



UNIVERSITÀ DEGLI STUDI DI TORINO

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

Expert consensus on the tapering of oral corticosteroids for the treatment of asthma: A delphi study

This is the author's manuscript		
Original Citation:		
Availability:		
This version is available http://hdl.handle.net/2318/1810894 since 2021-10-09T19:27:03Z		
Published version:		
DOI:10.1164/rccm.202007-2721OC		
Terms of use:		
Open Access		
Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.		

(Article begins on next page)

Expert Consensus on the Tapering of Oral Corticosteroids for the Treatment of Asthma: A Delphi Study

Carey M. Suehs¹, Andrew Menzies-Gow², David Price^{3,4}, Eugene R. Bleecker⁵, Giorgio Walter Canonica⁶, Mark Gurnell⁷, Arnaud Bourdin^{1,8} on behalf of the Oral Corticosteroids Tapering Delphi Expert Panel*

¹Department of Respiratory Diseases, University of Montpellier, Centre Hospitalier Universitaire Montpellier, Montpellier, France; ²Royal Brompton and Harefield National Health Service Foundation Trust, London, United Kingdom; ³Observational and Pragmatic Research Institute, Singapore; ⁴Centre of Academic Primary Care, Division of Applied Health Sciences, University of Aberdeen, Aberdeen, United Kingdom; ⁵University of Arizona Department of Medicine, Tucson, Arizona; ⁶Personalised Medicine, Asthma and Allergy Center, Humanitas University and IRCCS Research Hospital, Milan, Italy; ⁷Wellcome Trust – Medical Research Council Institute of Metabolic Science and Cambridge National Institute for Health Research Biomedical Research Centre, University of Cambridge and Addenbrooke's Hospital, Cambridge, United Kingdom; ⁸PhyMedExp, University of Montpellier, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, Centre Hospitalier Universitaire Montpellier, Montpellier, France

*A complete list of members of the Oral Corticosteroids Tapering Delphi Expert Panel may be found in the online supplement

Degrees and ORCID identifiers

Carey M. Suehs (PhD): 0000-0002-2175-3496 Andrew Menzies-Gow (MB BS, PhD): 0000-0001-9707-4986 David Price (FRCGP): 0000-0002-9728-9992 Eugene R. Bleecker (MD): 0000-0002-4767-3494

Giorgio Walter Canonica (MD): 0000-0001-8467-2557

Mark Gurnell (MD, PhD): 0000-0001-5745-6832

Arnaud Bourdin (MD, PhD): 0000-0002-4645-5209

Correspondence and requests for reprints should be addressed to: Carey M Suehs, Ph.D., Department of Respiratory Diseases, Hôpital Arnaud de Villeneuve, 371, av. du Doyen Gaston Giraud, F-34295 Montpellier Cedex 5, France. E-mail: c-suehs@chu-montpellier.fr Tel: +33 4.67.33.35.03 Fax: +33 4.67.33.58.27

This article has an online data supplement, which is accessible from this issue's table of content online at <u>www.atsjournals.org</u>.

Author Contributions: The study facilitator (C.M.S.) designed the study, developed the protocol and data collection tools, classified hundreds of raw brainstorming statements, organized survey logistics, collected and analyzed the data, and wrote the report. The steering committee (A.M.-G., D.P., E.R.B., G.W.C., M.G., and A.B.) provided initial recommendations of experts invited to enroll in the study and provided guidance to C.M.S. on study design, data collection, survey logistics, data analysis, and report writing. Expert panel members who contributed complete questionnaires to the study are listed in the online supplement. All authors participated in the

Funding: This study was funded by an unrestricted grant obtained through an investigatordriven submission to the AstraZeneca Cybergrant portal for educational programs. This research was conducted entirely independently of the funder, who had no role in the study design, data collection, analysis, or interpretation/write-up of the study report or manuscript. Medical writing support was funded via the unrestricted grant.

Running Head: Oral corticosteroid tapering Delphi consensus (45/50 characters)

Subject Category: Asthma; 1.11 Clinical Asthma

Word count: 4105

At a Glance

What is the current scientific knowledge on this subject?

Cumulative oral corticosteroid treatment for asthma is associated with costly and burdensome side effects and comorbidities. 'OCS stewardship' is advocated to protect patients from inappropriate OCS use and its consequences. The advent of effective OCS-sparing biological therapies also fosters new opportunities for tapering. Currently, evidence-based guidelines for OCS use, tapering, and associated comorbidity screening in asthma are lacking.

What does this study add to the field?

In the absence of clinical data to develop evidence-based guidelines, this modified Delphi consensus study brought together experts with relevant knowledge and clinical experience to generate a high-quality expert consensus statement on OCS use and tapering. The recommendations thus generated support minimizing OCS use in as much as possible. A cumulative yearly dose of 0.5 or 1g prednisolone equivalents would be indicative of poor asthma control. They also provide a first step towards development of an OCS tapering algorithm, as well as a minimum OCS adverse event screening list. Little consensus was achieved concerning the assessment and management of adrenal insufficiency, supporting a need for future related research in this specific domain. Finally, the experts strongly support shared decision making during OCS tapering.

Abstract

Rationale: There is a need to minimize oral corticosteroid use in patients with asthma to prevent their costly and burdensome adverse effects. Current guidelines do not provide recommendations for oral corticosteroid tapering in patients with asthma.

Objectives: To develop expert consensus on oral corticosteroid tapering among international experts.

Methods: A modified Delphi method was used to develop expert consensus statements relating to oral corticosteroid use, tapering, adverse effects, adrenal insufficiency, and patient-physician shared decision-making. Initial statements proposed by experts were categorized, filtered for repetition, and presented back to experts over three ranking rounds to obtain consensus (\geq 70% agreement).

Measurements and Main Results: 131 international experts participated in the study and 296 statements were ranked. Numerous recommendations and guidance regarding appropriate oral corticosteroid use were established. Experts agreed that oral corticosteroid tapering should be attempted in all patients with asthma receiving maintenance oral corticosteroid therapy, with personalization of tapering rhythm and speed. The importance of recognizing individual adverse effects was also established; however, a unified approach to the assessment of adrenal insufficiency was not reached. Shared decision-making was considered an important goal during the tapering process.

Conclusion: In this Delphi study expert consensus statements were generated on oral corticosteroid use, tapering, adverse effects screening, and shared decision-making, which may be used to inform clinical practice. Areas of non-consensus were identified, highlighting uncertainty among the experts around some aspects of oral corticosteroid use in asthma, such as adrenal insufficiency, which underscores the need for further research in these domains.

Abstract word count: 247/250

Keywords (3–5): adrenal insufficiency, adverse effects, shared decision-making, biological treatments

Introduction

Asthma is a chronic inflammatory disease, characterized by reversible airway obstruction and airway hyperresponsiveness (1), which affects ~339 million individuals worldwide (2). Approximately 5–10% of the overall asthma population have severe asthma (3), defined as uncontrolled asthma despite adherence to maximal optimized therapy and treatment of contributory factors (4). Severe asthma is associated with greater asthma-related morbidity, increased healthcare costs, more frequent exacerbations, and greater oral corticosteroid (OCS) use compared with mild/moderate asthma (5–8).

Early use of OCS in emergency department asthma treatment reduces hospital admission rates (9), supporting its routine guideline-recommended use for asthma exacerbations (4). Indeed, during acute exacerbations OCS have been observed to provide rapid benefit (10). Nevertheless, such benefits may be dose- or duration-dependent, and the current guidance remains somewhat empirical. Long-term, low-dose OCS add-on therapy is restricted to Global Initiative for Asthma (GINA) Step 5 and positioned after trials of other more preferential add-on treatments (e.g. tiotropium and biologicals), with consideration of side effects (4). However, long-term OCS therapy continues to be widely used in severe asthma, with global usage estimated at 20–60% (11).

Recent studies across multiple therapy areas demonstrate that cumulative OCS use (including long-term and intermittent use) is associated with a dose- and duration-dependent risk of potentially serious adverse effects including osteoporosis, hypertension, diabetes mellitus, cataracts, fractures, obesity, and gastrointestinal disorders(6, 11–13). Risk of adverse effects is evident at relatively low cumulative and mean daily OCS doses (12). Furthermore, long-term OCS use is associated with increased risk of mortality, reduced quality of life, and increased healthcare resource utilization and costs (5, 6, 14–16). The costly and burdensome adverse effects associated with OCS use have prompted international respiratory experts to call for a structured 'OCS stewardship' approach to protect patients from inappropriate OCS use and its consequences (16, 17). Tapering has been strengthened by the availability of effective OCS-sparing biological therapies; however, the process should still be approached with caution to prevent symptom recurrence and to avoid risking unrecognized adrenal insufficiency (12, 18). Reporting on successful OCS tapering protocols is most often indirect (i.e. the tapering algorithm is not the subject of study per se) and results in a diverse selection of study-specific algorithms (19–26), whose detail varies significantly between published studies. Current recommendations (4, 27) do not provide guidance on the choice of OCS tapering protocol or otherwise how to taper. From a clinical perspective, the lack of asthma-specific guidelines on OCS tapering and the systematic screening of adverse events represents a key barrier to reducing OCS use (16). In the absence of clinical data to develop evidence-based guidelines, this modified Delphi consensus study aimed to bring together experts with relevant knowledge and clinical experience to generate a high-quality expert consensus statement on OCS use and tapering.

Methods

Study Design

An international panel of experts participated in a four-round Delphi study to develop a systematic consensus on OCS tapering. The protocol was approved by the Institutional Review Board, University Hospital of Montpellier (reference number: 2019 IRB-MTP 04-12) and was registered on clinicaltrials.gov (NCT03934801). Surveys were administered anonymously to the expert panel using SurveyMonkey online software (<u>www.surveymonkey.co.uk</u>). Statistical analyses were performed using the R programming environment version 3.6.1 (28).

Participants and Expert Recruitment

The study steering committee (ERB, AB, GWC, MG, AMG, DP) provided initial recommendations of experts (based on their professional/association networks) to be invited to enroll in the study and eligible/responding experts were asked to recommend additional experts in the field. Pulmonologists/respiratory disease specialists, allergists, endocrinologists, pediatricians, rheumatologists, and patient advocacy organization representatives were eligible for study enrollment. Clinicians were required to manage patients on a weekly basis and have clinical experience in managing disease following OCS tapering/withdrawal to ensure a high-level knowledge in OCS management. Patient advocacy organization representatives were required to represent an asthma patient advocacy group. Experts were excluded if they were currently, or due to be (in the following 12 months) employed by, or had ownership in a pharmaceutical company. Participants were eligient daily.

Round 1: Expert Demographics and Brainstorming

Participants completed an electronically administered questionnaire to provide demographic information, including age, sex, qualifications, practice environment, specialty, years since training completion, time spent caring for patients treated with OCS, and number of patients seen per year. To initiate the brainstorming process, the questionnaire included open-ended questions to generate an initial list of statements pertaining to six categories: appropriate OCS use, OCS tapering, addressing adverse effects, adrenal insufficiency, patient-physician shared decision-making, and other aspects they felt to be important. Experts were informed that all OCS dosages should be expressed as prednisone-equivalent dosages, as reported in GINA guidelines (4). Raw statements (which refer to adult patients unless otherwise indicated) were categorized, filtered to avoid repetition, and amended for clarity (if necessary) to generate a

Page 10 of 71

final list of statements for ranking. The demographics/brainstorming and ranking questionnaires are available on the Open Science Framework platform (<u>https://osf.io/wrdbu/</u>).

Rounds 2, 3, and 4: Ranking

The final list of statements was presented to experts for ranking using a pre-defined Likert scale ranging from 'strongly disagree' (-2 points) to 'strongly agree' (+2 points). Experts were also asked to select specific responses for treatment duration, threshold values, and assessment frequencies. A stopping rule was enforced for a given statement when \geq 70% of experts indicated 'agree' or 'strongly agree' (positive consensus), or when \geq 70% indicated 'disagree' or 'strongly disagree' (negative consensus) during any round. For statements requiring a specific response consensus was defined as 70% of experts providing an identical response. Items that achieved consensus were not re-presented in subsequent ranking rounds.

Results

Participants

Of the 363 experts invited to participate in this Delphi study, 169 were enrolled in the expert panel and 131 completed at least one of the four survey rounds (Figure 1A). Participant attrition rates during the ranking process were low; of the 108 experts who participated in the first ranking round, 96 proceeded to complete all three rounds of ranking (Figure 1B). Most experts were pulmonologists (73%) or allergists (18%); however, a wide range of specialties were represented in the study. Demographics and professional characteristics of the expert panel are provided in Table 1.

Ranking Results

The initial brainstorming survey was completed over a 2-month period (April–May 2019) and three rounds of ranking surveys (rounds 2–4) were completed between 31 August and 26 September 2019. Ninety-one experts provided at least one brainstorming statement and 1447 statements were generated in total. Raw statements were categorized and filtered to avoid repetition resulting in a final list of 296 statements. The following sections summarize key points of consensus, but do not cover all 296 items presented to the experts. Full ranking results for all 296 statements are available in the online supplement (pp 1–21).

Section 1: Appropriate OCS Use for the Treatment of Asthma

Over 95% of experts agreed or strongly agreed with the following statement: 'In general, our goal should be not to use OCS. When nevertheless required, dose and duration should be minimized.'

Short-term OCS use: Positive consensus was reached for five out of six statements regarding appropriate short-term OCS use (online supplement p 1; 1.2.a–f). Short-term OCS use (<15 days) was deemed appropriate in patients experiencing acute non-resolving or life-threatening exacerbations and in patients experiencing eosinophilic or allergic exacerbations. Experts also agreed that short-term OCS use was appropriate within an asthma management plan or to avoid hospitalization. No consensus was reached on whether short-term OCS use was appropriate to palliate unavailability of hospitalization services. Experts agreed that 5–7 days constitutes the usual maximal duration for a short course of OCS for treatment of an exacerbation and that the optimal dosage of a short course of OCS should be 0.5 mg/kg/day. Items that remained controversial included whether dosages for short courses of OCS for treatment of an exacerbation should remain stable and whether the need for individual tailoring of OCS dose would render systematic application of 'ideal' doses unlikely.

Page 12 of 71

Maintenance OCS use: Nine statements were proposed regarding appropriate use of OCS as a maintenance (long-term) treatment, with five statements reaching consensus (online supplement pp 1–2; 1.6.a–i). Maintenance OCS use was considered appropriate in patients with severe asthma experiencing inadequate control despite optimization of GINA Step 5 treatments, or when adverse effects that could not be managed by another treatment presented during a tapering attempt. Consensus was also reached on eight of 13 statements characterizing an adequate response to long-term OCS use (online supplement pp 2–3; 1.9.a–m). In situations where OCS maintenance treatment is appropriate, experts considered ≤ 5 mg/day to be an acceptable dose (Figure 2).

Maintenance OCS use remained controversial in the context of adrenal insufficiency and to reduce overall OCS exposure. There was no consensus on whether maintenance OCS use is appropriate based on a patient's T2 phenotype.

Over 90% of experts agreed or strongly agreed that the annual cumulative OCS dose should be monitored as a marker of asthma control. Over 75% of experts selected a threshold of 0.5 g or 1 g as the annual cumulative OCS dose indicative of poor control in ranking round 3 (Figure 3).

It was agreed that biological therapies are useful OCS-sparing agents, and patients should be systematically assessed for suitability for biological therapy. Daily OCS dose may represent a reliable marker for the evaluation of biological treatment response (online supplement p 5; 1.16.g; 1.17.a–c).

Section 2: OCS Tapering

Two general statements reached positive consensus in the first round of ranking: 1) '*Tapering* (down to a minimal efficacious dose or complete weaning, if possible) should be attempted in

all asthma patients receiving maintenance OCS therapy, regardless of comorbidities'; 2) 'The rhythm and speed of OCS tapering requires individualization for each patient.'

Multiple statements reached positive consensus on when it may be appropriate to attempt OCS tapering, and when cautious slow attempts of tapering and complete OCS cessation are appropriate (Table 2). Tapering was deemed appropriate in multiple cases (online supplement p 5; 2.2.a–f) including: if the intensity or duration of OCS use is a cause for concern, if a patient exhibits OCS-related adverse effects or a lack of response to OCS, holds a reasonable likelihood of hypothalamic-pituitary-adrenal-axis recovery, or experiences improved asthma control following initiation of biological therapy. Tapering was also deemed appropriate in patients experiencing asthma control with OCS maintenance therapy for a minimum agreed-upon time; however, the duration of the minimum length of time remained controversial.

Tapering attempts were deemed inappropriate in patients with eosinophilic granulomatosis with polyangiitis or allergic bronchopulmonary aspergillosis that relapses during tapering (online supplement p 6; 2.4.b–c). Further statements that remained controversial included tapering in patients who demonstrated potentially harmful effects during previous tapering attempts and whether tapering should be attempted in patients with adrenal insufficiency (online supplement pp 5–6; 2.4.a,d).

Experts agreed that OCS tapering should incorporate some aspect of individualization and multiple factors were considered that may influence the rhythm and speed of OCS tapering (online supplement p 6; 2.5.a–g); such factors included: duration of previous maintenance OCS treatment, history and future risk of adverse effects, and type of adverse effect present. Three statements that remained controversial concerned the speed of OCS tapering in patients with a fast/slow response to OCS, whether OCS tapering should be guided by biomarkers at each weaning step, and whether the speed of tapering should be dependent on the known rapidity of action of the OCS-sparing drug introduced.

Five statements concerning characteristics of an acceptable OCS tapering algorithm reached positive consensus, and three statements remained controversial (Table 3). Experts agreed that biologicals should play an important role in OCS tapering and that failure to achieve a \geq 50% OCS dose reduction indicates failure of the biological and may warrant switching strategies (online supplement p 9; 2.11.c,e); furthermore, when writing prescriptions, the option to reduce dose should be considered (online supplement p 9; 2.12.c).

Section 3: Addressing OCS-Related Adverse Effects

All five general statements concerning adverse effects reached positive consensus in the first round of ranking (online supplement p 9; 3.1.a–e). Experts agreed that patients receiving OCS were at greater risk of adverse effects compared with patients receiving no OCS, and adverse effects should always be addressed, but should not preclude attempting to taper OCS to the lowest possible dose.

Experts reached positive consensus on two of three adverse effect subsets for whom OCS tapering should be a priority (online supplement pp 10–11; 3.4.a–c). A positive consensus was achieved in the first round of ranking for seven of ten elements that should be included in a minimum checklist for adverse effect screening in patients receiving OCS therapy, and three statements remained controversial (Table 4).

Section 4: Managing Adrenal Insufficiency

The majority of statements (44/55 [80%]) concerning adrenal insufficiency failed to reach consensus following three ranking rounds. Many statements that remained controversial concerned the sub-populations in which adrenal insufficiency should be assessed (online

supplement pp 13–14; 4.3.a–f, 4.4.a–d). Experts agreed that adrenal insufficiency should be assessed in individuals on regular, long-term OCS therapy. Additionally, a positive consensus was almost reached (69% agreement) on statements indicating that adrenal insufficiency should be assessed in patients exceeding an OCS dose of >2 g per year or >four repeated OCS short courses per year.

