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POSITION STATEMENT

EADV Task Force Pruritus White Paper on chronic pruritus and chronic prurigo: Current challenges and future solutions

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Abstract

Chronic pruritus (CP) is frequent in general medicine and the most common complaint in general dermatology. The prevalence of CP is expected to rise in the future due to the ageing population. The clinical presentation, underlying aetiology and treatment strategy of CP are heterogeneous. Also, individual treatment aims and physical, psychic and economic burdens of patients might vary. Chronic prurigo (CPG) is the most severe disease in the chronic pruritus spectrum, being associated with long-standing scratch-induced skin lesions and a therapy refractory itch-scratch-cycle. It is thus important to raise disease awareness for CP and CPG in the general public and among decision-makers in the health system. Further, there is a need to support a rational clinical framework to optimize both diagnostics and therapeutics. Currently, there is still a shortcoming regarding approved therapies and understanding CP/CPG as severe medical conditions. Therefore, the EADV Task Force Pruritus decided to publish this white paper based on several consensus meetings. The group consented on the following goals: (a) ensure that CP is recognized as a serious condition, (b) increase public awareness and understanding of CP and CPG as chronic and burdensome diseases that can greatly affect a person's quality of life, (c) clarify that in most cases CP and CPG are non-communicable and not caused by a psychiatric disease, (d) improve the support and treatment given to patients with CP to help them manage their disease and (e) publicize existing therapies including current guidelines. We aim to point to necessary improvements in access and quality of care directed to decision-makers in health policy, among payers and administrations as well as in practical care.

S. Ständer and M. P. Pereira: Equally contributed.

For affiliations refer to page 1690.

INTRODUCTION FROM THE EADV TASK FORCE PRURITUS

The EADV Task Force Pruritus (TFP) was founded in 2016 and unites experts and researchers in pruritus medicine originating from Dermatology, Psychology and Psychosomatics across Europe and additional countries. Since then, the TFP performed several clinical and translational projects including publication of the European guideline on chronic pruritus (CP) and, based on international collaborations in the International Forum for the Study of Itch (IFSI), International Dermatology Outcome Measures (IDEOM) and in the International League of Dermatological Societies (ILDS) an international guideline on chronic prurigo (CPG).[1,2] In all projects, patient representatives have been included. After years of fruitful collaboration and collective experience in exchange with different stakeholders including patients and colleagues from in- and outside dermatology, the TFP reached the decision to make aware on the current situation and unmet needs in pruritus medicine in a white paper. This white paper aims to describe research and healthcare gaps in patients with CP (Appendix S1).

CP is defined as pruritus lasting 6 weeks or longer.[2,3] This discomforting symptom induces the urge to scratch and is related to a plethora of dermatologic, systemic, neurologic as well as psychological/psychiatric etiological conditions.[3] Though pruritus is a skin sensation and a symptom of many diseases, CP should be considered as a disease on its own with functional and structural pathobiology in the skin and nervous system[3] (Appendix S1: Introduction).

CP occurs globally, in all ages, sex and ethnics. It is estimated that 95 million European adults have unpleasant skin sensations including pruritus.[4] Regarding the clinical phenotype, patients with CP can be clinically classified into three groups according to the International Forum for the Study of Itch (IFSI)[1,3]:

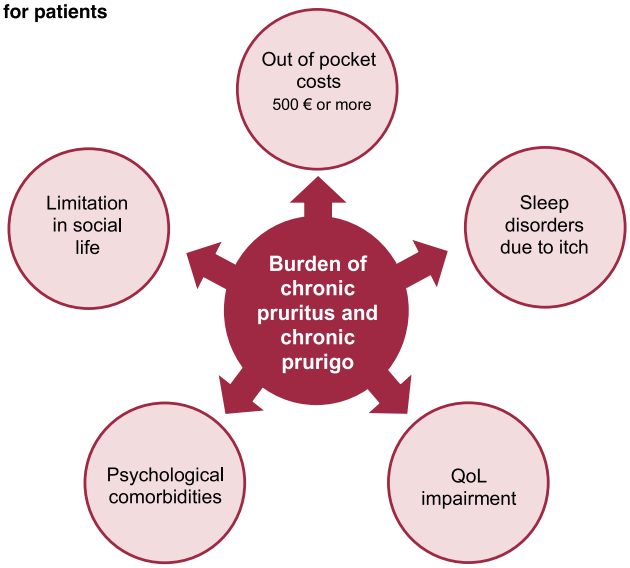
(i) CP along with a clinically visible dermatosis (termed CP on lesional skin).
(ii) CP without any skin lesions (termed CP on non-lesional skin).

