology/vascular surgery</i>	13.9 (18)
<i>Family and community medicine</i>	28.5 (37)
<i>Internal medicine</i>	20.8 (27)
<i>Cardiology</i>	14.6 (19)
<i>Endocrinology</i>	22.3 (29)
Experience, years [mean (SD)]	23.2 (9.9)
Workplace characteristics	
Type of center [% (n)]	
<i>Health center</i>	27.7 (36)
<i>Specialty center</i>	1.5 (2)
<i>Level 1 hospital</i>	6.2 (8)
<i>Level 2 hospital</i>	16.9 (22)
<i>Level 3 hospital</i>	47.7 (62)
Availability of angiology/vascular surgery [% (n)]	63.8 (83)
Possibility of conducting ABI in all patients who require it [% (n)]	86.2 (112)
With auxiliary healthcare personnel for PAD screening [% (n)]	65.4 (85)
<i>Nursing Department</i>	62.3 (81)
<i>Podology Department</i>	8.4 (11)
<i>Other</i>	2.3 (3)
With specific protocols for multidisciplinary follow-up on risk factors [% (n)]	20.0 (26)
With access to specific units/programs for managing PAD	83.8 (109)
<i>Podology/diabetic foot units</i>	60.7 (79)
<i>Tobacco cessation</i>	51.5 (67)
<i>Rehabilitation</i>	41.5 (54)
<i>Vascular risk units</i>	42.3 (55)
<i>Other</i>	8.5 (11)

SD: standard deviation; ABI: ankle-brachial index; PAD: peripheral artery disease.

ues (STATA, version 14). In addition, a subanalysis according to specialty was conducted for some issues.

Results

Context

Panelists' sociodemographic and workplace characteristics

A total of 130 experts from all regions of Spain (except Cantabria) completed the first questionnaire (response rate of 52%). Of them, 122 completed the second round (94%). The mean age of all participants (n = 130) was 50 years and 63% were men.

Most of them (80%) indicated that there were no specific protocols for the multidisciplinary management of risk factors of PAD in their workplace (Table 1).

Table 2 Involvement of different specialties in the identification and screening of patients with PAD: habitual practice, necessity, and feasibility.

	Habitual practice % (n)	Necessity % (n)	Feasibility % (n)
<i>Identification</i>			
Angiology/vascular surgery	100.0 (18)	100.0 (18)	100.0 (18)
Family and community medicine	72.9 (37)	97.3 (37)	89.2 (37)
Internal medicine	81.4 (27)	92.6 (27)	92.6 (27)
Cardiology	31.6 (19)	100.0 (19)	68.4 (19)
Endocrinology	58.6 (29)	93.1 (29)	86.2 (29)
<i>Screening</i>			
Angiology/vascular surgery	100.0 (18)	94.4 (18)	100.0 (18)
Family and community medicine	62.1 (37)	97.3 (37)	81.1 (37)
Internal medicine	70.3 (27)	92.6 (27)	88.9 (27)
Cardiology	5.3 (19)	84.2 (19)	52.6 (19)
Endocrinology	48.3 (29)	93.1 (29)	75.9 (29)

PAD: peripheral artery disease.

Perception of the therapeutic target for cLDL

According to the experts, half (54.4%) of patients with a medical history of PAD who were currently receiving lipid-lowering treatment would reach the therapeutic target for cLDL.

Of the experts, 75.4% considered that it was a priority to reach the cLDL target for all patient profiles using, if necessary, all available therapeutic alternatives until it is achieved.

Consensus: clinical practice and recommendable strategies

Of the 23 strategies proposed for managing the risk factors in patients with PAD, panelists agreed on ($\geq 75\%$) considering 22 of them necessary and 21 feasible to implement in clinical practice. Of these 22 strategies, nine were already implemented in clinical practice in a widespread manner ($>75\%$), six were moderately implemented (50%–75%), and five were hardly followed at present ($<50\%$).

Identification and screening of patients with PAD

The results indicate that at present, angiology/vascular surgery, internal medicine, and family medicine are the specialties most involved in both the identification and the specific screening of patients with PAD. Cardiology is the least involved specialty. In line with these results, though all cardiologists considered that their specialty should participate in the identification and screening of these patients, 31.6% stated that their involvement was not very feasible (Table 2).