Experts agreed that adrenal insufficiency is inadequately assessed (online supplement p 16; 4.11.a) and should be assessed regularly (online supplement p 121; 4.1.a) and when OCS tapering has failed in OCS-treated patients (online supplement p 14; 4.5.b). Experts also agreed that signs of adrenal insufficiency should be symptomatically treated as much as possible during the tapering process and should not be viewed as a reason to give up on tapering altogether (online supplement p 12; 4.1.b). Experts agreed that adrenal insufficiency should be assessed using fasting morning cortisol and in case of intermediate results, follow up with a (short) tetracosactide/cosyntropin (e.g. Synacthen®) test (online supplement p 15; 4.9.c). An additional general statement regarding whether hydrocortisone replacement is preferred to continued prednisolone almost reached positive consensus, with 65% of experts agreeing with the statement and 8% disagreeing; the remaining percentage remained neutral on the subject (online supplement p 12; 4.1.c).

Consensus was reached on the need for the treating respiratory physician to assess for adrenal insufficiency in patients with severe asthma, and that management of adrenal insufficiency in patients with severe asthma should involve an endocrinologist or a multidisciplinary approach (online supplement p 20; 6.1.c,d).

Section 5: Patient-Physician Shared Decision-Making

Experts agreed that shared decision-making should be a systematic practice and selfmanagement should be limited to individuals with good levels of comprehension (online supplement p 17; 5.1.a,d). Eight statements achieved positive consensus on the importance of shared decision-making (online supplement p 17; 5.2.a–h) and 14 statements reached positive consensus concerning the content to be included in the shared decision-making process (online supplement pp 17–18; 5.3.a–n).

Section 6: Miscellaneous

Experts agreed that primary care physicians prescribing at least three courses of OCS/year to a patient should consider specialist referral (online supplement p 20; 6.2.a). Experts also achieved positive consensus on 16/17 statements concerning future research of OCS tapering (online supplement pp 20-21; 6.3.a–q). The only subject that remained controversial concerning future work was the efficacy of internet-provided algorithms for delivering symptom-driven OCS tapering guidance to asthma patients.

Discussion

This Delphi study generated expert consensus and recommendations on numerous statements concerning appropriate OCS use, OCS tapering, adverse effects, patient-physician shared decision-making, and future research domains. Consensus was reached on general statements concerning adrenal insufficiency; however, beyond generalities, consensus was not reached. Hence, improving the assessment of adrenal insufficiency was one of multiple domains identified as requiring future research.

To our knowledge, no existing asthma-specific guidelines are currently available to guide OCS tapering in clinical practice. Consensus stated that tapering should be attempted in all asthma patients receiving maintenance OCS therapy, regardless of comorbidities; however, speed and rhythm of tapering should be individualized. Furthermore, expert consensus was reached on characteristics of an acceptable OCS tapering algorithm (Table 3), which constitutes a first step towards the development of OCS tapering algorithms for use in clinical practice. These consensuses and related information are summarized in Figure 4.

Successful OCS tapering algorithms have been reported in the past (19–25, 29, 30), but vary greatly in content and reporting quality. Currently, the most detailed and recent OCS tapering algorithm is being tested in the eagerly awaited PONENTE study (26). Certain previous studies also demonstrate that prescribing treatment guided by eosinophil levels can improve control, whilst simultaneously resulting in some corticosteroid sparing (31–33). Current GINA guidelines suggest OCS dose adjustment may be supported by internet-based monitoring of symptom control and exhaled nitric oxide; however, the latter contributed little to algorithm decisions, in favor of ACQ scores (34). In the current study, only asthma control questionnaires reached positive consensus as a useful tool during OCS tapering. The need for laboratory tests or at-home lung function measurements may render many biomarker approaches impractical for patients and clinicians. In addition, GINA recommends gradually decreasing or stopping OCS in patients with a good response to biological therapies. Successful corticosteroid reduction following initiation of biological therapies, using pre-set tapering protocols, has been demonstrated in multiple studies (18). However, the latter are often short-term in nature with little focus on adrenal function assessments, and the full potential of tapering was therefore not achieved/documented. As the use of biological therapies increases, studies evaluating OCS tapering regimens on a longer basis, which can be personalized based on factors such as baseline OCS dosage and level of asthma control, will become increasingly important (e.g. the PONENTE study) (26). The current consensus statement provides broader guidance on when and how to taper OCS in patients with asthma (Figure 4), regardless of whether a biological therapy has been initiated.

Regarding appropriate OCS use, experts felt that long-term use is not appropriate in situations where other treatment options are available. However, if no alternative treatment

Page 18 of 71

options are available, experts considered $\leq 5 \text{ mg/day}$ to be an acceptable dose. This threshold is considerably lower than the definition in current GINA guidelines, which defines low-dose maintenance OCS as $\leq 7.5 \text{ mg/day}$ (4) and may result from the way the question was designed to span the range of thresholds mentioned during the brain storming phase of the study. The reader should note that non-consensus fractions of experts are willing to use 10 mg/day doses and higher, suggesting that there is considerable non-guideline-conforming OCS usage in the field, even among experts. The low consensus threshold at 5mg may also reflect the increasing importance of biologics in the domain and the resulting opportunities for tapering down to the lowest efficacious dose possible or complete cessation. Regardless, the reader should also keep in mind that a 5mg/day OCS dose amounts to a cumulative dose exceeding 1.8 g/year.

In this study, when experts were asked to consider cumulative OCS doses, they voted that 0.5 or 1 g/year would be indicative of poor asthma control. This would correspond to approximately 3.5-7 months of maintenance treatment at 5 mg/day. A previous study by Price et al demonstrated that diabetes associated with OCS use emerged at lifetime cumulative systemic corticosteroid exposures of 0.5-<1 g, with most other adverse events emerging at 1.0 to <2.5 g (12). Furthermore, a 2020 study stated that a yearly cumulative OCS dose above 1 g should be considered unacceptable in severe asthma and indicates the need for specialist referral (35). Even a short term use, which amounts to a median of 20 mg per day for approximately 6-days in a large database study, is associated with an increase in sepsis, venous thromboembolism, and fracture in the next 30 days (36). These studies highlight the need for earlier specialist referral and earlier consideration of OCS-sparing strategies in patients receiving OCS.

Biological therapies were a common subject among the experts and the initiation of a successful biological therapy was the highest-ranked situation appropriate for initiating OCS

tapering (Table 2). The reader should keep in mind that there are other important reasons for initiating tapering, such as side effects or non-response (Table 2). Key criteria for success of a biological therapy include maintenance of asthma control, reduction in exacerbations, and decrease in dose of OCS (27, 37). However, there is no clear guidance on the magnitude of OCS reduction that constitutes success or failure of a biological therapy. In this study, consensus stated that failure to achieve \geq 50% reduction in OCS indicates failure of the biological therapy and may warrant a switch in strategy. The guidance provided here will support clinical decision-making.

Items included on the minimal checklist for adverse effect screening (Table 4) have been well documented in the literature among individuals receiving OCS. Early detection of adverse effects has been shown to be important in the treatment and management of OCSrelated complications; the items on the checklist provide a basis for adverse effect screening in clinical practice (6, 11, 12, 38). This checklist further underlines the importance of adverse effect prevention measures, including calcium and vitamin D supplementation and appropriate prescribing of bisphosphonates for osteoporosis, optimizing ICS dose and medication adherence. The latter may additionally allow further reduction in OCS dose.

Previous studies have shown that adrenal insufficiency is common among frequent users of OCS following tapering (39); however, lack of clear guidance for clinicians on how to manage adrenal insufficiency may hinder OCS reduction in patients with severe asthma (16). Experts agreed on the need to regularly assess for adrenal insufficiency, and that fasting morning cortisol tests may be used (followed up with a (short) tetracosactide/cosyntropin test in case of intermediate results). Experts also highlighted the need for a process to be in place for referral to an endocrinologist alongside further research and potential education in this domain. The majority of experts agreed use of hydrocortisone replacement therapy is preferential to continued prednisolone use to aid the tapering process in the case of adrenal

Page 20 of 71

insufficiency; however, consensus was not reached. The lack of consensus on this point is not surprising given that the optimal strategy for glucocorticoid replacement in patients with adrenal insufficiency remains controversial in the literature. In the UK, hydrocortisone is the first-line treatment in management of adrenal insufficiency, followed by prednisolone (40). Prednisolone is less expensive and some experts contend it may mimic the circadian rhythm more closely than the standard thrice-daily hydrocortisone therapy; however, prednisolone may also be associated with increased relative risk of cardiovascular disease (40–42). Results of ongoing head-to-head studies will improve understanding regarding this issue (43).

Shared decision-making in OCS tapering was viewed positively by the experts. The consensus was that although the OCS-tapering process should be primarily driven by the physician, patients should contribute to the decision-making process and be educated on OCS use and tapering. Patient's perceptions are frequently ambivalent towards OCS and how they navigated previous tapering attempts should be taken into account. This is in line with emerging evidence showing that shared decision-making is becoming more common in asthma management and has been shown to improve patient adherence, outcomes, and satisfaction with care (44). Shared decision making tools/platforms to facilitate this process (e.g. 43, 44) require further development and validation for general asthma populations.

The strengths of this study include participation of 131 experts across a range of specialisms, ensuring that a wide breadth of knowledge and relevant expertise was represented among the expert panel. Results from this study also benefit from the anonymity of expert responses, alongside a clear, *a priori* definition of consensus criteria and controlled feedback. Importantly, a lack of participant attrition was observed throughout all three ranking rounds, increasing the validity of the consensus by avoiding suppression of minority opinions and minimizing potential for bias (47). A limitation of the study was the large

number of raw statements that needed to be reduced and summarized; therefore, statements presented to experts were not fully representative of all the raw statements.

This Delphi consensus study provides expert consensus statements around OCS use and tapering, which may be used to inform clinical practice and optimize management of patients with severe asthma. The recommendations also provide a first step towards development of an OCS tapering algorithm and support the ongoing OCS stewardship effort by international respiratory experts to reduce the harm from inappropriate OCS use and its consequences. While consensus was generated on numerous statements, many remained controversial, highlighting the existing uncertainty, even among international experts, around certain aspects of OCS use in asthma, such as assessment and management of adrenal insufficiency. These findings underscore the need for further research to inform clinical practice and drive future evidence-based guideline development.

Acknowledgements

Expert panel members who contributed complete questionnaires to the study are listed in the online supplement. Medical writing support was provided by Neil Patel, M.Sc., and Liz Bolton, Ph.D. of Helios Medical Communications, Alderley Edge, Cheshire, United Kingdom.

References

- Holgate ST, Wenzel S, Postma DS, Weiss ST, Renz H, Sly PD. Asthma. Nat Rev Dis Primers 2015;1:15025.
- Global Asthma Network. *The Global Asthma Report 2018*. 2018. at http://www.globalasthmareport.org>.
- Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, Adcock IM, Bateman ED, Bel EH, Bleecker ER, Boulet L-P, Brightling C, Chanez P, Dahlen S-E, Djukanovic R, Frey U, Gaga M, Gibson P, Hamid Q, Jajour NN, Mauad T, Sorkness RL, Teague WG. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43:343–373.
- Global Initiative for Asthma. *Global Strategy for Asthma Management and Prevention*.
 2020. [Accessed 30 September 2020] at https://ginasthma.org>.
- 5. Canonica GW, Colombo GL, Bruno GM, Di Matteo S, Martinotti C, Blasi F, Bucca C, Crimi N, Paggiaro P, Pelaia G, Passalaqua G, Senna G, Heffler E, SANI Network. Shadow cost of oral corticosteroids-related adverse events: A pharmacoeconomic evaluation applied to real-life data from the Severe Asthma Network in Italy (SANI) registry. *World Allergy Organ J* 2019;12:100007.
- Ekström M, Nwaru BI, Hasvold P, Wiklund F, Telg G, Janson C. Oral corticosteroid use, morbidity and mortality in asthma: A nationwide prospective cohort study in Sweden. *Allergy* 2019;74:2181–2190.
- Suruki RY, Daugherty JB, Boudiaf N, Albers FC. The frequency of asthma exacerbations and healthcare utilization in patients with asthma from the UK and USA. *BMC Pulm Med* 2017;17:74.

- Nagase H, Adachi M, Matsunaga K, Yoshida A, Okoba T, Hayashi N, Emoto K, Tohda Y. Prevalence, disease burden, and treatment reality of patients with severe, uncontrolled asthma in Japan. *Allergol Int* 2020;69:53–60.
- Rowe BH, Spooner C, Ducharme FM, Bretzlaff JA, Bota GW. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev* 2001;CD002178.doi:10.1002/14651858.CD002178.
- Tattersfield AE, Postma DS, Barnes PJ, Svensson K, Bauer CA, O'Byrne PM, Löfdahl CG, Pauwels RA, Ullman A. Exacerbations of asthma: a descriptive study of 425 severe exacerbations. The FACET International Study Group. *Am J Respir Crit Care Med* 1999;160:594–599.
- Bleecker ER, Menzies-Gow AN, Price DB, Bourdin A, Sweet S, Martin AL, Alacqua M, Tran TN. Systematic Literature Review of Systemic Corticosteroid Use for Asthma Management. *Am J Respir Crit Care Med* 2020;201:276–293.
- Price DB, Trudo F, Voorham J, Xu X, Kerkhof M, Ling Zhi Jie J, Tran TN. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. *J Asthma Allergy* 2018;11:193–204.
- Liu D, Ahmet A, Ward L, Krishnamoorthy P, Mandelcorn ED, Leigh R, Brown JP, Cohen A, Kim H. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy Asthma Clin Immunol* 2013;9:30.
- 14. Lee H, Ryu J, Nam E, Chung SJ, Yeo Y, Park DW, Park TS, Moon J-Y, Kim T-H, Sohn JW, Yoon HJ, Kim S-H. Increased mortality in patients with corticosteroid-dependent asthma: a nationwide population-based study. *Eur Respir J* 2019;54:.

- 15. Hyland ME, Whalley B, Jones RC, Masoli M. A qualitative study of the impact of severe asthma and its treatment showing that treatment burden is neglected in existing asthma assessment scales. *Qual Life Res* 2015;24:631–639.
- Chung LP, Upham JW, Bardin PG, Hew M. Rational oral corticosteroid use in adult severe asthma: A narrative review. *Respirology* 2020;25:161–172.
- McBrien CN, Menzies-Gow A. Time to FOCUS on oral corticosteroid stewardship in asthma management. *Respirology* 2019;24:304–305.
- Bourdin A, Husereau D, Molinari N, Golam S, Siddiqui MK, Lindner L, Xu X. Matching-adjusted comparison of oral corticosteroid reduction in asthma: Systematic review of biologics. *Clin Exp Allergy* 2020;50:442–452.
- Cameron SJ, Cooper EJ, Crompton GK, Hoare MV, Grant IW. Substitution of beclomethasone aerosol for oral prednisolone in the treatment of chronic asthma. *Br Med* J 1973;4:205–207.
- Bel EH, Wenzel SE, Thompson PJ, Prazma CM, Keene ON, Yancey SW, Ortega HG, Pavord ID, SIRIUS Investigators. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med* 2014;371:1189–1197.
- 21. Nair P, Wenzel S, Rabe KF, Bourdin A, Lugogo NL, Kuna P, Barker P, Sproule S, Ponnarambil S, Goldman M, ZONDA Trial Investigators. Oral Glucocorticoid-Sparing Effect of Benralizumab in Severe Asthma. *N Engl J Med* 2017;376:2448–2458.
- 22. Vogelmeier C, Kardos P, Hofmann T, Canisius S, Scheuch G, Muellinger B, Nocker K, Menz G, Rabe KF. Nebulised budesonide using a novel device in patients with oral steroid-dependent asthma. *Eur Respir J* 2015;45:1273–1282.

- 23. Braunstahl G-J, Chlumský J, Peachey G, Chen C-W. Reduction in oral corticosteroid use in patients receiving omalizumab for allergic asthma in the real-world setting. *Allergy Asthma Clin Immunol* 2013;9:47.
- Lacronique J, Renon D, Georges D, Henry-Amar M, Marsac J. High-dose beclomethasone: oral steroid-sparing effect in severe asthmatic patients. *Eur Respir J* 1991;4:807–812.
- 25. Milgrom H, Fick RB, Su JQ, Reimann JD, Bush RK, Watrous ML, Metzger WJ. Treatment of allergic asthma with monoclonal anti-IgE antibody. rhuMAb-E25 Study Group. *N Engl J Med* 1999;341:1966–1973.
- 26. Menzies-Gow A, Corren J, Bel EH, Maspero J, Heaney LG, Gurnell M, Wessman P, Martin UJ, Siddiqui S, Garcia Gil E. Corticosteroid tapering with benralizumab treatment for eosinophilic asthma: PONENTE Trial. *ERJ Open Res* 2019;5:.
- Chipps BE, Bacharier LB, Murphy KR, Lang D, Farrar JR, Rank M, Oppenheimer J, Zeiger RS. The Asthma Controller Step-down Yardstick. *Ann Allergy Asthma Immunol* 2019;122:241-262.e4.
- 28. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2016. [Accessed 30 September 2020] at https://www.R-project.org/>.
- 29. Mullarkey MF, Lammert JK, Blumenstein BA. Long-term methotrexate treatment in corticosteroid-dependent asthma. *Ann Intern Med* 1990;112:577–581.
- Nelson HS, Busse WW, deBoisblanc BP, Berger WE, Noonan MJ, Webb DR, Wolford JP, Mahajan PS, Hamedani AG, Shah T, Harding SM. Fluticasone propionate powder:

oral corticosteroid-sparing effect and improved lung function and quality of life in patients with severe chronic asthma. *J Allergy Clin Immunol* 1999;103:267–275.

- Chlumský J, Striz I, Terl M, Vondracek J. Strategy aimed at reduction of sputum eosinophils decreases exacerbation rate in patients with asthma. *J Int Med Res* 2006;34:129–139.
- 32. Green RH, Brightling CE, McKenna S, Hargadon B, Parker D, Bradding P, Wardlaw AJ, Pavord ID. Asthma exacerbations and sputum eosinophil counts: a randomised controlled trial. *Lancet* 2002;360:1715–1721.
- 33. Jayaram L, Pizzichini MM, Cook RJ, Boulet L-P, Lemière C, Pizzichini E, Cartier A, Hussack P, Goldsmith CH, Laviolette M, Parameswaran K, Hargreave FE. Determining asthma treatment by monitoring sputum cell counts: effect on exacerbations. *Eur Respir J* 2006;27:483–494.
- 34. Hashimoto S, Brinke AT, Roldaan AC, van Veen IH, Möller GM, Sont JK, Weersink EJM, van der Zee JS, Braunstahl G-J, Zwinderman AH, Sterk PJ, Bel EH. Internet-based tapering of oral corticosteroids in severe asthma: a pragmatic randomised controlled trial. *Thorax* 2011;66:514–520.
- 35. Bourdin A, Adcock I, Berger P, Bonniaud P, Chanson P, Chenivesse C, de Blic J, Deschildre A, Devillier P, Devouassoux G, Didier A, Garcia G, Magnan A, Martinat Y, Perez T, Roche N, Taillé C, Val P, Chanez P. How can we minimise the use of regular oral corticosteroids in asthma? *Eur Respir Rev* 2020;29:.
- 36. Waljee AK, Rogers MAM, Lin P, Singal AG, Stein JD, Marks RM, Ayanian JZ, Nallamothu BK. Short term use of oral corticosteroids and related harms among adults in the United States: population based cohort study. *BMJ* 2017;j1415.doi:10.1136/bmj.j1415.