Box 1. Impact of Chronic Pruritus and Chronic Prurigo

Significance of pruritus

- CP is frequent in the general population; CPG is less frequent and not well-known
- CP and CPG can affect people of every age, sex and ethnicity.
- CP is a symptom and a disease in itself; CPG is a disease

Burden for patients



Statement Prevention

- CP and CPG are difficult to prevent.
- Current best prevention strategy is:
  1. Present early to a health care professional.
  2. Initiate an early and effective treatment of the disease causing pruritus and of the pruritus itself in order to limit the vicious circle of itch-scratching.
  3. Provide medical information and psychological support to patients. Patient education is very important to promote adherence to treatment, especially when topical treatment is involved.

Aims

- Increase public and healthcare awareness and understanding of CP and CPG as chronic and burdensome diseases that can greatly affect a person's QoL.
- Sustain that living with CP and CPG has large implications on holistic well-being and encourage patients with CP and CPG to seek help early.
- Long-term control is needed in order to prevent disease progression. This shall include information of patients on available treatments, their efficacy and the topic of potential placebo/nocebo effects.

FIGURE 1 Box 1. Impact of chronic pruritus and chronic prurigo.

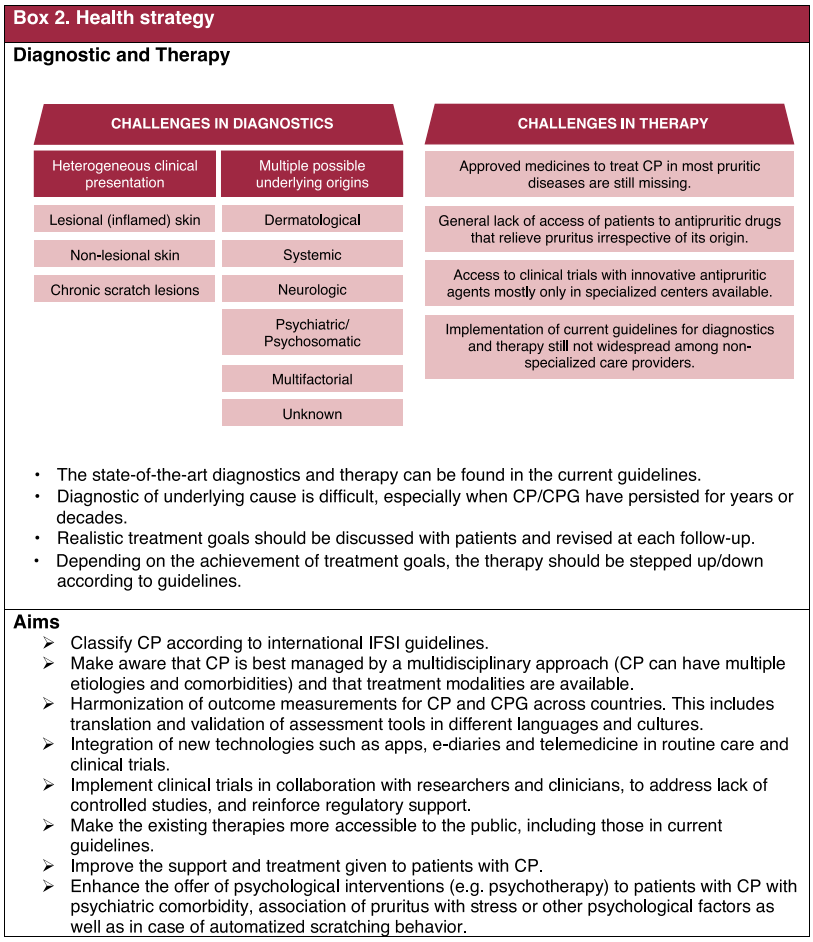


FIGURE 2 Box 2. Health strategy.

(iii) CP dominated by chronic scratch lesions, such as CPG, which is the most representative disease in the CP spectrum as it is associated with severe pruritus and a therapy refractory itch-scratch-cycle.[5]

CPG is thus a condition defined by the presence of CP and the development of pruriginous lesions due to a prolonged scratching behaviour.[5]

In past projects, we achieved that CPG has received more attention and research activity.[5,6] Our activity has recently led to substantial pharmaceutical-driven clinical trials and the first approved therapy for CPG in 2022. Our scientific work is further reflected by the fact that 64/100 papers from 12 of the 18 countries publishing on CPG originate from Europe.[7]

With this paper, we want to raise awareness of CP and CPG and explain important needs and areas of necessary action in pruritus-related medicine.

METHODS

TFP members were invited to participate in this initiative and select one of the predefined topics as follows: impact of CP, health strategy, research and development, awareness and advocacy. Thirty of the 36 invited TFP members agreed to participate. In a first virtual meeting with all experts (January 2022), groups and a group leader were determined. Each group was composed of six to nine members (Table S1). The four groups met several times digitally independently from each other in order to discuss and consent on content and action plans. After a period of 6 months, each group shared with the whole author group an outline of specific topic issues, a summary and suggested actions. In a consensus conference (August 2022), the summary and suggested actions were discussed, modified and consented. The paper was framed and circulated among the group leaders and finally across the whole group for comments and approvals.