Most of the panelists (90.7%) indicated that in current clinical practice, the ankle-brachial index (ABI) is assessed in patients with symptoms suggestive of claudication or signs of PAD (Strategy 1). However, it is not common in asymp-

tomatic patients with risk factors (Strategies 2, 3, 4, and 5). There was consensus on the suitability of evaluating ABI in both cases, though its implementation in the screening of elderly asymptomatic patients seemed less feasible (Strategy 5) (Table 3).

Although annual reassessment in high-risk patients with nonpathological ABI values (Strategy 7) and a reassessment every three years in low-risk patients (Strategy 6) was considered necessary and feasible to conduct, in current clinical practice, it is not reassessed at this frequency (Table 3).

Strategies to control risk factors

Tobacco us. The panelists considered that at present, healthcare professionals informed patients with PAD about the need to stop using tobacco (Strategy 8), though the other strategies were less widespread (Strategy 9 and 10). The experts agreed that the three proposed strategies were necessary and feasible to implement in the short- to medium-term (Table 4).

Diabetes mellitus. In line with habitual clinical practice, the experts agreed that it was necessary and feasible to establish an HbA1c therapeutic target below 8% in frail patients with DM and PAD (Strategy 11) (Table 4).

cLDL. In current clinical practice, a therapeutic target for cLDL below 70 mg/dL is established for the majority of patients, although it is more common in symptomatic patients (83.8%) (Strategy 13) than in asymptomatic patients (70.0%) (Strategy 12). In both types of patient, the panel of experts agreed on the necessity and feasibility of establishing this therapeutic objective (Table 4).

Lifestyle. Specific recommendations about nutrition (Strategy 15) were given to patients less frequently than recommendations on exercise (Strategy 14) (63.9% vs. 83.1%). However, the experts agreed on the necessity and feasibility of implementing both equally (Table 4).

Table 3 Screening of patients with PAD: habitual practice, necessity, and feasibility.

	Habitual practice %	Necessity %	Feasibility %
Screening to detect PAD is done in patients...			
...with symptoms suggestive of claudication or signs of PAD (Strategy 1)	90.7	95.4	94.6
...who are asymptomatic with diabetes mellitus (Strategy 2)	61.6	93.1	87.7
...who are asymptomatic, >50 years of age, and smokers (Strategy 3)	37.7	89.2	75.3
...who are asymptomatic, >50 years of age, and have other risk factors (Strategy 4)	38.4	90.0	76.2
who are asymptomatic and elderly (Strategy 5)	26.9	89.3 ^a	73.7 ^a
When the ABI is normal in a patient who has risk factors for PAD, the frequency at which it is reassessed is...			
...three years for low-risk patients (Strategy 6)	27.0	76.1	76.3
...one year for high-risk patients (Strategy 7)	39.3	89.2 ^a	84.4 ^a

PAD: peripheral artery disease; ABI: ankle-brachial index.

^a Consensus achieved on the second round.

Table 4 Risk factor control strategies: habitual practice, necessity, and feasibility.

	Habitual practice %	Necessity %	Feasibility %
In patients with PAD who are active smokers, the healthcare professional is involved in controlling their smoking cessation by...			
...informing the patient about the importance of cutting back/quitting (Strategy 8)	94.6	99.3	96.9
...prescribing/recommending the use of drugs to help quit (Strategy 9)	61.5	90.7	83.1
...involving the patient in cessation programs or referring them to consultations/specific units (Strategy 10)	73.1	95.4	79.9
The therapeutic target (HbA1c) for frail patients with PAD and diabetes mellitus is, in general, <8% (Strategy 11)	83.8	90.8	89.3
The therapeutic target (cLDL) in patients with confirmed PAD is <70 mg/dL (or reduce by at least 50% in the case of having baseline values of 70–135 mg/dL)			
...in patients with asymptomatic PAD (Strategy 12)	70.0	97.7	89.3
...in patients with symptomatic PAD (Strategy 13)	83.8	97.7	97.7
For patients with PAD that does not limit them, aerobic exercise, such as walking five km per day (for the rest of their life) or all tolerated exercise with rest when symptoms require it, is recommended (Strategy 14)	83.1	98.4	93.9
For patients with PAD, following the Mediterranean diet which includes nuts (25–30 g/day) and extra virgin olive oil (40 mL/day, modifiable in obese patients) is recommended (Strategy 15)	63.9	97.0	99.3
Hypertensive patients with PAD may be prescribed, when necessary, β -blockers that are...			
...cardioselective (Strategy 16)	68.4	85.4	86.1
...not cardioselective (Strategy 17)	23.9	59.8 ^{a,b}	43.5 ^{a,b}
Treatment with antiplatelet drugs is recommended in patients with PAD...			
...who are asymptomatic and have a pathological ABI (Strategy 18)	72.2	85.3	86.9
...who are asymptomatic and have diabetes mellitus (Strategy 19)	70.8	81.5	88.5
...who have claudication (Strategy 20)	95.4	98.5	98.4