- 37. Bousquet J, Brusselle G, Buhl R, Busse WW, Cruz AA, Djukanovic R, Domingo C,
 Hanania NA, Humbert M, Menzies Gow A, Phipatanakul W, Wahn U, Wechsler ME.
 Care pathways for the selection of a biologic in severe asthma. *Eur Respir J* 2017;50:.
- 38. Pisani P, Renna MD, Conversano F, Casciaro E, Muratore M, Quarta E, Paola MD, Casciaro S. Screening and early diagnosis of osteoporosis through X-ray and ultrasound based techniques. *World J Radiol* 2013;5:398–410.
- Mortimer KJ, Tata LJ, Smith CJP, West J, Harrison TW, Tattersfield AE, Hubbard RB.
 Oral and inhaled corticosteroids and adrenal insufficiency: a case-control study. *Thorax* 2006;61:405–408.
- 40. Iqbal K, Halsby K, Murray RD, Carroll PV, Petermann R. Glucocorticoid management of adrenal insufficiency in the United Kingdom: assessment using real-world data. *Endocr Connect* 2019;8:20–31.
- 41. Williams EL, Choudhury S, Tan T, Meeran K. Prednisolone replacement therapy mimics the circadian rhythm more closely than other glucocorticoids. *The Journal of Applied Laboratory Medicine* 2016;1:152–161.
- 42. Quinkler M, Ekman B, Marelli C, Uddin S, Zelissen P, Murray RD, EU-AIR Investigators. Prednisolone is associated with a worse lipid profile than hydrocortisone in patients with adrenal insufficiency. *Endocr Connect* 2017;6:1–8.
- 43. ClinicalTrials.gov. Hydrocortisone vs prednisolone in AI (HYPER-AID). 2019;
 [Accessed 30 September 2020] at https://clinicaltrials.gov/ct2/show/NCT03608943>.
- 44. Blaiss MS, Steven GC, Bender B, Bukstein DA, Meltzer EO, Winders T. Shared decision making for the allergist. *Ann Allergy Asthma Immunol* 2019;122:463–470.

- 45. Tapp H, Shade L, Mahabaleshwarkar R, Taylor YJ, Ludden T, Dulin MF. Results from a pragmatic prospective cohort study: Shared decision making improves outcomes for children with asthma. *Journal of Asthma* 2017;54:392–402.
- 46. Fiks AG, Mayne SL, Karavite DJ, Suh A, O'Hara R, Localio AR, Ross M, Grundmeier RW. Parent-Reported Outcomes of a Shared Decision-Making Portal in Asthma: A Practice-Based RCT. *PEDIATRICS* 2015;135:e965–e973.
- 47. Gargon E, Crew R, Burnside G, Williamson PR. Higher number of items associated with significantly lower response rates in COS Delphi surveys. *Journal of clinical epidemiology* 2019;108:110–120.

Figure legends

Figure 1. (A) Study flow diagram. (B) Expert participation in three statement-ranking rounds.

A



B



Figure 2. Percentage agreement among experts on acceptable doses for maintenance OCS treatment. OCS = oral corticosteroid.



Figure 3. Percentage agreement among experts for threshold options indicating a yearly cumulative OCS dose that is suggestive of poor asthma control. NA = not applicable; OCS = oral corticosteroid.





Figure 4. Graphic summary of consensus information on oral corticosteroid tapering.

*Adrenal insufficiency should be regularly assessed using fasting morning cortisol. In case of intermediate results, follow up with a (short) tetracosactide/cosyntropin test. Adrenal insufficiency management should be multidisciplinary, involving an endocrinologist.

**Comorbidity screening should include at least the following: glycemic control, bone density, blood pressure, cataracts and glaucoma, weight change, fracture risk score and

growth in pediatric populations. However, no consensus was achieved concerning the periodicity of comorbidity screening measures.

ABPA = allergic bronchopulmonary aspergillosis; ACQ = asthma control questionnaire; EGPA = eosinophilic granulomatosis with polyangiitis; HPA = hypothalamic–pituitary– adrenal axis; OCS = oral corticosteroids.

Variable	Sample	Centrality
	size (n)	
Age	131	50.6 ± 9.64
Sex (female)	35/131	26.72%
Academic qualification	131	
MD (or equivalent)	129	98.47%
PhD	71	54.20%
Masters	8	6.11%
Practice environment	131	
University hospital	117	89.31%
Private practice	11	8.40%
Academic environment	37	28.24%
Patient care environment	13	9.92%
Medical practice environment	14	10.69%
Other	7	5.34%
Specialties	131	
Allergist	24	18.32%
Endocrinologist/Metabolic	8	6.11%
Pediatrician	1	0.76%

Table 1. Expert Panel Demographic Data
Patient advocacy organization representatives	2	1.53%
Pulmonologist/Respiratory disease specialist	95	72.52%
Rheumatologist	1	0.76%
Years since completion of training	131	19 (10 to 27)
Approximate % of work spent in caring for patients treated with OCS	131	15 (5 to 30)
How often tapering is attempted in OCS patients	131	
NA (patient advocacy organization representative)	2	1.53%
Occasionally	4	3.05%
Frequently	48	36.64%
Systematically	77	58.78
Participation in studies with aim of OCS tapering	80	61.07%
Concerning OCS		
Protocols, no.	131	2 (1 to 4)
Scientific articles, no.	131	2 (0 to 5)
Patients seen per year, no.	131	50 (25 to 100)
Concerning asthma		
Protocols, no.	131	10 (4 to 20)
Scientific articles, no.	131	30 (6 to 60)
Patients seen per year, no.	131	300 (100 to 500)

In all

Protocols, no.	131	20 (10 to 40)
Scientific articles, no.	131	67 (25 to 132)
Patients seen per year, no.	131	600 (400 to 1200)

Definition of abbreviations: NA = not applicable; OCS = oral corticosteroid.

Table 2. Consensus Statements on OCS Tapering

	Strongly	Disagree,	Neutral,	Agree,	Strongly	Weighted
	disagree,	%	%	%	agree, %	mean
	%					rank*
Proceeding towards a tapering attempt is particularly appropriate when:						
Biological treatment has been initiated and results in asthma control	0.00	0.95	0.95	25.71	72.38	1.70
The patient does not appear to respond to OCS treatment	0.00	0.95	0.95	35.24	62.86	1.60
A patient exhibits symptoms/comorbidities likely linked to OCS	0.00	1.90	2.86	41.90	53.33	1.47
Patients on maintenance OCS have gained control (for a minimum agreed-upon time)	0.00	0.00	3.81	59.05	37.14	1.33
The intensity or duration of OCS treatment gives reason for concern	0.00	0.00	3.81	59.05	37.14	1.33
There is reasonable likelihood of hypothalamic-pituitary-adrenal axis recovery	0.00	1.90	11.43	54.29	32.38	1.17

Tapering should not be attempted in patients who:

	Have EGPA that relapses during tapering (and no other changes can	0.95	3.81	12 38	66 67	16 19	0.93
	be proposed)	0.95	5.01	12.50	00.07	10.17	0.95
	Have ABPA that relapses during tapering (and no other changes can	0.00	0.50	10.05	(1.00	0.50	0.71
	be proposed)	0.00	9.52	19.05	61.90	9.52	0.71
Cau	tious slow tapering is particularly appropriate for patients who:						
	Have had life-threatening attacks	0.95	3.81	3.81	60.00	31.43	1.17
	Have been dependent on systemic steroids for an extended period (e.g.	0.00	2.96	((7	(2.91	26.67	1 1 4
	6 months or more)	0.00	2.80	0.07	03.81	20.07	1.14
	Have comorbidities that respond to OCS	0.00	3.81	9.52	70.48	16.19	0.99
Cor	nplete OCS cessation (weaning) can be implemented:						
	Following a short course of OCS treatment that lasted for 5–7 days	0.95	1.90	1.90	44.76	50.48	1.42
	Following a short course of OCS treatment if patients are on inhaled	1.00	1.00	2.86	10 57	11 76	1 2 2
	anti-inflammatory therapy	1.90	1.90	2.80	40.37	44./0	1.32

When a sparing strategy has been initiated	0.95	2.86	14.29	54.29	27.62	1.05
When there is no evidence of adrenal insufficiency	0.95	6.67	13.33	59.05	20.00	0.90
When the patient has agreed to cessation	1.90	4.76	20.00	50.48	22.86	0.88
When there is no evidence of EGPA or ABPA	0.00	7.62	19.05	56.19	17.14	0.83
When the OCS dose is ≤ 5 mg prednisolone	0.95	15.24	13.33	53.33	17.14	0.70

Definition of abbreviations: ABPA = allergic bronchopulmonary aspergillosis; EGPA, eosinophilic granulomatosis with polyangiitis; OCS = oral corticosteroid.

*Note that statements are ordered by mean rank score.

Table 3. Consensus Statements Concerning Development of an OCS Tapering Algorithm

Positive consensus	Controversial
• The initial tapering of high OCS doses (e.g. >20 mg/day) can proceed at a faster pace	• In general, the speed of tapering
(e.g10 mg/week, or 30–50% reductions every 2–4 weeks)	should not exceed a reduction of
• OCS tapering should be gradual, with 2.5–5 mg steps every 0.5–2 weeks until an agreed-upon	5 mg/week
threshold is achieved (e.g. $5-10 \text{ mg/day}$), and then proceeds at a slower pace (1–2.5 mg every	• OCS tapering should incorporate
1–2 weeks)	every-other-day OCS reductions
• When a reduction in OCS by 5 mg weekly fails, a slower and lower dose reduction of	(especially prior to
1 mg/week should be attempted	discontinuation) to allow recovery
• If mild symptoms occur, maintain the current dosage; they are likely to resolve as endogenous	of the endogenous axis
axis recovery occurs	• OCS tapering should be gradual by
• If intolerable symptoms occur, return to the previous (efficacious) dose, and then later	reducing the OCS dose by 30–50%
consider re-attempting tapering at a slower pace	every 2–4 weeks

Definition of abbreviations: OCS = oral corticosteroid.

Table 4. Minimal Checklist for Adverse Effect Screening

Positive consensus	Controversial
Growth (pediatric population)	
Glycemic control	Cardiovascular risk score
• Bone density	• Lipid panel
Blood pressure	LaLa
Cataracts and glaucoma	• Fluid retention
• Weight change	
• Fracture risk score (e.g. FRAX)	

Definition of abbreviations: FRAX = Fracture Risk Assessment Tool.

Adverse effects are not ordered/hierarchized, and should be given equal consideration.

Online Data Supplement:

Expert Consensus on the Tapering of Oral Corticosteroids for the Treatment of Asthma: A Delphi Study

Carey M. Suehs, Andrew Menzies-Gow, David Price, Eugene R. Bleecker, Giorgio Walter Canonica, Mark Gurnell, Arnaud Bourdin on behalf of the Oral Corticosteroids Tapering Delphi Expert Panel*

Results from the three rounds of ranking in the OCS Tapering Delphi project (for items ranked with a five-point Likert scale). For each item, the round and sample size are given along with the percentage of experts that chose a given rank. Darker shades of green signify greater percentage consensus. The weighted mean rank and consensus category are given (positive = blue; negative = red; controversial = white).

			~ .	Strongly				~ · ·	Weighted	
Statement	Number	Round	Sample	disagree,	Disagree,	Neutral, %	Agree,	Strongly	mean rank	Consensus
In general our goal should be to not use OCS. When nevertheless required dose and	Rumber	Kounu	SIZC	/0	/0	/0	70	agree, 70	тапк	Consensus
duration should be minimized.	1.1.a	1	108	2.78	0.93	0.93	19.44	75.93	1.65	Positive
Short-term (e.g. <15 days) OCS use is appropriate in asthma patients during acute, non-resolutive exacerbation.	1.2.a	1	108	0	0.93	5.56	54.63	38.89	1.31	Positive
Short-term (e.g. <15 days) OCS use is appropriate in asthma patients during acute, life-threatening, exacerbation.	1.2.b	1	108	0	0	0	22.22	77.78	1.78	Positive
Short-term (e.g. <15 days) OCS use is appropriate in asthma patients during eosinophilic										
or allergic exacerbation.	1.2.c	1	108	0	3.7	12.04	46.3	37.96	1.19	Positive
Short-term (e.g. <15 days) OCS use is appropriate in asthma patients in the context of an		1	108	4.63	10.19	15.74	45.37	24.07	0.74	Controversial
asthma management plan.	1.2.d	2	113	2.65	7.96	8.85	69.03	11.5	0.79	Positive
Short-term (e.g. <15 days) OCS use is appropriate in asthma patients to avoid hospitalization.	1.2.e	1	108	2.78	11.11	10.19	48.15	27.78	0.87	Positive
		1	108	19.44	34.26	24.07	19.44	2.78	-0.48	Controversial
Short-term (e.g. <15 days) OCS use is appropriate in asthma patients to palliate the		2	113	16.81	32.74	18.58	27.43	4.42	-0.3	Controversial
unavailability of hospitalization services.	1.2.f	3	111	14.41	32.43	22.52	22.52	8.11	-0.23	Controversial
Short-term (e.g. <15 days) OCS use is never appropriate in asthma patients.	1.2.g	1	108	71.3	23.15	2.78	2.78	0	-1.63	Negative
As concerns dosages for short courses of OCS for the treatment of asthma exacerbations,		1	108	2.78	37.96	14.81	35.19	9.26	0.1	Controversial
individual tailoring is required to such an extent that the systematic application of "ideal"		2	112	5.36	31.25	19.64	38.39	5.36	0.07	Controversial
doses is unlikely.	1.5.a	3	111	4.5	39.64	12.61	39.64	3.6	-0.02	Controversial
		1	108	1.85	21.3	20.37		11.11	0.43	Controversial
Dosages for short courses of OCS for the treatment of asthma exacerbations should remain stable.		2	112	3.57	19.64	22.32		7.14	0.35	Controversial
	1.5.b	3	111	0.9	16.22	19.82	52.25	10.81	0.56	Controversial
Dosages for short courses of OCS for the treatment of asthma exacerbations should be progressively escalated.	1.5.c	1	108	26.85	53.7	8.33	7.41	3.7	-0.93	Negative
Maintenance OCS therapy is appropriate (and does not require further improvement) in severe										
asthmatics who are well controlled with a low dose of OCS (e.g. 5 mg/day or less of prednisone).	1.6.a	1	108	15.74	54.63	12.96	13.89	2.78	-0.67	Negative
Maintenance OCS therapy is appropriate (and does not require further improvement) in		1	108	5.56	14.81	13.89	59.26	6.48	0.46	Controversial
severe asthmatics with inadequate control despite optimization of alternative (Step 5).	1.6.b	2	111	0.9	17.12	11.71	61.26	9.01	0.6	Positive
Maintenance OCS therapy is appropriate (and does not require further improvement) in										
severe asthmatics with poor inhaler compliance/technique.	1.6.c	1	108	56.48	35.19	4.63	3.7	0	-1.44	Negative

				Strongly					Weighted	
			Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
		1	108	30.56		24.07	6.48	0	-0.94	Controversial
Maintenance OCS therapy is appropriate (and does not require further improvement) in		2	111	9.01		29.73	14.41	1.8	-0.45	Controversial
severe asthmatics with low-T2 phenotypes.	1.6.d	3	111	13.51	52.25	24.32	9.01	0.9	-0.68	Controversial
		1	108	18.52	29.63	19.44	31.48	0.93	-0.33	Controversial
Maintenance OCS therapy is appropriate (and does not require further improvement) in		2	111	6.31	36.94	24.32	30.63	1.8	-0.15	Controversial
severe asthmatics with high T2 phenotypes/eosinophils.	1.6.e	3	111	13.51	36.04	24.32	24.32	1.8	-0.35	Controversial
Maintenance OCS therapy is appropriate (and does not require further improvement) in		1	108	3.7	22.22	30.56	36.11	7.41	0.21	Controversial
severe asthmatics when it results in an overall reduction in OCS exposure (i.e. the total		2	111	0.9	14.41	22.52		3.6	0.5	Controversial
mg of OCS exposure per year; e.g. 5 mg/day is a 33% reduction when compared to 10)	1.6.f	3	111	3.6	15.32	18.02	58.56	4.5	0.45	Controversial
Maintenance OCS therapy is appropriate (and does not require further improvement) in		1	108	1.85	7.41	25		6.48	0.61	Controversial
severe asthmatics if when trying to taper OCS there is an adverse effect or comorbidity.	1.6.g	2	111	0	8.11	18.02	69.37	4.5	0.7	Positive
		1	108	6.48	11.11	12.96	56.48	12.96	0.58	Controversial
Maintenance OCS therapy is appropriate (and does not require further improvement) in		2	111	3.6	12.61	18.02		13.51	0.59	Controversial
severe asthmatics with primary or secondary adrenal insufficiency.	1.6.h	3	111	6.31	16.22	18.02	48.65	10.81	0.41	Controversial
Maintenance OCS therapy is never appropriate in severe asthmatics.	1.6.i	1	108	27.78	43.52	15.74	10.19	2.78	-0.83	Negative
As concerns maintenance OCS therapy, individual tailoring is required to such an extent										
that the systematic application of "ideal" doses is unlikely.	1.8.a	1	108	1.85	16.67	13.89	42.59	25	0.72	Controversial
As concerns maintenance OCS therapy, individual tailoring is required to such an extent										
that the systematic application of "ideal" doses is unlikely.	1.8.a	2	111	0.9	17.12	9.91	56.76	15.32	0.68	Positive
		1	108	3.7	35.19	19.44	38.89	2.78	0.02	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:		2	110	5.45	29.09	26.36	37.27	1.82	0.01	Controversial
normalization of lung function.	1.9.a	3	109	1.83	30.28	20.18	47.71	0	0.14	Controversial
		1	108	4.63	24.07	19.44	49.07	2.78	0.21	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:		2	110	0	30	30.91	38.18	0.91	0.1	Controversial
a stable peak flow during the last week of treatment.	1.9.b	3	109	0.92	23.85	25.69	49.54	0	0.24	Controversial
		1	108	5.56	20.37	27.78	39.81	6.48	0.21	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:		2	110	3.64	25.45	25.45	43.64	1.82	0.15	Controversial
suppression of blood eosinophils/other T2 biomarkers.	1.9.c	3	109	1.83	26.61	20.18	50.46	0.92	0.22	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:										
improvement in the Asthma Control Questionnaire score (MCID = 0.5) or the Asthma										
Control Test (ACT) (MCID = 5).	1.9.d	1	108	0.93	6.48	7.41	72.22	12.96	0.9	Positive
An adequate response to long-term OCS in asthmatics can be characterized as:										
decreasing the exacerbation rate to <2/year.	1.9.e	1	108	0.93	4.63	12.96	63.89	17.59	0.93	Positive
		1	108	0.93	24.07	32.41	37.04	5.56	0.22	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:		2	110	0.91	26.36	16.36		7.27	0.35	Controversial
decreasing the exacerbation rate by at least 30%.	1.9.f	3	109	0	11.93	19.27	62.39	6.42	0.63	Controversial