Specific issues in pruritus care, unmet needs and goals

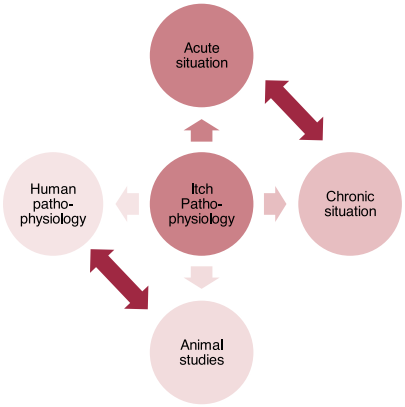
Patients with CP are highly burdened due to CP itself, but also due to the lack of largely approved therapies, a lack of expert centres, of medical education of health care professionals, and available and valid patient resources.[8,9] Missing implementation of national and international guidelines

Box 3. Research and Development

Pathophysiology

- Our understanding of CP mostly comes from animal studies and from translational and clinical studies enrolling patients with various pruritic conditions
- While these studies are essential for exploring the underlying causes and mechanisms, it is crucial to apply this knowledge to human studies.
- We need to determine if the findings from animal research are applicable to patients with acute pruritus, CP, and CPG.

Pathophysiological considerations



Aims

- Improve understanding of pathophysiological processes behind CP and CPG in humans.
- Focus on human studies assessing the activation of histaminergic and non-histaminergic itch pathways, the role of inflammatory mediators and effects of new drugs.
- Improve research concerning skin-nerve-interactions including the communication between skin components and receptors involved in itch.
- Work to find disease biomarkers that are lacking for the moment.
- Initiate studies on the effect of psychological interventions: Research in the skin-brain-relationship.

FIGURE 3 Box 3. Research and development.

contributes to an undertreatment of patients and inconsistencies in the therapeutic quality. Also, the lack of patient organizations, national education programmes and priority by stakeholders further complicates the situation. In order to address these issues, the TFP outlines here specific issues in pruritus care, defines unmet needs and aims and recommends actions, which will help address the goals. The overarching goal is to provide a framework for improved access and quality of care and to increase the awareness of the burdensome disease of CP.

One of our major aims is to ensure that CP and CPG are recognized as diseases and serious conditions in the wider healthcare area. We aim to increase public awareness and understanding of CP as a chronic and burdensome disease that can greatly affect a person's quality of life (QoL). It is important to clarify that, in most cases, CP is non-communicable and not caused by a psychiatric disease. By achieving this, patients will profit from diagnostic efforts and consideration for therapy. We also underline the importance to publicize existing therapies including current guidelines.

Promoting greater clinical awareness and research into CP and CPG by spreading the knowledge on pathophysiology, diagnostics, current guidelines and novel therapies is of highest importance to improve, on the long run, the health care of affected patients. This shall enhance the support and treatment given to patients with CP and CPG to help them manage their disease. To achieve this goal, all stakeholders are invited to participate in promoting the field of pruritus medicine and engage in novel and innovative ideas and groups to the field.

In detail, we state-specific issues as follows (Figures 1–4):

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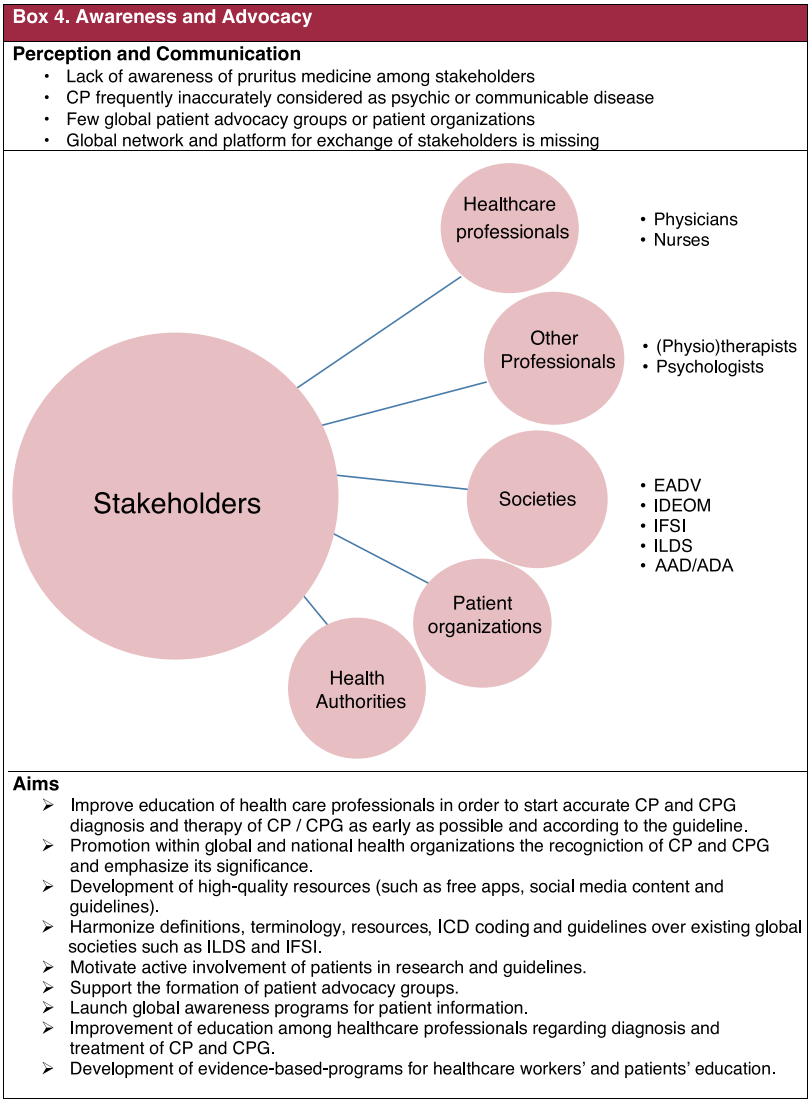