PAD: peripheral artery disease; HbA1c: hemoglobin A1c; cLDL: low-density lipoprotein bound cholesterol; ABI: ankle-brachial index.

^a Consensus achieved on the second round.

^b Consensus on disagreement.

Table 5 Follow-up on patients with confirmed PAD: habitual practice, necessity, and feasibility.

	Habitual practice %	Necessity %	Feasibility %
Follow-up on risk factors in patients with PAD (revascularized and nonsurgical) is done in...			
...primary care in controlled patients (Strategy 21)	81.6	92.3	88.4
...hospital specialties in patients who are difficult to control (Strategy 22)	83.9	91.6	90.0
Follow-up on risk factors in revascularized patients with PAD is done at least annually by primary care/hospital specialty departments (Strategy 23)	82.1	97.4	93.7

PAD: peripheral artery disease.

Hypertension. In line with current clinical practice, the experts agreed that if needed, cardioselective β -blockers may be prescribed (Strategy 16 and 17) (Table 4).

Treatment and follow-up on patients

Treatment with antiplatelet drugs is a widespread practice in claudicating patients (95.4%) (Strategy 20), but it is less common in asymptomatic patients with pathological ABI (72.2%) (Strategy 18) or patients with asymptomatic PAD and with DM (70.8%) (Strategy 19). Nevertheless, the experts agreed that antiplatelet treatment is necessary and feasible to implement in the three patient profiles (Table 4).

In line with current clinical practice, the experts considered it necessary and feasible to follow-up on risk factors in controlled patients through primary care (Strategy 21) and by hospital specialty departments in patients who are difficult to control (Strategy 22) and that, in revascularized patients, the frequency of follow-up should be annually at minimum (Strategy 23) (Table 5).

Discussion

One of the key actions for preventing the progression of PAD and its complications is early diagnosis and treatment¹⁵. However, despite the known association between PAD and other diseases such as DM, ischemic cardiopathy, and cerebrovascular disease¹⁶, our results indicate that specialties such as cardiology or endocrinology are not as involved in the identification of patients with PAD, revealing the need to promote a more active role of these specialties.

Given that a multidisciplinary approach to controlling risk factors is crucial for the optimization of PAD management, this document intends to highlight the role of other specialties in the control of risk factors for PAD and the need for a holistic management of the disease.

The majority of individuals with PAD do not present with signs of claudication⁶. Therefore, specific screening using the ABI could be a useful tool for the early initiation of strategies that prevent disease progression¹⁷. Our study suggests that in clinical practice, screening is only conducted systematically in people with symptoms suggestive of claudication. This could be due to three factors: the majority of

current guidelines do not recommend universal screening, the population profiles in which it is recommended are very heterogeneous among the guidelines^{9–12}, and the excessive workload that all specialties are facing at present. In this work, there was consensus on the patient profiles for which screening would be necessary and feasible.

In regard to reassessment of the ABI, the main clinical practice guidelines do not establish a specific frequency^{9,10,12} with the exception of the Spanish multidisciplinary consensus guidelines on PAD¹¹, which recommend performing it at least every three years in asymptomatic patients with low-intermediate cardiovascular risk. Though this frequency does not appear to be habitual in clinical practice, the experts agreed on reassessment at least every three years in low-risk patients and annually in high-risk patients.

One of the most important modifiable cardiovascular risk factors is tobacco, with the dose and number of years the patient has smoked being proportional to the risk^{18,19}. Our data suggest that the most widespread strategy to promote tobacco cessation is to provide the patient with information on the need to quit smoking. However, in line with the main clinical practice guidelines^{9–12}, it seems that other strategies are necessary, such as joining programs, referral to specific clinics/units, or the prescribing of/recommendation to use antitobacco drugs. The recent inclusion of coverage for antitobacco drugs in the Spanish public healthcare system and the line of action defined by the public health commission on tobacco use prevention could drive its implementation²⁰.