			Sampla	Strongly	Disagroo	Noutral	Agrees	Strongly	Weighted	
Statement	Number	Round	size	wisagree,	bisagree, %	weuti ai, %	Agree,	agree, %	rank	Consensus
An adequate response to long-term OCS in asthmatics can be characterized as:							-			
decreasing the exacerbation rate by at least 50%.	1.9.g	1	108	0	7.41	14.81	57.41	20.37	0.91	Positive
An adequate response to long-term OCS in asthmatics can be characterized as:										
decreasing hospitalizations for asthma to 0 per year.	1.9.h	1	108	0.93	5.56	11.11	56.48	25.93	1.01	Positive
		1	108	0.93	12.96	19.44		10.19	0.62	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:		2	110	0.91	14.55	16.36		7.27	0.59	Controversial
a decreased need for rescue treatments.	1.9.i	3	109	0.92	9.17	12.84	72.48	4.59	0.71	Positive
An adequate response to long-term OCS in asthmatics can be characterized as:										
when a clinical improvement is obtained that outweighs risks/harms.	1.9.j	1	108	0	3.7	12.96	60.19	23.15	1.03	Positive
An adequate response to long-term OCS in asthmatics can be characterized as:										
improvement in asthma-related daily limitations/quality of life.	1.9.k	1	108	1.85	6.48	14.81	70.37	6.48	0.73	Positive
		1	108	2.78	19.44	33.33	41.67	2.78	0.22	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:		2	110	0.91	18.18	33.64		1.82	0.29	Controversial
improvement in symptoms related to chronic sinusitis/nasal polyps.	1.9.1	3	109	0.92	16.51	29.36	52.29	0.92	0.36	Controversial
An adequate response to long-term OCS in asthmatics can be characterized as:										
return to work (which would have been impossible without OCS).	1.9.m	1	108	0.93	2.78	16.67	68.52	11.11	0.86	Positive
OCS may be used as a temporary measure in patients having recurrent eosinophilic										
asthma exacerbations whilst completing severe asthma assessments.	1.10.a	1	108	1.85	8.33	13.89	62.96	12.96	0.77	Positive
The yearly cumulative dose of OCS should be monitored as a marker of asthma control.	1.10.b	1	108	0	2.78	6.48	63.89	26.85	1.15	Positive
		1	108	0	17.59	25.93		8.33	0.47	Controversial
		2	108	1.85	17.59	22.22		3.7	0.41	Controversial
OCS therapy can be used to estimate the best obtainable improvement of asthma symptoms.	1.10.c	3	109	0.92	22.02	11.93	59.63	5.5	0.47	Controversial
Short-term, prophylactic OCS use is appropriate in asthma patients when early		1	108	4.63	30.56	20.37	42.59	1.85	0.06	Controversial
signs/symptoms of significant exacerbation appear, if the patient is adherent with proper		2	108	4.63	27.78	22.22	42.59	2.78	0.11	Controversial
use of daily asthma therapy.	1.10.d	3	109	4.59	30.28	15.6	47.71	1.83	0.12	Controversial
		1	108	4.63	24.07	35.19	34.26	1.85	0.05	Controversial
OCS can also be considered in patients with fixed airflow obstruction which becomes		2	108	1.85	26.85	29.63	40.74	0.93	0.12	Controversial
reversible on OCS (infrequent).	1.10.e	3	109	2.75	21.1	31.19	44.04	0.92	0.19	Controversial
		1	108	2.78	21.3	33.33		2.78	0.19	Controversial
Asthma patients who have a second exacerbation within 6 weeks of a short "burst"		2	108	2.78	28.7	18.52	46.3	3.7	0.19	Controversial
prednisone-treated exacerbation should have a longer, tapering course of prednisone.	1.11.a	3	109	1.83	18.35	23.85	53.21	2.75	0.37	Controversial
		1	108	2.78	20.37	18.52		5.56	0.38	Controversial
In adults and adolescents receiving maintenance OCS for asthma, the dose should be at		2	108	0.93	19.44	26.85	46.3	6.48	0.38	Controversial
least doubled to define an exacerbation.	1.11.b	3	109	2.75	11.93	16.51	62.39	6.42	0.58	Controversial

				Strongly					Weighted	
			Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean	~
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
		1	108	1.85	14.81	19.44		10.19	0.56	Controversial
Patients hospitalized for asthma exacerbation and treated with systemic corticosteroids should be		2	108	0.93	22.22	18.52	51.85	6.48	0.41	Controversial
prescribed a short course (for example 5 days) of OCS upon discharge from the hospital.	1.11.c	3	109	0	18.35	20.18	51.38	10.09	0.53	Controversial
		1	108	5.56	25	26.85	33.33	9.26	0.16	Controversial
		2	108	6.48	34.26	29.63	24.07	5.56	-0.12	Controversial
Prednisolone assays should be used in standard practice to verify OCS adherence.	1.12.a	3	109	5.5	35.78	22.94	29.36	6.42	-0.05	Controversial
		1	108	11.11	30.56	42.59	15.74	0	-0.37	Controversial
		2	108	13.89	32.41	36.11	16.67	0.93	-0.42	Controversial
A 9AM cortisol test is sufficient for determining if a patient is OCS compliant.	1.12.b	3	109	11.93	37.61	29.36	20.18	0.92	-0.39	Controversial
		1	108	0.93	13.89	17.59	36.11	31.48	0.83	Controversial
Long-acting or methylprednisolone injections are not necessary.	1.13.a	2	108	0	13.89	15.74	47.22	23.15	0.8	Positive
Patients receiving frequent methylprednisolone injections for asthma treatment or										
exacerbations are at the same or similar risk of suffering side effects from steroids and	1 12 1	1	100	0.70	14.01	7.41	25.10	20.01	0.04	D 14
developing adrenal insufficiency as those receiving OCS.	l . 13 . b	1	108	2.78	14.81	/.41	35.19	39.81	0.94	Positive
Long-acting or methylprednisolone injections are not superior to orally administered glucocorticoids.	1.13.c	1	108	0	6.48	13.89	52.78	26.85	1	Positive
Chronic OCS treatment of asthma in the pediatric age should be a rare exception.	1.14.a	1	108	0	0	14.81	29.63	55.56	1.41	Positive
OCS can lead to several systemic side-effects and growth deficits in pediatric patients.	1.14.b	1	108	0	0	11.11	25	63.89	1.53	Positive
		1	108	25.93	35.19	29.63	9.26	0	-0.78	Controversial
		2	108	14.81	41.67	29.63	12.96	0.93	-0.56	Controversial
Methotrexate is a useful steroid-sparing agent in asthma.	1.16.a	3	109	14.68	48.62	26.61	8.26	1.83	-0.66	Controversial
		1	108	25.93	37.04	31.48	5.56	0	-0.83	Controversial
		2	108	16.67	50.93	25.93	5.56	0.93	-0.77	Controversial
Azathioprine is a useful steroid-sparing agent in asthma.	l.16.b	3	109	15.6	56.88	21.1	6.42	0	-0.82	Negative
		1	108	25	35.19	33.33	6.48	0	-0.79	Controversial
		2	108	16.67	39.81	38.89	3.7	0.93	-0.68	Controversial
Mycophenolat motetil is a useful steroid-sparing agent in asthma.	1.16.c	3	109	14.68	47.71	33.94	3.67	0	-0.73	Controversial
		1	108	5.56	25.93	31.48	36.11	0.93	0.01	Controversial
	1 16 1	2	108	2.78	27.78	30.56	37.04	1.85	0.07	Controversial
Azithromycin is a useful steroid-sparing agent in asthma.	1.16.d	3	109	2.75	26.61	32.11	35.78	2.75	0.09	Controversial
		1	108	1.85	23.15	20.37	42.59	12.04	0.4	Controversial
The most well ACC mention statement is high deep inheled standid in a state	1 16 -	2	108	3.7	23.15	24.07	51.29	9.26	0.28	Controversial
i ne mosi useiui OCS-sparing strategy is nign-dose innaied steroid in astima.	1.10.e	3	109	1.85	13.76	24.77	51.38	8.26	0.5	Controversial
		1	108	6.48	24.07		20.37	3./	-0.09	Controversial
	1 16 6	2	108	3./	21.3	41.67	31.48	1.85	0.06	Controversial
Bronchiai inermopiasty is a userui steroid-sparing strategy in astima.	1.10.1	5	109	3.07	25.69	43.12	26.61	0.92	-0.05	Controversial

			Sample	Strongly disagree	Disagree.	Neutral	Agree.	Strongly	Weighted mean	
Statement	Number	Round	size		%	%	%	agree, %	rank	Consensus
Biologicals, such as IL5 and IL4Ra targeting drugs, are useful sparing agents in asthma.	1.16.g	1	108	0.93	0	3.7	19.44	75.93	1.69	Positive
There is a need for OCS-sparing agents.	1.16.h	1	108	0	0	1.85	39.81	58.33	1.56	Positive
Patients on maintenance OCS for severe asthma should be systematically assessed for suitability of biologicals.	1.17.a	1	108	0	0	1.85	18.52	79.63	1.78	Positive
OCS may be used as a provisional strategy for difficult to control, eosinophilic/T2 asthma										
until an effective biological treatment is available for the patient.	1.17.b	1	108	1.85	2.78	9.26	67.59	18.52	0.98	Positive
The daily dose of OCS treatment may represent a reliable marker for the evaluation of										
biological treatment response.	1.17.c	1	108	0.93	7.41	12.04	49.07	30.56	1.01	Positive
		1	108	8.33		13.89	19.44	8.33	-0.31	Controversial
Patients should not have extra OCS at home because the risk of self treatment becoming		2	107	9.35		10.28	23.36	6.54	-0.33	Controversial
a habit is too high.	1.18.a	3	109	11.93	44.95	13.76	22.02	7.34	-0.32	Controversial
If OCS is to be used, preparations with lower adrenal suppression should be chosen at the										
lowest effective dose administered in the morning.	1.18.b	1	108	0.93	0.93	14.81	58.33	25	1.06	Positive
Establishing equivalence between ICS and OCS in children and in adults (systemic										
distribution of ICS) is of major importance.	1.18.c	1	108	0	4.63	23.15	52.78	19.44	0.87	Positive
Tapering (down to a minimal efficacious dose or complete weaning if possible) should be										
attempted in all asthma patients receiving maintenance OCS therapy, regardless of comorbidities.	2.1.a	1	105	0	1.9	1.9	37.14	59.05	1.53	Positive
The rhythm and speed of OCS tapering requires individualization for each patient.	2.1.b	1	105	0	1.9	2.86	54.29	40.95	1.34	Positive
Proceeding towards a tapering attempt is particularly appropriate when: patients on										
maintenance OCS have gained control (for a minimum, agreed-upon time).	2.2.a	1	105	0	0	3.81	59.05	37.14	1.33	Positive
Proceeding towards a tapering attempt is particularly appropriate when: biological										
treatment has been initiated and results in asthma control.	2.2.b	1	105	0	0.95	0.95	25.71	72.38	1.7	Positive
Proceeding towards a tapering attempt is particularly appropriate when: a patient										-
exhibits symptoms/comorbidities likely linked to OCS.	2.2.c	1	105	0	1.9	2.86	41.9	53.33	1.47	Positive
Proceeding towards a tapering attempt is particularly appropriate when: there is a										-
reasonable likelihood of hypothalamic-pituitary-adrenal axis recovery.	2.2.d	1	105	0	1.9	11.43	54.29	32.38	1.17	Positive
Proceeding towards a tapering attempt is particularly appropriate when: the intensity or						• • •				-
duration of OCS treatment gives reason for concern.	2.2.e	1	105	0	0	3.81	59.05	37.14	1.33	Positive
Proceeding towards a tapering attempt is particularly appropriate when: the patient does			105		0.05	0.05		(2.0)		De lat
not appear to respond to OCS treatment.	2.2.f	1	105	0	0.95	0.95	35.24	62.86	1.6	Positive
Tapering OCS should NOT be attempted in patients who: have demonstrated potentially		1	105	1.9	18.1	18.1		5.71	0.46	Controversial
harmful outcomes during previous weaning attempts (and all available medications have		2	106	0.94	17.92	22.64	51.89	6.6	0.45	Controversial
been appropriately initiated/tested).	2.4.a	3	109	0.92	22.94	13.76	59.63	2.75	0.4	Controversial

			с I	Strongly	D.	N / I		G(1	Weighted	
Statement	Number	Round	sample	disagree,	Disagree,	Neutral, %	Agree,	strongly agree, %	mean rank	Consensus
Tapering OCS should NOT be attempted in patients who: have EGPA that relapses during	i (unio ei	nounu	51110	70	,,	/0	70	ugree, /v		Consensus
tapering (and no other changes can be proposed).	2.4.b	1	105	0.95	3.81	12.38	66.67	16.19	0.93	Positive
Tapering OCS should NOT be attempted in patients who: have ABPA that relapses during				0						
tapering (and no other changes can be proposed).	2.4.c	1	105		9.52	19.05	61.9	9.52	0.71	Positive
		1	105	4.76	11.43	22.86		8.57	0.49	Controversial
Tapering OCS should NOT be attempted in patients who: have proven primary or		2	106	5.66	21.7	17.92	47.17	7.55	0.29	Controversial
secondary adrenal insufficiency.	2.4.d	3	109	4.59	29.36	18.35	42.2	5.5	0.15	Controversial
		1	105	3.81	17.14	20		11.43	0.46	Controversial
		2	106	1.89	20.75	14.15	55.66	7.55	0.46	Controversial
Tapering OCS should NOT be attempted in patients who: have uncontrolled asthma.	2.4.e	3	109	0	21.1	13.76	55.96	9.17	0.53	Controversial
		1	105	5.71	24.76	27.62	32.38	9.52	0.15	Controversial
	2 4 6	2	106	4.72	27.36	29.25	30.19	8.49	0.1	Controversial
Tapering OCS should NOT be attempted in patients who: have uncontrolled 12 high inflammation.	2.4.f	3	109	1.83	28.44	25.69	40.37	3.6/	0.16	Controversial
OCS tapering should be faster in patients who have been on maintenance OCS for shorter	2 5	1	105	0	17.14	12.20	56.10	14.20	0.00	D 10
periods (less than 6 months for example).	2.5.a	1	105	0	17.14	12.38	56.19	14.29	0.68	Positive
		1	105	0.95	30.48	31.43	34.29	2.86	0.08	Controversial
2008 to a size should be device in activate who had a close source to 2008 (and size source)	251	2	106	2.83	34.91	29.25	31.13	1.89	-0.06	Controversial
OCS tapering should be slower in patients who had a slow response to OCS (and vice-versa).	2.5.0	3	108	0.93	37.96	29.03	31.48	10.00	-0.08	Controversial
		1	105	0	18.1	23.81		13.33	0.53	Controversial
The mode of QCS tancing depends on the lengum remidity of action of the appring days introduced	25.0	2	106	0.94	10.38	19.81	54.62	7.00	0.64	Controversial
The speed of OCS tapering depends on the known rapidity of action of the spaning drug introduced.	2.5.0	3	108	0	5.71	20.37	70.49	12.22	0.32	Daniting
The speed of OCS tapering depends on the history of and future risk for adverse events.	2.5.0	I	105	0	5./1	10.48	/0.48	13.33	0.91	Positive
example tangeting plans proposed in RCTs are used)	25 e	1	105	0	19	13 33	66 67	18.1	1.01	Positive
OCS tamping should be based on patient collaboration and experience with side effects	2.5.C	1	105	0	1.9	13.33	62.86	21.9	1.01	Positive
des apering should be based on parent conaboration and experience with side effects.	2.3.1	1	105	0.95	28.57	36.10	32.38	1.0	0.06	Controversial
		2	105	1.89	37.74	30.19	28.3	1.9	-0.09	Controversial
QCS tangening should be guided by biomarkers at each weaping step	2 5 g	3	108	0.93	50	21.3	25.93	1.85	-0.22	Controversial
	2.0.8	1	105	0.95	28 57	29.52	40	0.95	0.11	Controversial
		2	106	1.89	27.36	20.75		1.89	0.21	Controversial
OCS tapering should be gradual, by reducing the OCS dose by 30–50% every 24 weeks.	2.6.a	3	107	0	19.63	12.15	67.29	0.93	0.5	Controversial
OCS tapering should be gradual, with 2.5–5 mg steps every 0.5–2 weeks until an agreed-upon threshold is										
achieved (e.g. 5–10 mg/day), and then proceeds at a slower pace (1–2.5 mg every 1–2 weeks).	2.6.b	1	105	0	3.81	13.33	72.38	10.48	0.9	Positive