FIGURE 4 Box 4. Awareness and advocacy.

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CONFLICT OF INTEREST STATEMENT
Sonja Ständer was speaker and/or consultant and/or Investigator and/or has received research funding from AbbVie, Almirall, Beiersdorf, BMS, Clexio, Eli Lilly, FomF, Galderma, German Research Foundation (DFG), Integrity CE, Kiniksa, Leo Pharma, L'Oréal, MEDahead, Moroscience, NACCME, Novartis, Omnicuris, P.G. Unna Academy, Pfizer, Sanofi, TouchIME, UCB, Vifor and WebMD. Manuel P. Pereira was speaker and/or consultant and/or investigator and/or has received research funding from AbbVie, Allakos, Almirall, Aslan Pharmaceuticals, Beiersdorf, Celldex Therapeutics, Celltrion Healthcare, Eli Lilly, Galderma, GA^{2}LEN, Incyte, Menlo Therapeutics, Novartis, P.G. Unna

Akademie, Pfizer, Sanofi and Trevi Therapeutics. Claudia Zeidler is an investigator for Novartis, Janssen, Pfizer, UCB, Lilly, AbbVie, Boehringer Ingelheim, Sanofi, Regeneron, Leo, Galderma and has received speaker honoraria/travel fees from Dermasence, Beiersdorf, Leo, Sanofi, Novartis, Unna Akademie, Allmiral and AbbVie and a grant from the European Academy of Dermatology and Venereology. Franz J Legat received honoraria as a consultant and/or advisory board member and/or speaker for Almirall, Celgene, Eli Lilly, Galderma, Menlo Therapeutics, Novartis, Pelpharma, Pfizer, Sanofi, Trevi Therapeutics, Vifor Pharma; received support for participating in scientific meetings from Amgen, AbbVie, Celgene, Eli Lilly, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pelpharma, Pfizer, Sanofi; and has served as Principal investigator in clinical studies for Amgen, Almirall, DS Biopharma, Eli Lilly, Galderma, Incyte, Kiniksa, Menlo Therapeutics, Leo Pharma, Pfizer and Trevi Therapeutics. 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Andrey Lvov was a speaker and/or consultant for AbbVie, Bayer, Beiersdorf, Galderma, Leo Pharma, Pierre Fabre, LOreal, Pfizer, Sanofi, Swixx BioPharma, Sun Pharma, Teva and received grants from AbbVie, Galderma, Pfizer, Leo Pharma, Bayer and Sanofi. Martin Metz was a speaker and/or consultant for AbbVie, Allmiral, ALK-Abello, Amgen, AstraZeneca, argenx, Bayer, Beiersdorf, Celldex, Celltrion, Escient, Galderma, gsk, Incyte, Jasper, Novartis, Pharvaris, Pfizer, Regeneron, Sanofi, Teva, ThirdHarmonicBio and Vifor. 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Matthias Augustin has served as consultant and/or paid speaker, and/or has received research grants and/or honoraria for consultations and/or scientific presentations and/or has received travel reimbursement and/or participated in clinical trials for companies that manufacture medicines for the treatment of pruritus/prurigo, including AbbVie, Almirall, Eli Lilly, Galderma, Novartis, Pfizer, Sanofi and Trevi. Andrea W.M. Evers, Jörg Kupfer, Anna Michenko, Evangelia Papadavid, Gudrun Schneider and Joanna Wallengren have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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