Another important risk factor is dyslipidemia. Indeed, lipid-lowering treatment is one of the main therapeutic strategies in patients with PAD. cLDL has been shown to have a causal role in atherosclerotic cardiovascular disease, further highlighting its importance¹⁴. More than 70% of the experts consulted believed that the therapeutic target set in clinical practice is less than 70 mg/dL, a figure that is somewhat higher than the 53% observed in a previous study²¹. Given its significance, it is necessary to underscore the importance of establishing and using the therapeutic tools necessary to achieve this target, both in symptomatic and asymptomatic patients with established PAD. It is important

to note that this therapeutic target was recommended by the guidelines at the time of consultation^{9–12}. More recently, the European ESC/EAS guidelines for the management of dyslipidemia have set the target at less than 55 mg/dL in patients with very high cardiovascular risk²², which would include patients with PAD.

Doing exercise improves symptoms of PAD as well as distance walked, especially if the exercise is supervised²³. An association between healthy eating habits and prevention of PAD and its symptoms has also been suggested^{24,25}. Providing exercise recommendations is very common in clinical practice, but providing nutrition recommendations is less common. According to the results of the PREDIMED study²⁶, the panel of experts considers it necessary to stress the importance of following the Mediterranean diet which includes nuts and extra virgin olive oil. The active role of endocrinologists and nutritionists is crucial in this regard.

Hypertension is another known risk factor. An increase in blood pressure of 20 mmHg is associated with a 63% increase in risk of PAD²⁷. However, the suitability of β -blockers for treating hypertension in patients with PAD is a subject of debate²⁸. The panel of experts concluded that hypertensive patients with PAD could be prescribed cardioselective β -blockers when necessary.

Antiplatelet therapies have been the cornerstone of treatment of patients with arteriosclerotic diseases such as PAD for a long time. This practice is followed by nearly all professionals in the case of symptomatic patients and to a lesser extent in asymptomatic patients. This trend could be due to the inconsistencies in the recommendations of the main guidelines as a result of the fact that the body of evidence on asymptomatic patients comes from studies with small sample sizes and heterogeneous populations²⁹. In line with the Spanish multidisciplinary consensus guidelines and the American Heart Association and American College of Cardiology (AHA/ACC) guidelines^{10,11}, in our study, treatment with antiplatelet drugs was considered necessary for asymptomatic patients with a pathological ABI and especially in patients with asymptomatic PAD and DM, given their greater atherothrombotic risk³⁰.

This study has some limitations inherent to its methods, in which consensus was based on the participants' experience. Although the response rate was not very high (52%), which could have led to a response bias, it is important to note that the results come from the perspective of more than 100 professionals with ample experience in PAD; this is the study's main strength. Likewise, even though not all specialties involved in the management of these patients participated in the Delphi process, the inclusion of specialists in family and community medicine, internal medicine, cardiology, endocrinology and nutrition, and angiology and vascular surgery has allowed for reaching a multidisciplinary consensus in which the main specialties are represented. The consensus reached must be contextualized within the Spanish healthcare system and is intended to serve as support for improving the multidisciplinary management of risk factors for PAD.

Conclusions

The results of the project suggest that in order to optimize the control of risk factors in patients with PAD, it is necessary to: (1) involve and increase awareness among all specialties on the identification of and screening for the disease; (2) make it possible to evaluate ABI in all the medical specialties involved; (3) promote strategies for tobacco use cessation; (4) follow an appropriate Mediterranean-based diet and the prescription of daily exercise; (5) raise awareness on the importance of achieving cLDL values below 70 mg/dL in symptomatic as well as asymptomatic patients (<55 mg/dL as per the August 2019 publication of the ESC/EAS guidelines on dyslipidemia management); (6) recommend the use of antiplatelet therapy in asymptomatic patients with PAD with DM and/or a pathological ABI; and (7) protocolize the annual reassessment of ABI in high-risk patients.

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Conflicts of interest

MC, an employee of an independent research organization (Outcomes'10 S.L.) has received professional fees for her contribution to the execution and coordination of the project and the writing of this manuscript. JMM, NP, and RC have received professional fees from Amgen for conferences and advising work.

Appendix A. Researchers who form part of the CREVASP working group and participated in the consensus

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