			Sample	Strongly disagree,	Disagree,	Neutral,	Agree,	Strongly	Weighted mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
		1	105	0	26.67	24.76		9.52	0.31	Controversial
In general, the speed of tapering should not exceed a reduction of 5 mg per week	260	2	106	1.89	23.38	17.92	50.94 48.6	5.60	0.35	Controversial
in general, the speed of tapering should not exceed a reduction of 5 mg per week.	2.0.0	1	107	0.05	16.10	14.95	40.0	0.57	0.29	Controversial
The initial tangging of high OCS doese (e.g. >20 mg ner day) can proceed at a faster page		1	105	0.95	10.19	16.08		8.37 2.83	0.54	Controversial
The initial tapering of high OCS doses (e.g. >20 higher day) can proceed at a faster pace	26 d	3	107	1.87	8 <i>4</i> 1	14.95	70.09	2.03 1.67	0.59	Positive
When a reduction in OCS by S my weakly fails a slower and lower does reduction of 1 mg	2.0.u	5	107	1.07	0.41	14.75	70.07	ч.07	0.07	10311100
per week should be attempted	26 e	1	105	0	5 71	12 38	72 38	9 52	0.86	Positive
per week should be utempted.	2.0.0	1	105	1.0	16.10	27.62	12.50	0.52	0.44	Controversial
OCS tapering should incorporate every-other-day OCS reductions (especially prior to		2	105	2.83	19.81	27.02		2.83	0.26	Controversial
discontinuation) to allow recovery of the endogenous axis	2.6 f	3	107	2.8	15.89	26.17	50.47	4 67	0.38	Controversial
If intolerable symptoms occur, return to the previous (efficacious) dose, and then later	2.0.1	5	107	2.0	10.07	20.17			0.50	Contro Visiai
consider re-attempting tapering at a slower pace.	2.6.g	1	105	0	0	3.81	75.24	20.95	1.17	Positive
	8	1	105	0	6.67	23.81	65.71	3.81	0.67	Controversial
If mild symptoms occur, maintain the current dosage; they are likely to resolve as		2	106	0.94	7.55	23.58		1.89	0.6	Controversial
endogenous axis recovery occurs.	2.6.h	3	107	0	7.48	19.63	69.16	3.74	0.69	Positive
		1	105	2.86	28.57	43.81	24.76	0	-0.1	Controversial
		2	106	1.89	44.34	28.3	23.58	1.89	-0.21	Controversial
A tapering trial should end when: biomarkers trend toward abnormal.	2.7.a	3	107	1.87	44.86	23.36	28.97	0.93	-0.18	Controversial
A tapering trial should end when: symptoms trend toward loss of control (retain lowest										
dose that maintains clinical benefit).	2.7.b	1	105	0	5.71	2.86	81.9	9.52	0.95	Positive
		1	105	4.76	40.95	25.71	24.76	3.81	-0.18	Controversial
		2	106	5.66	43.4	29.25	18.87	2.83	-0.3	Controversial
A tapering trial should end when: the patient is not motivated to continue.	2.7.c	3	107	1.87	43.93	24.3	28.04	1.87	-0.16	Controversial
		1	105	3.81	30.48	35.24	25.71	4.76	-0.03	Controversial
		2	106	2.83	32.08	23.58	39.62	1.89	0.06	Controversial
Peak expiratory flow is a useful biomarker during OCS tapering.	2.8.a	3	106	0.94	33.02	16.04	49.06	0.94	0.16	Controversial
		1	105	1.9	23.81	22.86	44.76	6.67	0.3	Controversial
		2	106	0	26.42	22.64		4.72	0.29	Controversial
Forced expiratory volume in 1 second (spirometry) is a useful biomarker during OCS tapering.	2.8.b	3	106	0.94	26.42	16.98	50.94	4.72	0.32	Controversial
		1	105	0	11.43	29.52		5.71	0.53	Controversial
	•	2	106	0	15.09	20.75	55.66	8.49	0.58	Controversial
Fraction exhaled nitric oxide is a useful biomarker during OCS tapering.	2.8.c	3	106	0.94	14.15	24.53	54.72	5.66	0.5	Controversial
		1	105	0	13.33	27.62		8.57	0.54	Controversial
	• • •	2	106	1.89	18.87	24.53	48.11	6.6	0.39	Controversial
Peripheral eosinophils are a useful biomarker during OCS tapering.	2.8.d	3	106	0	15.09	23.58	55.66	5.66	0.52	Controversial

				Strongly					Weighted	
Station and	Name	Dennal	Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean	C
Statement	Number	Kouna	105	% 0	% 0	% 0	%	agree, %		Consensus
		1	105	2.80	20	32.38	33.24	9.52	0.29	Controversial
Sputum assignabils are a useful biomarker during OCS tapering	289	2	106	0.0 5.66	10.81	23.38	38.68	3.00	0.19	Controversial
Spitum cosmophis are a useful biomarker during Oes tapering.	2.8.0	1	105	15.00	24.20	27.14	11.42	1.0	0.15	Controversial
Bronchoalvaolar lavaga fluid (BAL) accinophils are a usaful biomatkar during OCS		1	105	13.24	34.29	28.3	11.45	0.04	-0.5	Controversial
tanerina	28 f	3	106	16.98	43.4	27.36	10.38	1.89	-0.63	Controversial
Asthma control questionnaires (ACT_ACO) are a useful biomarker during OCS tanering	2.0.1	1	105	0.95	4.76	12.38	61.9	20	0.05	Positive
Asuma control questionnanes (ACT, ACQ) are a useful biomarker during o'es tapering.	2.0.g	1	105	2.86	12.38	20.95	5/ 20	9.52	0.55	Controversial
		2	105	1.72	10.81	20.93		5.66	0.35	Controversial
Adrenal insufficiency assessments are a useful biomarker during OCS tapering	28 h	3	106	4 72	22.64	22.64	45.28	4 72	0.20	Controversial
		1	105	24.76	31.43	24.76	15.24	3.81	-0.58	Controversial
		2	106	21.7	36.79	22.64	16.04	2.83	-0.58	Controversial
Biomarker guidance is useless or too troublesome during OCS tapering.	2.8.i	3	106	11.32	51.89	21.7	13.21	1.89	-0.58	Controversial
Cautious, slow tapering is particularly appropriate for patients who: have comorbidities that respond to OCS.	2.9.a	1	105	0	3.81	9.52	70.48	16.19	0.99	Positive
Cautious, slow tapering is particularly appropriate for patients who: have had life-threatening attacks.	2.9.b	1	105	0.95	3.81	3.81	60	31.43	1.17	Positive
Cautious, slow tapering is particularly appropriate for patients who: have been										
dependent on systemic steroids for an extended period of time (e.g. 6 months or more).	2.9.c	1	105	0	2.86	6.67	63.81	26.67	1.14	Positive
Complete OCS cessation (weaning) can be implemented: when the OCS dose is less than										
or equal to 5 mg prednisolone.	2.10.a	1	105	0.95	15.24	13.33	53.33	17.14	0.7	Positive
Complete OCS cessation (weaning) can be implemented: following a short course of OCS										
treatment that lasted for 5–7 days.	2.10.b	1	105	0.95	1.9	1.9	44.76	50.48	1.42	Positive
Complete OCS cessation (weaning) can be implemented: following a short course of OCS										
treatment if patients are on inhaled anti inflammatory therapy.	2.10.c	1	105	1.9	1.9	2.86	48.57	44.76	1.32	Positive
		1	105	0	18.1	27.62	41.9	12.38	0.49	Controversial
Complete OCS cessation (weaning) can be implemented: when no severe exacerbations		2	106	1.89	22.64	16.98		6.6	0.39	Controversial
have occurred during the last 4 weeks.	2.10.d	3	106	0.94	22.64	15.09	58.49	2.83	0.4	Controversial
Complete OCS cessation (weaning) can be implemented: when there is no evidence of adrenal insufficiency.	2.10.e	1	105	0.95	6.67	13.33	59.05	20	0.9	Positive
Complete OCS cessation (weaning) can be implemented: when there is no evidence of EGPA or ABPA.	2.10.f	1	105	0	7.62	19.05	56.19	17.14	0.83	Positive
Complete OCS cessation (weaning) can be implemented: when a sparing strategy has been initiated.	2.10.g	1	105	0.95	2.86	14.29	54.29	27.62	1.05	Positive

			Sample	Strongly disagree,	Disagree,	Neutral,	Agree,	Strongly	Weighted mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
Complete OCS cessation (weaning) can be implemented: when the patient has agreed to cessation.	2.10.h	1	105	1.9	4.76	20	50.48	22.86	0.88	Positive
		1	105	0	14.29	34.29		6.67	0.44	Controversial
Pulmonary rehabilitation can be helpful before OCS tapering to improve physical activity		2	106	0	16.98	19.81		12.26	0.58	Controversial
and decrease dyspnea. It can facilitate OCS tapering.	2.11.a	3	106	1.89	11.32	20.75	53.77	12.26	0.63	Controversial
OCS tapering should be re-attempted every time a new biological treatment for										
eosinophilic asthma patients becomes available.	2.11.b	1	105	0	2.86	7.62	57.14	32.38	1.19	Positive
Biological therapies have become an essential support for OCS tapering.	2.11.c	1	105	0.95	0.95	4.76	29.52	63.81	1.54	Positive
Following the initiation of a biological therapy, if weaning is not achieved within										
12 months, consider switching to a different biological.	2.11.d	1	105	0	5.71	10.48	57.14	26.67	1.05	Positive
Not achieving a >50% reduction in OCS dose (or a tolerable daily dose) is a failure for a										
given biological therapy that may mandate switching strategies.	2.11.e	1	105	0	5.71	20	59.05	15.24	0.84	Positive
		1	105	1.9	15.24		38.1	5.71	0.3	Controversial
Thermoplasty needs to be considered when OCS tapering fails and no other alternative is		2	106	0	13.21	29.25		6.6	0.51	Controversial
indicated (biologicals etc).	2.11.f	3	106	0.94	10.38	34.91	44.34	9.43	0.51	Controversial
Poor adherence and inhaler technique should be actively sought and managed to facilitate OCS tapering.	2.12.a	1	105	0	0.95	0.95	32.38	65.71	1.63	Positive
		1	105	0.95	23.81	16.19		14.29	0.48	Controversial
		2	106	4.72	27.36	7.55		8.49	0.32	Controversial
Monitoring during OCS tapering can be based on symptoms in almost all patients.	2.12.b	3	106	0.94	23.58	14.15	55.66	5.66	0.42	Controversial
OCS should be used at a minimum dose, so whenever writing a prescription for OCS, the										
option of reducing the dose should always be considered.	2.12.c	1	105	0	2.86	7.62	58.1	31.43	1.18	Positive
Comorbidities should be addressed at all times (not just during tapering).	3.1.a	1	103	0	0	1.94	42.72	55.34	1.53	Positive
Asthma patients receiving OCS therapy are at a higher risk of complications compared to										
those without OCS exposure.	3.1.b	1	103	0	0	2.91	29.13	67.96	1.65	Positive
OCS tapering becomes a primary outcome/goal of asthma management when a patient is										
affected by OCS-related comorbidities.	3.1.c	1	103	0	2.91	4.85	28.16	64.08	1.53	Positive
The evaluation of comorbidities is mandatory prior to tapering OCS.	3.1.d	1	103	0	3.88	7.77	53.4	34.95	1.19	Positive
In general, the presence of comorbidities should not preclude attempting to taper down										
to the lowest efficacious dose or complete withdrawal (if possible).	3.1.e	1	103	0.97	1.94	0.97	60.19	35.92	1.28	Positive
Comorbidities to address prior to or when initiating tapering: those that require or										
respond well to OCS treatment (immune diseases, vasculitis, adrenal suppression, etc)	3.2.a	1	103	0	0.97	2.91	55.34	40.78	1.36	Positive

			~ .	Strongly				a	Weighted	
Statement	Number	Dound	Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean	Consonsus
Statement	Number	Koullu	SIZE	/0	/0	/0	/0	agree, 70	тапк	Consensus
or those that may cause (or minic) asthma (rhonoing tapening) is non-characteristic as a set of the										
vocal cord dysfunction inducible larvngeal obstruction dysfunctional breathing etc)	32 h	1	103	0	3.88	4 85	60 19	31.07	1 18	Positive
Comorbidities to address prior to or when initiating tanging chronic pon-communicable	5.2.0	-	105	Ŭ	5.00		00.17	51.07	1.10	1 0011110
diseases often exacerbated by (or even caused by) OCS use (hvners/lvcemia/diabetes metabolic										
disease, cardiovascular diseases, high blood pressure, glaucoma, cataract, osteoporosis, etc).	3.2.c	1	103	0	1.94	6.8	54.37	36.89	1.26	Positive
The minimum checklist for comorbidity screening in the OCS-treated population should										
include: glycemic control/HbA1c.	3.3.a	1	103	0	0.97	0.97	54.37	43.69	1.41	Positive
The minimum checklist for comorbidity screening in the OCS-treated population should include: blood pressure.	3.3.b	1	103	0	0.97	6.8	58.25	33.98	1.25	Positive
		1	103	0	7.77	27.18	54.37	10.68	0.68	Controversial
The minimum checklist for comorbidity screening in the OCS-treated population should		2	106	1.89	24.53	21.7		0	0.24	Controversial
include: fluid retention.	3.3.c	3	106	1.89	18.87	26.42	50.94	1.89	0.32	Controversial
		1	103	0	6.8	25.24	47.57	20.39	0.82	Controversial
The minimum checklist for comorbidity screening in the OCS-treated population should		2	106	1.89	24.53	27.36	44.34	1.89	0.2	Controversial
include: cardiovascular risk score (e.g. CHADS2).	3.3.d	3	106	2.83	21.7	25.47	45.28	4.72	0.27	Controversial
		1	103	0	7.77	29.13		14.56	0.7	Controversial
The minimum checklist for comorbidity screening in the OCS-treated population should		2	106	0.94	23.58	24.53		0.94	0.26	Controversial
include: lipid panel.	3.3.e	3	106	2.83	25.47	22.64	47.17	1.89	0.2	Controversial
The minimum checklist for comorbidity screening in the OCS-treated population should										
include: fracture risk score (e.g. FRAX).	3.3.f	1	103	0	0	17.48	50.49	32.04	1.15	Positive
The minimum checklist for comorbidity screening in the OCS-treated population should			102	0	<u>^</u>	4.05	40.51	15.00		D 111
include: bone density.	3.3.g	1	103	0	0	4.85	49.51	45.63	1.41	Positive
The minimum checklist for comorbidity screening in the OCS-treated population should	2 2 1	1	102	0	2 01	10.00	50.40	25.02	1.10	D 141
include: cataracts and glaucoma.	3.3.h	1	103	0	2.91	10.68	50.49	35.92	1.19	Positive
The minimum checklist for comorbidity screening in the OCS-treated population should	a a :	1	102	0	0	2.00	40.70	52.4	1.7	D 141
include: growth (pediatric population).	3.3.1	I	103	0	0	3.88	42.72	53.4	1.5	Positive
The minimum checklist for comorbidity screening in the OCS-treated population should	· · ·	1	102	0	0.07	()	(5.05	27.10	1 10	Desition
Include: weight change.	5.5.J	1	103	0	0.97	0.8	05.05	27.18	1.18	Positive
Comorbiaity subsets for whom OCS tapering is a priority: those with evidence of a	2 4	1	102	0	0	0.07	20.02	(0.10	1.50	Desition
cinically significant OCS adverse effect.	3.4.a	1	103	0	0	0.97	38.83	60.19	1.39	Positive

			Sample	Strongly disagree.	Disagree.	Neutral.	Agree.	Strongly	Weighted mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
Comorbidity subsets for whom OCS tapering is a priority: those with chronic non-communicable										
diseases often exacerbated by (or even caused by) OCS use (glucose metabolism, metabolic										
disease, cardiovascular diseases, high blood pressure, glaucoma, cataract, osteoporosis, etc).	3.4.b	1	103	0	0	0.97	45.63	53.4	1.52	Positive
		1	103	0	5.83	25.24	48.54	20.39	0.83	Controversial
		2	106	0.94	17.92	26.42		6.6	0.42	Controversial
Comorbidity subsets for whom OCS tapering is a priority: those with a non-T2 phenotype.	3.4.c	3	105	0.95	15.24	21.9	54.29	7.62	0.52	Controversial
Comorbidity subsets for whom OCS tapering is a priority: those with important risk										
factors associated with increased OCS-susceptibility	3.4.d	1	103	0	0	10.68	63.11	26.21	1.16	Positive
Comorbidity subsets for whom OCS tapering is a priority: those with important risk										
factors associated with increased OCS-susceptibility such as age (youth).	3.4.e	1	103	0	0	10.68	50.49	38.83	1.28	Positive
Comorbidity subsets for whom OCS tapering is a priority: those with important risk										
factors associated with increased OCS-susceptibility such as age (elderly).	3.4.f	1	103	0	3.88	16.5	54.37	25.24	1.01	Positive
Comorbidity subsets for whom OCS tapering is a priority: those with important risk										
factors associated with increased OCS-susceptibility such as post-menopausal women.	3.4.g	1	103	0	8.74	19.42	51.46	20.39	0.83	Positive
		1	103	0	8.74	32.04		13.59	0.64	Controversial
Comorbidity subsets for whom OCS tapering is a priority: those with important risk		2	106	0.94	14.15	16.98		6.6	0.58	Controversial
factors associated with increased OCS-susceptibility such as gender (female).	3.4.h	3	105	0	8.57	25.71	60	5.71	0.63	Controversial
		1	103	0	11.65	30.1		10.68	0.57	Controversial
Comorbidity subsets for whom OCS tapering is a priority: those with important risk		2	106	0.94	15.09	27.36		3.77	0.43	Controversial
factors associated with increased OCS-susceptibility such as vitamin D deficiency.	3.4.i	3	105	0.95	8.57	34.29	53.33	2.86	0.49	Controversial
Comorbidity subsets for whom OCS tapering is a priority: those with important risk		1	103	0	7.77		23.3	7.77	0.31	Controversial
factors associated with increased OCS-susceptibility such as known PDGF-D gene		2	106	1.89	13.21		27.36	2.83	0.16	Controversial
polymorphism.	3.4.j	3	105	0.95	8.57	62.86	23.81	3.81	0.21	Controversial
		1	103	0.97	35.92	32.04	25.24	5.83	-0.01	Controversial
		2	106	7.55	51.89	15.09	18.87	6.6	-0.35	Controversial
Obese patients should have a polysomnography test prior to tapering.	3.6.a	3	105	1.9	60	22.86	11.43	3.81	-0.45	Controversial
Obesity should be aggressively managed with dietary advice and, where suitable and safe,										
consideration of bariatric surgery.	3.6.b	1	103	0	0.97	6.8	63.11	29.13	1.2	Positive
		1	103	0	15.53	29.13		4.85	0.45	Controversial
The risk of triggering a bipolar disorder in predisposed patients on continuous OCS	2 7	2	106	2.83	25.47	24.53	42.45	4.72	0.21	Controversial
treatment should be discussed with a psychiatrist.	<u>3.7.a</u>	3	105	1.9	24.76	23.81	45.71	3.81	0.25	Controversial
OCS addiction requires assessment of patient psychological profiles.	3.7.b	1	103	0	7.77	21.36	63.11	7.77	0.71	Positive
		1	103	5.83	36.89	31.07	25.24	0.97	-0.21	Controversial
All patients over 65 years with severe asthma Step 5 and cardiac failure, should begin	2 0	2	106	4.72	45.28	16.98	31.13	1.89	-0.2	Controversial
tapering only in case of stable cardiac disease.	3.8.a	3	105	4.76	38.1	20.95	33.33	2.86	-0.09	Controversial

				Strongly	D:	N (N		G()	Weighted	
Statement	Number	Round	Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean rank	Consensus
In OCS patients with cardiovascular diseases a coronarography should be performed	Tumber	Round	SILU	70	70	70	70	agree, 70	тапк	Consensus
even if the patient has no symptoms.	3.8.b	1	103	11.65	49.51	28.16	9.71	0.97	-0.61	Controversial
In OCS patients with cardiovascular diseases, a coronarography should be performed										
even if the patient has no symptoms.	3.8.b	2	106	17.92	56.6	16.98	8.49	0	-0.84	Negative
		1	103	4.85	38.83	26.21	26.21	3.88	-0.15	Controversial
Patients >75 years of age with uncontrolled, Step 4–5 asthma and cardiac disease should		2	106	4.72	33.02	23.58	34.91	3.77	0	Controversial
have a cardiology evaluation prior to tapering.	3.8.c	3	105	5.71	45.71	17.14	27.62	3.81	-0.22	Controversial
		1	103	0	17.48	33.01		3.88	0.36	Controversial
		2	106	0	23.58	25.47	41.51	9.43	0.37	Controversial
For GINA Step 5 patients, fungal disease must be ruled out in the first weeks of OCS treatment.	3.9.a	3	105	0.95	20	21.9	51.43	5.71	0.41	Controversial
		1	103	0.97	25.24	29.13	42.72	1.94	0.19	Controversial
		2	106	0.94	26.42	36.79	33.02	2.83	0.1	Controversial
OCS tapering should occur prior to cataract surgery.	3.9.b	3	105	0	20	41.9	34.29	3.81	0.22	Controversial
		1	103	3.88	21.36	21.36		4.85	0.29	Controversial
		2	106	4.72	22.64	23.58	41.51	7.55	0.25	Controversial
In patients with EGPA, tapering must be performed in collaboration with a rheumatologist.	3.9.c	3	105	2.86	25.71	20.95	44.76	5.71	0.25	Controversial
		1	103	0	2.91			5.83	0.53	Controversial
For patients treated with DDAVP (desmopressin), sodium levels should be monitored		2	106	0	4.72	46.23	43.4	5.66	0.5	Controversial
during tapering to avoid significant hyponatremia.	3.9.d	3	105	0	4.76	50.48	41.9	2.86	0.43	Controversial
		1	103	0.97	15.53	20.39		5.83	0.51	Controversial
	•	2	106	3.77	19.81	19.81	51.89	4.72	0.34	Controversial
ACOS/COPD rule-out should be performed for patients with a history of tobacco use or biomass exposure.	3.9.e	3	105	1.9	21.9	8.57	60	7.62	0.5	Controversial
The cost of OCS side effects should be more properly invested in more effective	2 0 6		102	0	0.07	10.00	50.40	27.06	1.05	D 14
treatments such as biologicals.	3.9.1	1	103	0	0.97	10.68	50.49	37.86	1.25	Positive
OCS tapering may be necessary for assessing the possibility of EGPA or other systemic vasculitis.	3.9.g	I	103	1.94	3.88	22.33	65.05	6.8	0.71	Positive
Adrenal insufficiency among OCS-treated asthma patients should be regularly assessed.	4.1.a	1	101	1.98	11.88	12.87	57.43	15.84	0.73	Positive
In as much as possible during the tapering process, troublesome signs (such as aches and										
pains) of adrenal insufficiency should be symptomatically treated and not viewed as a				0.00	0.01	1405	(2.20)	10.05		
reason to give up on tapering altogether.	4.I.b	1	101	0.99	8.91	14.85	62.38	12.87	0.77	Positive
		1	101	1.98	3.96	28.71		18.81	0.76	Controversial
In case of adrenal insufficiency during tapering, hydrocortisone replacement is preferred	4 1	2	106	1.89	7.55	27.36	50	13.21	0.65	Controversial
to continued prednisoione, and may ease the tapering process.	4.1.C	3	105	1.9	5./1	27.62	55.24	9.52	0.65	Controversial

			Sample	Strongly disagree	Disagree.	Neutral	Agree.	Strongly	Weighted mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
Adrenal insufficiency should be assessed: systematically when the daily dose of OCS is						•				
tapered down to an agreed-upon threshold	4.2.a	1	101	1.98	9.9	12.87	55.45	19.8	0.81	Positive
		1	101	4.95	31.68	35.64	18.81	8.91	-0.05	Controversial
Adrenal insufficiency should be assessed: systematically when the daily dose of OCS is		2	105	2.86	34.29	27.62	28.57	6.67	0.02	Controversial
tapered down to an agreed-upon threshold such as 3 mg/day.	4.2.b	3	105	4.76	33.33	24.76	33.33	3.81	-0.02	Controversial
		1	101	3.96	12.87	24.75		11.88	0.5	Controversial
Adrenal insufficiency should be assessed: systematically when the daily dose of OCS is		2	105	1.9	18.1	15.24	52.38	12.38	0.55	Controversial
tapered down to an agreed-upon threshold such as 5 mg/day.	4.2.c	3	105	3.81	13.33	19.05	54.29	9.52	0.52	Controversial
		1	101	3.96	31.68	33.66	22.77	7.92	-0.01	Controversial
Adrenal insufficiency should be assessed: systematically when the daily dose of OCS is	4 2 1	2	105	4.76	34.29	36.19	18.1	6.67	-0.12	Controversial
tapered down to an agreed-upon threshold such as /.5 mg/day.	4.2.d	3	105	5./1	36.19	24.76	27.62	5./1	-0.09	Controversial
		1	101	3.96	17.82	19.8		2.97	0.36	Controversial
A drame incufficiency should be accorded only in calcord sub nonvolutions	1 2 0	2	105	3.81 2.91	22.86	11.43	59.1	10.48	0.42	Controversial
Advand insufficiency should be assessed only in selected sub-populations	4.3.a	3	105	3.61	21.9	10.48	36.1	5.71	0.4	Controversiai
Auterial insufficiency should be assessed only in selected sub-populations such as those	1 2 h	1	101	0.00	4.05	0.0	62.28	21.79	0.00	Dositivo
on regular, long-term oc's therapy.	4.3.0	1	101	1.09	4.93	9.9	22.58	21.70	0.99	Controversial
Adranal insufficiency should be assessed only in selected sub nonulations — such as those		1	101	2.86	25.70	25.71	30.48	5.90	0.15	Controversial
Autorial instituctory should be assessed only in selected sub-populations such as those exceeding a cumulative yearly dose of 500 mg OCS	43 c	3	105	0	39.05	32.38	26.67	1.9	-0.02	Controversial
exectang a canadative yearly dose of 500 mg 666.	ч. <i>Э</i> . с	1	103	1.98	19.8	26.73	38.61	12.87	0.41	Controversial
Adrenal insufficiency should be assessed only in selected sub-nonulations such as those		2	101	1.9	25.71	24.76		8 57	0.77	Controversial
exceeding a cumulative yearly dose of 1 g OCS.	4.3.d	3	105	0	20	30.48	43.81	5.71	0.35	Controversial
		1	101	1.98	13.86	20.79	41.58	21.78	0.67	Controversial
Adrenal insufficiency should be assessed only in selected sub-populations such as those		2	105	0.95	17.14	19.05		18.1	0.62	Controversial
exceeding a cumulative yearly dose of 2 g OCS.	4.3.e	3	105	0	16.19	19.05	48.57	16.19	0.65	Controversial
		1	101	1.98	8.91	21.78	39.6	27.72	0.82	Controversial
Adrenal insufficiency should be assessed only in selected sub-populations such as those		2	105	0.95	13.33	17.14		22.86	0.76	Controversial
exceeding a cumulative yearly dose of >2 g OCS.	4.3.f	3	105	0.95	14.29	16.19	47.62	20.95	0.73	Controversial
		1	101	8.91		28.71	8.91	0	-0.62	Controversial
Adrenal insufficiency should be assessed only in selected sub-populations such as those		2	105	11.43		26.67	5.71	0.95	-0.7	Controversial
who have had two repeated short courses of OCS in a given year.	4.4.a	3	105	7.62	60.95	19.05	12.38	0	-0.64	Controversial
		1	101	6.93		28.71	16.83	0.99	-0.42	Controversial
Adrenal insufficiency should be assessed only in selected sub-populations such as those		2	105	10.48	40	28.57	18.1	2.86	-0.37	Controversial
who have had three repeated short courses of OCS in a given year.	4.4.b	3	105	5.71	48.57	21.9	22.86	0.95	-0.35	Controversial
		1	101	5.94	28.71	26.73	29.7	8.91	0.07	Controversial
Adrenal insufficiency should be assessed only in selected sub-populations such as those		2	105	3.81	28.57	18.1	41.9	7.62	0.21	Controversial
who have had four repeated short courses of OCS in a given year.	4.4.c	3	105	3.81	28.57	20.95	40.95	5.71	0.16	Controversial

				Strongly					Weighted	
			Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
		1	101	2.97	12.87	20.79	43.56	19.8	0.64	Controversial
Adrenal insufficiency should be assessed only in selected sub-populations such as those		2	105	1.9	12.38	16.19		20.95	0.74	Controversial
who have had >4 repeated short courses of OCS in a given year.	4.4.d	3	105	1.9	13.33	15.24	54.29	15.24	0.68	Controversial
Adrenal insufficiency should be assessed when signs/symptoms of adrenal insufficiency appear.	4.5.a	1	101	0.99	6.93	5.94	43.56	42.57	1.2	Positive
Adrenal insufficiency should be assessed when OCS tapering trials are unsuccessful.	4.5.b	1	101	0	14.85	10.89	52.48	21.78	0.81	Positive
		1	101	1.98	21.78	55.45	18.81	1.98	-0.03	Controversial
In case of adrenal insufficiency during tapering, OCS should be switched to physiological		2	105	0.95	28.57		16.19	3.81	-0.07	Controversial
doses of hydrocortisone with the following characteristics: 0.25 mg/kg/d.	4.6.a	3	105	1.9	32.38	42.86	20.95	1.9	-0.11	Controversial
		1	101	3.96	21.78	43.56	29.7	0.99	0.02	Controversial
In case of adrenal insufficiency during tapering, OCS should be switched to physiological		2	105	3.81	29.52		16.19	1.9	-0.17	Controversial
doses of hydrocortisone with the following characteristics: 0.50 mg/kg/d.	4.6.b	3	105	1.9	26.67	43.81	26.67	0.95	-0.02	Controversial
		1	101	0.99	21.78	32.67	38.61	5.94	0.27	Controversial
In case of adrenal insufficiency during tapering, OCS should be switched to physiological		2	105	2.86	16.19	41.9	31.43	7.62	0.25	Controversial
doses of hydrocortisone with the following characteristics: 15–20 mg/day	4.6.c	3	105	1.9	17.14	43.81	31.43	5.71	0.22	Controversial
In case of adrenal insufficiency during tapering, OCS should be switched to physiological		1	101	4.95	18.81	46.53	28.71	0.99	0.02	Controversial
doses of hydrocortisone with the following characteristics: 30 mg/day in men and 20 mg/day		2	105	4.76	24.76	44.76	23.81	1.9	-0.07	Controversial
in women.	4.6.d	3	105	2.86	25.71	41.9	26.67	2.86	0.01	Controversial
In case of adrenal insufficiency during tapering, OCS should be switched to physiological										
doses of hydrocortisone with the following characteristics: doubling in cases of stress/sick days.	4.6.e	1	101	0.99	5.94	16.83	56.44	19.8	0.88	Positive
		1	101	4.95	32.67	33.66	24.75	3.96	-0.1	Controversial
In case of adrenal insufficiency during tapering, OCS should be switched to physiological		2	105	6.67	36.19	27.62	23.81	5.71	-0.14	Controversial
doses of hydrocortisone with the following characteristics: one intake per day.	4.6.f	3	105	9.52	39.05	26.67	21.9	2.86	-0.3	Controversial
		1	101	2.97	23.76	31.68	36.63	4.95	0.17	Controversial
In case of adrenal insufficiency during tapering. OCS should be switched to physiological		2	105	1.9	23.81	36.19	31.43	6.67	0.17	Controversial
dose of hydrocortisone with the following characteristics: two intakes per day	4 6 g	3	105	2.86	14 29	32.38	45 71	4 76	0.35	Controversial
	1.0.8	1	101	4.95	10.59	31.68	17.82	/ 95	-0.23	Controversial
In case of adrenal insufficiency during tanering OCS should be switched to physiological		2	101	2.86		32.38	19.05	3.81	-0.23	Controversial
does of hydrocortisone with the following characteristics: three intakes per day	46 h	3	105	6.67	34 29	33 33	22.86	2.86	-0.19	Controversial
	1.0.11	1	101	5.04	10.0	00.7	41.50	2.00	0.16	Controversital
		1	101	5.94	19.8	29.7	41.58	2.97	0.16	Controversial
	4 7	2	105	6.67	21.9	25.71	41.9	3.81	0.14	Controversial
Hydrocortisone is not obligatory; OCS can be maintained at 2–4 mg once daily (starting at 4 mg)	4./.a	3	105	3.81	22.86	29.52	40	3.81	0.17	Controversial

				Strongly		NT		<i>a</i>	Weighted	
Statement	Number	Round	Sample size	disagree, %	Disagree, %	Neutral, %	Agree, %	Strongly agree, %	mean rank	Consensus
		1	101	7.92	19.8	21.78	48.51	1.98	0.17	Controversial
		2	105	7.62	18.1	23.81		3.81	0.21	Controversial
Hydrocortisone is not obligatory; OCS can be maintained at 5 mg once daily.	4.7.b	3	105	4.76	17.14	25.71	49.52	2.86	0.29	Controversial
		1	101	13.86	29.7	29.7	25.74	0.99	-0.3	Controversial
		2	105	11.43	42.86	26.67	17.14	1.9	-0.45	Controversial
Hydrocortisone is not obligatory; OCS can be maintained at 7.5 mg once daily.	4.7.c	3	105	10.48	37.14	26.67	23.81	1.9	-0.3	Controversial
		1	101	2.97	12.87	38.61	37.62	7.92	0.35	Controversial
		2	105	1.9	28.57	30.48	34.29	4.76	0.11	Controversial
Switching to hydrocortisone should be performed: as soon as adrenal insufficiency is diagnosed.	4.8.a	3	105	3.81	23.81	25.71	42.86	3.81	0.19	Controversial
		1	101	3.96	7.92	26.73		5.94	0.51	Controversial
Switching to hydrocortisone should be performed: when the patient has been weaned		2	105	2.86	10.48	29.52		3.81	0.45	Controversial
down to 5 mg OCS (and signs of adrenal insufficiency are present).	4.8.b	3	105	2.86	10.48	23.81	61.9	0.95	0.48	Controversial
		1	101	5.94		32.67	10.89	0	-0.51	Controversial
Switching to hydrocortisone should be performed: when the patient has been weaned		2	105	5.71		33.33	8.57	4.76	-0.41	Controversial
down to 5 mg OCS (regardless of adrenal insufficiency assessments).	4.8.c	3	105	7.62	46.67	24.76	20	0.95	-0.4	Controversial
		1	101	3.96	24.75	35.64	27.72	7.92	0.11	Controversial
Switching to hydrocortisone should be performed: when the patient has been weaned		2	105	3.81	35.24	32.38	23.81	4.76	-0.1	Controversial
down to 7 mg OCS (and signs of adrenal insufficiency are present).	4.8.d	3	105	5.71	35.24	23.81	33.33	1.9	-0.1	Controversial
		1	101	6.93		31.68	2.97	2.97	-0.6	Controversial
Switching to hydrocortisone should be performed: when the patient has been weaned		2	105	6.67		34.29	4.76	3.81	-0.51	Controversial
down to 7 mg OCS (regardless of adrenal insufficiency assessments).	4.8.e	3	105	9.52	54.29	24.76	9.52	1.9	-0.6	Controversial
		1	101	8.91	36.63	31.68	18.81	3.96	-0.28	Controversial
		2	105	10.48	29.52	31.43	20.95	7.62	-0.14	Controversial
Switching to hydrocortisone is not obligatory/important when managing adrenal insufficiency.	4.8.f	3	105	15.24	30.48	33.33	16.19	4.76	-0.35	Controversial
		1	101	3.96	44.55	27.72	21.78	1.98	-0.27	Controversial
		2	105	7.62	42.86	22.86	23.81	2.86	-0.29	Controversial
Adrenal insufficiency should be assessed: using only a fasting morning cortisol.	4.9.a	3	105	4.76	46.67	21.9	23.81	2.86	-0.27	Controversial
		1	101	0.99	32.67	35.64	24.75	5.94	0.02	Controversial
		2	105	4.76	34.29	28.57	25.71	6.67	-0.05	Controversial
Adrenal insufficiency should be assessed: using only a (short) Synacthen test.	4.9.b	3	105	1.9	40.95	24.76	29.52	2.86	-0.1	Controversial
Adrenal insufficiency should be assessed: using fasting morning cortisol, and in case of										
intermediate results, follow up with a (short) Synacthen test.	4.9.c	1	101	0.99	6.93	19.8	55.45	16.83	0.8	Positive
		1	101	0	6.93	31.68		6.93	0.61	Controversial
Adrenal insufficiency assessments should be interpreted with caution; current laboratory		2	105	2.86	13.33	29.52	47.62	6.67	0.42	Controversial
tests require improvement in terms of sensitivity and specificity.	4.9.d	3	105	0	13.33	25.71	54.29	6.67	0.54	Controversial
Adrenal insufficiency should be assessed: never; patients should be systematically										
substituted during tapering irrespective of any test.	4.9.e	1	101	17.82	56.44	22.77	2.97	0	-0.89	Negative

				Strongly	D .	N (1		G()	Weighted	
Statement	Number	Round	Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean rank	Consensus
Adrenal insufficiency should be assessed: never: patients should be substituted during	rtumber	Round	SILC	/0	70	/0	70	ugree, /o	Tunk	Consensus
tapering only according to signs/symptoms.	4.9.f	1	101	20.79	50.5	19.8	7.92	0.99	-0.82	Negative
Adrenal insufficiency is insufficiently assessed or under-recognized.	4.11.a	1	101	0.99	1.98	15.84	54.46	26.73	1.04	Positive
Steroid withdrawal syndrome (symptoms of glucocorticoid deficiency in the setting of a		1	101	0	2.97	38.61	51.49	6.93	0.62	Controversial
proven normal hypothalamic-pituitary-adrenal axis) occurs more often than adrenal		2	105	0	10.48	31.43		7.62	0.55	Controversial
insufficiency.	4.11.b	3	105	0	7.62	29.52	57.14	5.71	0.61	Controversial
		1	101	0.99	15.84	24.75	53.47	4.95	0.46	Controversial
Administration of exogenous glucocorticoids even in small doses for only a few days leads		2	105	1.9	24.76	22.86	44.76	5.71	0.28	Controversial
to a measurable suppression of the hypothalamic-pituitary-adrenal axis.	4.11.c	3	105	0.95	17.14	28.57	49.52	3.81	0.38	Controversial
		1	101	0.99	13.86	29.7		5.94	0.46	Controversial
OCS treatment may not suppress the hypothalamic-pituitary-adrenal axis at all, or it		2	105	1.9	10.48	33.33		8.57	0.49	Controversial
may cause central suppression and adrenal gland atrophy of varying degrees.	4.11.d	3	105	0.95	6.67	34.29	52.38	5.71	0.55	Controversial
		1	101	2.97	31.68	18.81	43.56	2.97	0.12	Controversial
		2	105	9.52	32.38	19.05	35.24	3.81	-0.09	Controversial
A correct OCS tapering regime does not require frequent assessments of adrenal insufficiency.	4.12.a	3	105	4.76	27.62	20	43.81	3.81	0.14	Controversial
Reduce the dose of glucocorticoid replacement to the minimum dose possible. This		1	101	2.97	19.8		26.73	0.99	0.03	Controversial
should be judged on hydrocortisone day curves (if on hydrocortisone), or prednisolone day		2	105	3.81	22.86	51.43	20.95	0.95	-0.08	Controversial
curves/8- hour prednisolone levels.	4.12.b	3	105	1.9	25.71	48.57	22.86	0.95	-0.05	Controversial
		1	101	0	11.88	24.75		3.96	0.55	Controversial
If systemic effects (e.g. arthritis pain) occur during OCS tapering, patients are advised to		2	105	0.95	10.48	22.86	59.05	6.67	0.6	Controversial
slow down the tapering pace because the complaints will disappear after some time.	4.12.c	3	105	0	10.48	24.76	61.9	2.86	0.57	Controversial
If adrenal insufficiency occurs during tapering, first increase OCS, and then later re-					12.04	10.0	57 40			
attempt tapering at a slower pace.	4.12.d	I	101	2.97	13.86	19.8	57.43	5.94	0.5	Controversial
If adrenal insufficiency occurs during tapering, first increase OCS, and then later re-	4 12 1	2	105	2.00	0.52	15.24	(5.71	((7	0.64	D 14
attempt tapering at a slower pace.	4.12.d	2	105	2.86	9.52	15.24	65./1	6.67	0.64	Positive
		1	101	0	19.8	23.76		0.99	0.38	Controversial
when symptoms occur, stop rurtner tapering until they resolve (this can take	4 12 -	2	105	1.9	23.81	16.19	55.24	2.91	0.32	Controversial
weeks/months), and then continue.	4.12.e	3	105	0.95	15.24	24.76	35.24	3.81	0.46	Controversial
		1	101	4.95	41.58	22.11	28.71	1.98	-0.19	Controversial
An undetectable essimential equat may be a given of alugescarticated success	4 12 0	2	105	6.57	29.32	20.07	20.00	0.05	-0.1	Controversial
An undetectable cosmophil count may be a sign of glucocorticold excess.	4.13.a	1	103	0.07	21.79	22.80	36.1	0.93	-0.03	Controversial
		1	101	0.99	21.78	32.07	37.02	0.93	0.28	Controversial
The interpretation of short Synacthen test results should take into account the effect of inhaled absocortionids	1 13 h	23	105	0	19.05	35.24	10.95	0.37	0.3	Controversial
The interpretation of short synacticities results should take into account the creet of initiated glucocorticolds.	+.15.0	1	103	2.07	14.85	63.24	18.93	4.70	0.01	Controversial
Patients who fail their first short Synacthen test with a 30-min cortisol of <350 nmol/I		2	101	0.95	12.38		22.86	2.86	-0.02	Controversial
$1 \text{ areas who fail then this short synacticities with a so-fine correspondence of 1 > 350 \text{ mino}/L$	4 13 c	3	105	0.95	14.30	60	22.80	0.95	0.14	Controversial
or 12 g/aL, should be counselled that there is a 50% chance of metong replacement therapy.	+.15.0	5	105	0.95	14.27	00	25.01	0.95	0.1	Connoversial

			Sample	Strongly disagree,	Disagree,	Neutral,	Agree,	Strongly	Weighted mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
		1	101	2.97	15.84		17.82	0.99	-0.02	Controversial
Patients with a subsequent morning cortisol of <200 nmol/L should be informed that		2	105	0.95	17.14	64.76	15.24	1.9	0	Controversial
there is a >90% chance that they will need lifelong steroids.	4.13.d	3	105	1.9	11.43	60.95	24.76	0.95	0.11	Controversial
Patient-physician shared decision-making for OCS tapering should be a systematic practice.	5.1.a	1	101	0	1.98	4.95	52.48	40.59	1.32	Positive
		1	101	8.91	39.6	8.91	38.61	3.96	-0.11	Controversial
		2	105	13.33		9.52	32.38	5.71	-0.22	Controversial
In most cases, the decision to taper OCS treatment is not shared, but taken alone by the clinician.	5.1.b	3	105	6.67	50.48	11.43	26.67	4.76	-0.28	Controversial
		1	101	1.98	25.74	10.89		22.77	0.54	Controversial
		2	105	2.86	31.43	13.33	35.24	17.14	0.32	Controversial
The self-management of OCS treatments should be discouraged.	5.1.c	3	105	1.9	33.33	14.29	40.95	9.52	0.23	Controversial
The self-management of OCS tapering should be limited to patients with a good level of comprehension.	5.1.d	1	101	1.98	14.85	11.88	57.43	13.86	0.66	Positive
Patient-physician shared decision-making for OCS tapering is important because: it										
educates the patient on the benefits/risks associated with OCS use.	5.2.a	1	101	0	0	0.99	58.42	40.59	1.4	Positive
Patient-physician shared decision-making for OCS tapering is important because: it allows										
the patients to understand the purpose of OCS tapering.	5.2.b	1	101	0	0	0	66.34	33.66	1.34	Positive
Patient-physician shared decision-making for OCS tapering is important because: it										
provides necessary support and guidance to the patient.	5.2.c	1	101	0	0	3.96	65.35	30.69	1.27	Positive
Patient-physician shared decision-making for OCS tapering is important because: it can										
increase the chances of success; improve outcomes.	5.2.d	1	101	0	1.98	1.98	61.39	34.65	1.29	Positive
Patient-physician shared decision-making for OCS tapering is important because:										
ambivalent attitudes towards tapering are frequent.	5.2.e	1	101	0	6.93	13.86	59.41	19.8	0.92	Positive
Patient-physician shared decision-making for OCS tapering is important because: "aches and pains" during										
OCS withdrawal can occur, and planning how to manage them is likely to improve withdrawal progress.	5.2.f	1	101	0.99	0.99	3.96	62.38	31.68	1.23	Positive
Patient-physician shared decision-making for OCS tapering is important because: patient										
engagement/empowerment in the process can optimize the outcome.	5.2.g	1	101	0	0	1.98	62.38	35.64	1.34	Positive
Patient-physician shared decision-making for OCS tapering is important because: patients										
are often expected to self-medicate at home.	5.2.h	1	101	1.98	4.95	15.84	63.37	13.86	0.82	Positive
Patient-physician shared decision-making should include: a decision aid including full										
disclosure of short- and long-term exacerbation/adverse events profile.	5.3.a	1	101	0	1.98	11.88	66.34	19.8	1.04	Positive
Patient-physician shared decision-making should include: patient education on the										
benefits/risks associated with OCS use.	5.3.b	1	101	0	0	0	65.35	34.65	1.35	Positive

			G	Strongly	D:	Nandaral	A	Store - In	Weighted	
Statement	Number	Round	size	disagree, %	Disagree, %	Neutral, %	Agree, %	agree, %	rank rank	Consensus
Patient-physician shared decision-making should include: the benefits/risks associated				, ,	, .	, .	,,,			
with OCS tapering and why it is important.	5.3.c	1	101	0	0	0	56.44	43.56	1.44	Positive
Patient-physician shared decision-making should include: the dangers of abrupt tapering										
OCS discontinuation.	5.3.d	1	101	0	0	0	56.44	43.56	1.44	Positive
Patient-physician shared decision-making should include: the patient's thoughts										
(concerns, fears, hopes, expectations) and preferences.	5.3.e	1	101	0	0	3.96	60.4	35.64	1.32	Positive
Patient-physician shared decision-making should include: symptoms that may occur due										
to weaning, how to recognize and manage them (including adrenal insufficiency).	5.3.f	1	101	0	0.99	0.99	60.4	37.62	1.35	Positive
Patient-physician shared decision-making should include: multidisciplinary work (for										
example, collaboration between respiratory, endocrinology, and rheumatology experts).	5.3.g	1	101	0.99	3.96	12.87	49.5	32.67	1.09	Positive
Patient-physician shared decision-making should include: a joint evaluation of the										
patient's global health status and/or quality of life.	5.3.h	1	101	0	3.96	11.88	66.34	17.82	0.98	Positive
Patient-physician shared decision-making should include: using biomarkers for		1	101	0.99	10.89	26.73		7.92	0.56	Controversial
monitoring and individualization of the action plan.	5.3.i	2	105	0.95	12.38	16.19	60.95	9.52	0.66	Positive
Patient-physician shared decision-making should include: steroid-sparing strategies and their benefits/risks.	5.3.j	1	101	0	0.99	5.94	61.39	31.68	1.24	Positive
Patient-physician shared decision-making should include: clear, agreed-upon										
protocols/action plan on how tapering will be carried out and what to expect.	5.3.k	1	101	0	0.99	4.95	62.38	31.68	1.25	Positive
Patient-physician shared decision-making should include: a warning regarding the										
consequences of not following the action plan.	5.3.1	1	101	0.99	2.97	7.92	70.3	17.82	1.01	Positive
Patient-physician shared decision-making should include: a means of contacting the										
doctor/team so the patient can reach out and get support.	5.3.m	1	101	0	0.99	3.96	59.41	35.64	1.3	Positive
Patient-physician shared decision-making should include: discussion with both patients										
and their families/caregivers.	5.3.n	1	101	0	1.98	11.88	59.41	26.73	1.11	Positive
Advice for OCS self-managers: if possible, do not opt for regular OCS use.	5.4.a	1	101	0	1.98	7.92	51.49	38.61	1.27	Positive
Advice for OCS self-managers: the lowest active dose of OCS for the shortest duration is preferable.	5.4.b	1	101	0	0	1.98	53.47	44.55	1.43	Positive
Advice for OCS self-managers: closely monitor symptoms while tapering, including those										
of adrenal insufficiency.	5.4.c	1	101	0	0	5.94	59.41	34.65	1.29	Positive
Advice for OCS self-managers: help the process of OCS tapering by overcoming minor discomfort related to it.	5.4.d	1	101	0.99	0	3.96	67.33	27.72	1.21	Positive
Advice for OCS self-managers: respect your doctor's recommendations in as much as										
possible, and contact him/her (or team) when there is a problem.	5.4.e	1	101	0	0.99	3.96	63.37	31.68	1.26	Positive

			Sample	Strongly disagree,	Disagree,	Neutral,	Agree,	Strongly	Weighted mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
Advice for OCS self-managers: increase the OCS dose to the previous dose if a weaning										
step causes (intolerable) symptoms.	5.4.f	1	101	0	3.96	10.89	54.46	30.69	1.12	Positive
		1	101	0.99	10.89	22.77	44.55	20.79	0.73	Controversial
Advice for OCS self-managers: never use a dose lower than the agreed-up threshold		2	105	4.76	23.81	29.52	35.24	6.67	0.15	Controversial
(e.g. 7.5 mg) without substitution.	5.4.g	3	105	0.95	33.33	23.81	37.14	4.76	0.11	Controversial
Advice for OCS self-managers: always make dosage changes under medical supervision.	5.4.h	1	101	0	10.89	15.84	52.48	20.79	0.83	Positive
Physicians should drive the decision-making when it comes to OCS tapering.	5.5.a	1	101	0	8.91	12.87	59.41	18.81	0.88	Positive
		1	101	1.98	10.89	21.78		8.91	0.59	Controversial
		2	105	0.95	27.62	17.14	48.57	5.71	0.3	Controversial
Physicians should limit prescriptions to ensure that tapering is occurring.	5.5.b	3	105	1.9	19.05	21.9	56.19	0.95	0.35	Controversial
		1	101	1.98	23.76	26.73	29.7	17.82	0.38	Controversial
		2	105	2.86	30.48	14.29	41.9	10.48	0.27	Controversial
The self-management of OCS treatments should be discouraged.	5.5.C	3	105	1.9	39.05	12.38	39.05	7.62	0.11	Controversial
		1	101	4.95	41.58	10.89	35.64	6.93	-0.02	Controversial
	5 5 J	2	105	3.81	47.62	15.24	30.48	2.86	-0.19	Controversial
Forewarning patients of acres and pains during OCS withdrawar is fikely to impede withdrawar progress.	5.5.U	1	103	2.80	49.32	24.75	55.55	2.80	-0.10	Controversial
		1	101	0.05	9.9	24.75		9.9	0.65	Controversial
When OCS tenoring decisions are not taken mutually, this can lead to medical malaractics and litization	5 5 0	2	105	0.95	7.02 8.57	23.71	59.05	5.71	0.05	Controversial
when OCS tapering decisions are not taken mutuany, uns can read to medical mapfactice and nugation.	5.5.6	1	103	2.06	0.57	25.64	21.69	2.06	0.01	Controversial
		1	101	0.52	41.0	15.24	31.00	0.05	0.07	Controversial
In some cases, you might need to have a consent form signed before patients start OCS treatment	55 f	3	105	6.67	36.19	23.81	30.48	2.86	-0.13	Controversial
Many times, note there are to have a concern form signed before particulations of effort to convince them to taper	5 5 9	1	101	0.07	9.9	19.8	55.45	14.85	0.15	Positive
The majority of patients want to reduce their OCS use and will actively participate in doing so	<u>5.5.g</u>	1	101	0	2.97	10.89	62.38	23.76	1.07	Positive
OCS tapering can be successful even if the patient doesn't think it will work	5 5 i	1	101	0.99	4 95	16.83	62.38	14.85	0.85	Positive
	0.0.1	1	101	4 95	36.63	26.73	25.74	5.94	-0.09	Controversial
It is better to allow patients to control their own prednisolone doses to control symptoms		2	105	4.76		29.52	23.81	0.95	-0.25	Controversial
than to give high dose bursts for exacerbations.	5.5.i	3	105	2.86	45.71	26.67	22.86	1.9	-0.25	Controversial
		1	101	0	13.86	35.64	43.56	6.93	0.44	Controversial
The patient generally has full confidence in his/her doctor and experiences tapering as a		2	105	0	10.48	35.24		1.9	0.46	Controversial
success on his/her illness.	5.5.k	3	105	0	14.29	30.48	48.57	6.67	0.48	Controversial
		1	101	0.99	12.87	30.69	46.53	8.91	0.5	Controversial
The patient is usually the major player and follows an action plan with an easy contact		2	105	0.95	10.48	26.67		5.71	0.55	Controversial
with the multidisciplinary team.	5.5.1	3	105	1.9	15.24	20.95	57.14	4.76	0.48	Controversial

				Strongly					Weighted	
Station and	Namban	Dennal	Sample	disagree,	Disagree,	Neutral,	Agree,	Strongly	mean	C
Statement Devisions should be trained on how to couch nationts during the tenoring process	Number		101	-70 	7 0	70 8 01	70	10 01	Ганк 1.1	Dositivo
Physicials should be trained on now to coach patients during the tapering process.	5.5.m	1	101	0	0	6.91	72.28	16.01	1.1	Positive
Patients should be educated with standard material (generated and endorsed e.g. by ERS) about the OCS therapy.	5.5.n	1	101	0	0.99	6.93	/5.25	16.83	1.08	Positive
		1	101	1.98	20.79	15.84		9.9	0.47	Controversial
Shared decision-making is made difficult by the level of individualization and adaptation	~ ~	2	105	1.9	32.38	22.80	40	2.80	0.1	Controversial
required during OCS tapering.	5.5.0	3	105	0.95	38.1	20.95	38.1	1.9	0.02	Controversial
Shared decision-making is dependent on the willingness and ability of both sides to interact.	5.5.p	l	101	0	0	3.96	69.31	26.73	1.23	Positive
Patients are suffering a lot and a strong patient-doctor relationship is required to achieve			101	0.00	0	12.07	50.45	21 (0		D 111
a safe, optimum outcome from OCS tapering.	5.5.q	l	101	0.99	0	13.86	53.47	31.68	1.15	Positive
All OCS-treated asthma patients should be referred to an expert center able to propose										
multidisciplinary assessment and access to innovations.	6.1.a	1	101	0	1.98	5.94	38.61	53.47	1.44	Positive
Maintenance OCS for severe asthma should only be considered after evaluation by a										
severe asthma specialist (the definition of this specialist may vary from region to region).	6.1.b	1	101	0	2.97	4.95	32.67	59.41	1.49	Positive
The respiratory physician treating severe asthma patients must assess for adrenal insufficiency.	6.1.c	1	101	0.99	6.93	13.86	49.5	28.71	0.98	Positive
Adrenal insufficiency management in patients with severe asthma should involve an										
endocrinologist/multidisciplinary approach.	6.1.d	1	101	0	3.96	23.76	38.61	33.66	1.02	Positive
Primary care physicians prescribing more than three courses of OCS to a patient with										
asthma in 1 year should consider a referral to a specialist.	6.2.a	1	101	0	0.99	0	27.72	71.29	1.69	Positive
The primary care physician should be part of the multidisciplinary team.	6.2.b	1	101	0	3.96	16.83	55.45	23.76	0.99	Positive
		1	101	6.93	28.71	6.93	36.63	20.79	0.36	Controversial
		2	105	10.48	28.57	8.57	33.33	19.05	0.22	Controversial
OCS use in asthma should also be discouraged at the primary care level.	6.2.c	3	105	7.62	29.52	9.52	34.29	19.05	0.28	Controversial
The following is an important subject of future research: improving the delivery of asthma care.	6.3.a	1	101	0	0.99	5.94	54.46	38.61	1.31	Positive
The following is an important subject of future research: integration and dissemination of										
how to use predictive biomarkers in clinical practice.	6.3.b	1	101	0	2.97	8.91	57.43	30.69	1.16	Positive
The following is an important subject of future research: improving the use of biological treatments in asthma.	6.3.c	1	101	0	0	4.95	38.61	56.44	1.51	Positive
The following is an important subject of future research: while striving to obtain a										
balance between over and under-treatment with OCS, patients often experience adverse										
quality of life. How best to manage this requires future research.	6.3.d	1	101	0	0	19.8	55.45	24.75	1.05	Positive

			Sample	Strongly disagree.	Disagree.	Neutral.	Agree.	Strongly	Weighted mean	
Statement	Number	Round	size	%	%	%	%	agree, %	rank	Consensus
The following is an important subject of future research: whether hydrocortisone										
supplementation is less harmful than prednisone should be established.	6.3.e	1	101	0.99	2.97	15.84	50.5	29.7	1.05	Positive
The following is an important subject of future research: The impact of shared decision-										
making on important outcomes.	6.3.f	1	101	0	0.99	20.79	52.48	25.74	1.03	Positive
The following is an important subject of future research: OCS tapering regime algorithms and optimization.	6.3.g	1	101	0.99	0.99	5.94	50.5	41.58	1.31	Positive
The following is an important subject of future research: real-life, cost-										
benefit/effectiveness evaluations for steroid-sparing strategies taking into account side-										
effects and comorbidities, quality of life, and the societal costs of maintenance OCS.	6.3.h	1	101	0	0	6.93	40.59	52.48	1.46	Positive
The following is an important subject of future research: direct comparisons between										
biologicals, especially anti-IL-5.	6.3.i	1	101	0.99	0.99	10.89	38.61	48.51	1.33	Positive
The following is an important subject of future research: strategic ways to reduce OCS use										
for the overall at-risk populations.	6.3.j	1	101	0	0.99	2.97	58.42	37.62	1.33	Positive
The following is an important subject of future research: methods for determining OCS starting doses.	6.3.k	1	101	0	7.92	17.82	55.45	18.81	0.85	Positive
The following is an important subject of future research: the role of the endocrinologist										
and when referral should occur.	6.3.1	1	101	0	4.95	11.88	64.36	18.81	0.97	Positive
The following is an important subject of future research: improving the assessment of adrenal insufficiency.	6.3.m	1	101	0.99	0	7.92	54.46	36.63	1.26	Positive
		1	101	0.99	9.9	22.77		18.81	0.73	Controversial
The following is an important subject of future research: the efficacy of internet-provided		2	105	0	13.33	22.86		13.33	0.64	Controversial
algorithms for delivering symptom-driven OCS tapering guidance to asthma patients.	6.3.n	3	105	0	11.43	20.95	59.05	8.57	0.65	Controversial
The following is an important subject of future research: how should OCS tapering be										
addressed in countries where there is limited access to biological treatments?	6.3.0	1	101	0	2.97	8.91	58.42	29.7	1.15	Positive
The following is an important subject of future research: what aspect/phenotype of										
asthma is being treated by OCS that the currently available biological therapies are not treating?	6.3.p	1	101	0	0.99	7.92	42.57	48.51	1.39	Positive
The following is an important subject of future research: in the context of successful OCS										
weaning subsequent to the initiation of a biological, what kind of follow-up should be proposed?	6.3.q	1	101	0	1.98	15.84	56.44	25.74	1.06	Positive

ABPA = allergic bronchopulmonary aspergillosis; ACOS = Asthma-COPD overlap syndrome; ACQ = Asthma Control Questionnaire; ACT = Asthma Control Test; BAL = bronchoalveolar lavage fluid; COPD = chronic obstructive pulmonary disease; DDAVP = desmopressin; EGPA = eosinophilic granulomatosis with polyangiitis; ERS = European Respiratory Society; FRAX = Fracture Risk Assessment Tool; GERD = gastroesophageal reflux disease; GINA = Global Initiative for Asthma; HbA1c = hemoglobin A1c; ICS = inhaled corticosteroid; IL = interleukin; MCID = minimal clinically important difference; OCS = oral corticosteroid; PDGF-D = platelet-derived growth factor D

The OCS Tapering Delphi Expert Panel (Alphabetical order)

Al-Ahmad, Mona

- Microbiology Department, Faculty of Medicine, Kuwait University, Kuwait
- Babu, K Suresh

٠

- Queen Alexandra Hospital, Portsmouth, Hampshire, PO6 3LY, United Kingdom
- Bakakos, Petros
 - 11 Kononos St, Athens, Attiki, 11634, Greece
- Ball, Stephen
 - Manchester University Foundation Trust, Endocrinology Department, Oxford Road, Manchester, M13 9WL, United Kingdom
- Bel, Elisabeth
 - Department of Pulmonology, F5-168, Amsterdam UMC, Univ. of Amsterdam, Meibergdreef 9, Amsterdam, 1105AZ, Netherlands
- Bjermer, Leif
 - Department of Lung and Allergology, Skane University Hospital, Lund, 22185, Sweden
- Blanc, François-Xavier
 - Nantes University, Nantes, 44093, France
- Blasi, Francesco
 - Internal Medicine Department, Respiratory Unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, and Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Italy
- Bourdin, Arnaud
 - Department of Respiratory Diseases, University of Montpellier, CHU Montpellier, Montpellier, France
- Brown, Thomas
 - Portsmouth Hospitals NHS Trust, Queen Alexandra Hospital, Southwick Hill Road, Cosham, Portsmouth, Hampshire, PO63LY, United Kingdom
- Brussino, Luisa
 - Department of Medical Science, University of Torino-Allergy and Immunology Unit, Mauriziano Hospital, C.so Re Umberto 109, Torino, 10100, Italy
- Burhan, Hassan
 - Royal Liverpool University Hospital, Prescot Street, Link 6Z, Royal Liverpool University Hospital, Prescot Street, Liverpool, L7 8XP, United Kingdom
- Calvert, James
 - North Bristol NHS Trust, Westbury on Trym, Bristol, Avon, BS10 5NB, United Kingdom
- Caminati, Marco
 - Department of Medicine, University of Verona & Asthma Center and Allergy Unit, Verona University Hospital, Verona, Italy
- Campos Cerda, Ricardo
 - Centro de Atención de Enfermedades Cardiopulmonares, 880 Garibaldi St, Office 9, 1st Floor, Guadalajara, Jalisco, 44200, Mexico
- Canonica, Giorgio Walter
 - Personalised Medicine, Asthma and Allergy Center, Humanitas Research Hospital, Milan, Italy

- Caruso, Cristiano
 - Fondazione Policlinico Universitario A. Gemelli IRCSS, Rome, Italy
- Cataldo, Didier
 - University of Liege (GIGA-research center) and CHU of Liege, Tower of Pathology (B23), Hippocrates Avenue 13, Liege, 4000, Belgium
- Chanez, Pascal
 - Department of Respiratory Diseases, AP-HM, INSERM, INRA, C2VN Aix Marseille Université, Marseille, France
- Chanson, Philippe
 - Assistance Publique-Hôpitaux de Paris, Hôpital de Bicêtre, Service d'Endocrinologie et des Maladies de la Reproduction, Centre de Référence des Maladies Rares de l'Hypophyse; Université Paris-Saclay, Univ. Paris-Sud, Inserm, Signalisation Hormonale, Physiopathologie Endocrinienne et Métabolique, 94276, Le Kremlin-Bicêtre, France
- Chapman, Ken
 - Asthma & Airway Centre, University Health Network, University of Toronto, Room 7-451
 - East Wing, 399 Bathurst Street, Toronto, Ontario M5T 2S8, Canada
- Chaudhuri, Rekha
 - NHS Greater Glasgow and Clyde, Asthma/COPD Clinical Research Centre, Gartnavel
 - General Hospital, Glasgow, G62 6QL, United Kingdom
- Chenivesse, Cécile
 - CHU Lille, Service de Pneumologie et Immuno-allergologie, Centre de référence constitutif pour les maladies pulmonaires rares, Univ. Lille, Inserm 1019, Centre Infection et Immunité de Lille, Institut Pasteur de Lille, Lille, France
- Choudhury, Sirazum
 - Imperial College London, Section of Investigative Medicine, 6th Floor Commonwealth Building,
 - Du Cane Road, London, W12 0NN, United Kingdom
- Christoff, George
 - Medical University Sofia, Faculty of Public Health, 8 "Bialo more" str, Sofia, 1527, Bulgaria
- Chung, Li Ping
 - Department of Respiratory Medicine, Fiona Stanley Hospital, Perth, Western Australia 6150, Australia
- Clairelyne Dupin
 - Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis, 1 avenue Claude Vellefaux,75475 Paris Cedex 10, France
- Clifton, Ian
 - St James's University Hospital, Beckett Street, Leeds, West Yorkshire, LS9 7TF, United Kingdom
- Cochrane, Belinda
 - Campbelltown Hospital, Therry Rd, Campbelltown, NSW, 2560, Australia
- Colantuono, Stefania
 - Allergy Unit, Fondazione Policlinico Gemelli, IRCCS; Department of Translational and Precision medicine, Sapienza University of Rome, Rome, Italy
- Cosmi, Lorenzo
 - University of Firenze, AOU Careggi, Largo Brambilla, Firenze 50100, Italy

- Costello, Richard
 - RCSI, Beaumont Hospital, Dublin 9, Ireland
- Côté, Andréanne
 - Institut Universitaire Cardiologie et Pneumologie de Québec, Laval University, 2725 ch Ste- Foy, Quebec, G1V 4V5, Canada
- Crimi, Nunzio
 - Via Etnea 676, Catania, 95125, Italy
- Crooks, Michael G.
 - Hull York Medical School, Academic Respiratory Medicine, Castle Hill Hospital, Cottingham, HU16 5JQ, United Kingdom
- D'Amato, Maria
 - Respiratory Department, Monaldi Hospital, Via D. Fontana, 134, Naples, Campania, 80128, Italy
- De Gennaro, Mónica S.
 - Fundacion CIDEA, Paraguay 2035 3Cuerpo 2SS, CABA, Buenos Aires, C1121ABE, Argentina
- Debono, Miguel
 - Sheffield Teaching Hospitals, Royal Hallamshire Hospital, Glossop Road, Sheffield, S10 2JF, United Kingdom
- Del Giacco, Stefano
 - Department of Medical Sciences and Public Health, University of Cagliari, Asse Didattico E1, Cittadella Universitaria, 09042 Monserrato (Cagliari), Italy
- Dennison, Patrick
 - University Hospitals Southampton Foundation Trust, Tremona road, Southampton, Hampshire, SO16 6YD, United Kingdom
- Deschildre, Antoine
 - CHU Lille, Pneumologie et Allergologie Pédiatriques, Hôpital Jeanne de Flandre, Avenue Avinée, F-59000 Lille, France
- Detoraki, Aikaterini
 - Azienda Ospedaliera Universitaria Federico II, Via Pansini 5, Naples, 80131, Italy
- Devouassoux, Gilles
 - University Claude Bernard Lyon 1; HCL, Service de Pneumologie, Bâtiment I 103 Grande
 - Rue de la Croix Rousse, F-69004 Lyon, France
- Didier, Alain
 - Center for Pathophysiology Toulouse Purpan, INSERM U1043, CNRS UMR 5282, Toulouse III University and CHU Toulouse, France
- Dorscheid, Del
 - University of British Columbia, 166 1081 Burrard Street, Vancouver, BC, V6Z 1Y6, Canada
- Fardon, Tom
 - NHS Tayside, East Block, Ninewells Hospital; Department of Respiratory Research, University of Dundee, Dundee, DD1 9SY, Scotland, United Kingdom
- Faruqi, Shoaib
 - The Hull University Teaching Hospital NHS Trust, Department of Respiratory Medicine, Castle Hill Hospital, Castle Road, Cottingham, East Yorkshire, HU16 5JQ, United Kingdom

- FitzGerald, JM Mark
 - The Lung Centre, Vancouver General Hospital, Institute for Heart and Lung Health, Gordon and Leslie Diamond Health Care, Vancouver, BC, Canada
- Gaga, Mina
 - Athens Chest Hospital, 152 Mesogion Ave, Athens 11527, Greece
- Genova, Sonya
 - UHATEM N.I.Pirogov, 21 Totleben blvd, Sofia, 1606, Bulgaria
- Gibson, Peter
 - University of Newcastle, Lookout RD, New Lambton Hts, Newcastle, NSW 2305, Australia
- Gore, Robin
 - Cambridge University NHS Foundation Trust, Box 40, Addenbrooke's Hospital, Cambridge, CB2 0QQ, United Kingdom
- Guilleminault, Laurent
 - Toulouse University Hospital Centre, Larrey Hospital, F-31059 Toulouse, France
- Gurnell, Mark
 - University of Cambridge & Addenbrooke's Hospital, Cambridge, United Kingdom
- Hamerlijnck, Dominique
 - Atini, Zeeburgerkade 540, Amsterdam, Noord-Holland, 1019HR, Netherlands
- Hanania, Nicola
 - Baylor College of Medicine, 7200 Cambridge, Suite 8A. 269, Houston, 77030 Texas, United States of America
- Heaney, Liam
 - Centre for Experimental Medicine, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Wellcome-Wolfson Institute for Experimental Medicine, 97 Lisburn Road, Belfast BT9 7BL, Northern Ireland, United Kingdom
- Heffler, Enrico
 - Humanitas University, Via Rita Levi Montalcini 4, Pieve Emanuele, MI, 20090, Italy
- Hernandez Colin, Dante Daniel
 - Instituto Jalisciense de Investigacion Clinica Penitenciaria, Centro 20, Guadalajara, Jalisco, 44100, México
- Hew, Mark
 - Alfred Health, 55 Commercial Road, Prahran, Melbourne, Victoria 3004, Australia
- Hoyte, Flavia
 - National Jewish Health, Division of Allergy and Immunology, Denver, CO, 80206, United States of America
- Humbert, Marc
 - Université Paris-Saclay, Inserm, Hôpital Bicêtre (Assistance Publique Hôpitaux de Paris), 78 rue du Général Leclerc, F-94270 Le Kremlin-Bicêtre, France
- Idzko, Marco
 - Department of Pneumology, Medical Clinic II, Medical University Vienna, 6L, Währingerstraße 18-20, Vienna, 1090, Austria
- Jenkins, Christine
 - The George Institute for Global Health, PO Box M201, Missenden Rd, NSW, 2050, Australia
- Kauppi, Paula
 - HUH, Inflammation Center, Department of Allergy (Adult Unit), P.O. Box 160, 00029 HUH; Skin and Allergy Hospital, Meilahdentie 2, Helsinki, Finland

- Kostikas, Konstantinos
 - Respiratory Medicine Department, University of Ioannina, Ioannina, Greece
- Kuna, Piotr
 - Department of Internal Medicine, Asthma and Allergy, Medical University of Lodz, Poland
- Kupczyk, Maciej
 - Medical University of Lodz, Kopcinskiego 22, Lodz, 90-350, Poland
- Kupryś-Lipińska, Izabela
 - Medical University of Lodz, Department of Internal Medicine, Asthma and Allergy, 22 Kopcinskiego Str, Lodz 90-153, Poland
- Labor, Marina
 - University Hospital Centre Osijek, Huttlerova 4, Osijek 31000, Croatia
- Langton, David
 - Peninsula Health, 2 Hastings St, Frankston, Victoria, 3199, Australia
- Latorre, Manuela
 - Pulmonary Unit, NOA Hospital (Nuovo Ospedale Apuano), Massa, Italy
- Lehtimäki, Lauri
 - Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland
- Louis, Renaud
 - CHU of Liege, University of Liege, GIGA I3 Research Group, Liege, 4000, Belgium
- Loukides, Stylianos
 - National and Kapodistrian University of Athens Medical School, 2nd Respiratory Department, Rimini 1 Xaidari 12462, Greece
- Lugogo, Njira Lucia
 - Department of Medicine, Division of Pulmonary and Critical Care Medicine, University of Michigan, 300 North Ingalls St Suite 2C40, Ann Arbor, Michigan, 48109, United States of America
- Mahay, Guillaume
 - Centre Hospitalier Universitaire de Rouen, Service de Pneumologie, Oncologie Thoracique, Soins Intensifs Respiratoires, 1 rue de Germont, F-760031 Rouen, France
- Mahboub, Bassam
 - DHA & University of Sharjah, PO box 4545, Dubai 4546, United Arab Emirates
- Masoli, Matthew
 - Royal Devon & Exeter Hospital, Respiratory Department, Barrack Road, Exeter, Devon, EX2 5DW, United Kingdom
- Maspero, Jorge
 - Fundacion Cidea, Paraguay 2035, Segundo Subsuelo, Buenos Aires, Caba C1121ABE, Argentina
- Meeran, Karim

•

- Imperial College London, Department of Endocrinology, 9th floor, East Wing,
- Charing Cross campus, Fulham Palace Road, London W6 8RF, United Kingdom Menzella, Francesco
- Azienda USL di Reggio Emilia-IRCCS, Pneumology Unit, Santa Maria Nuova Hospital, Via Amendola 2, Reggio Emilia 42122, Italy
- Menzies-Gow, Andrew
 - Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom
- Middleton, Peter
 - Westmead Hospital, Hawkesbury Rd, Westmead, Sydney, NSW 2145, Australia

- Milanese, Manlio
 - Pulmonology Unit S. Corona Hospital, ASL2 Savonese, Via XXV Aprile 38, Pietra ligure, Savona 17027, Italy
- Mitchell, Patrick D.
 - Rockyview General Hospital, 7007 14 ST SW, Calgary, Alberta, T2V 1P9, Canada
- Mohan, Arjun
 - ECU Pulmonary Clinic & Severe Asthma Program, Division of Pulmonary and Critical Care Medicine, Brody School of Medicine-East Carolina University, 3E-111A, BSOM, Greenville, NC, 27834, United States of America
- Paggiaro, Pierluigi
 - University of Pisa, via Paradisa 2, Pisa, 56124, Italy
- Papadopoulos, Nikolaos G.
 - Division of Infection, Inflammation and Respiratory Medicine, University of Manchester, Manchester, United Kingdom; Allergy Dpt, 2nd Pediatric Clinic, National Kapodistrian University of Athens, Athens, Greece
- Papaioannou, Andriana I.
 - Attikon Hospital, Rimini 1, Chaidari, Athens, 12462 Greece
- Pavord, Ian
 - University of Oxford, Respiratory Medicine Unit, Nuffield Department of Medicine, Oxford OX3 7FZ, United Kingdom
- Peché, Rudi
 - CHU Charleroi site Vesale, Rue de Gozee 706, Montingny-l-Tilleul, Hainaut, 6110 Belgium
- Pelaia, Corrado
 - University Magna Graecia of Catanzaro, Viale Europa, Catanzaro, 88100, Italy
- Pelaia, Girolamo
 - University Magna Graecia of Catanzaro, Viale Europa, Catanzaro, 88100, Italy
- Perng, Diahn-Warng
 - Taipei Veterans General Hospital, 201 Shi-Pai Rd, Sec 2, Taipei, 11217 Taiwan
- Pfeffer, Paul
 - Barts Health NHS Trust, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE, United Kingdom
- Pilette, Charles
 - Université catholique de Louvain, Cliniques Universitaires St-Luc and Institute of Experimental and Clinical Research, Department of Pulmonology, 10 Avenue Hippocrate, Brussels, B-1200, Belgium
- Pison, Christophe
 - UGA, Service Hospitalier Universitaire Pneumologie Physiologie, Pôle Thorax et Vaisseaux, Centre Hospitalier et Universitaire de Grenoble, Grenoble, CS10217, 38043 Grenoble Cedex 9, France
- Plavec, Davor
 - Srebrnjak Children's Hospital, Srebrnjak 100, Zagreb, 10000, Croatia; Medical Faculty, University JJ Strossmayer, Osijek, 31000, Croatia
- Popov, Todor A
 - University Hospital Sv. Ivan Rilski, 13, Urvich St., Sofia, 1612, Bulgaria
- Popović-Grle, Sanja
 - University Hospital Centre Zagreb, Clinic for Lung Diseases Jordanovac, Jordanovac 104, Zagreb, 10000; School of Medicine, University of Zagreb, Croatia

- Powlson, Andrew S
 - University of Cambridge, Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, CB2 0QQ, United Kingdom
- Puggioni, Francesca
 - Personalized Medicine, Asthma, and Allergy, Humanitas Clinical and Research Center, IRCCS, Milan, Italy
- Reddel, Helen
 - Woolcock Institute of Medical Research, University of Sydney, 431 Glebe Point Rd, Glebe, NSW 2037, Australia
- Rhee, Chin Kook
 - Seoul St. Mary's Hospital, The Catholic University of Korea, 222 Banpodaero, Seochogu, Seoul, South Korea
- Roche, Nicolas
 - Respiratory Medicine, Cochin Hospital (APHP Centre), University Paris Descartes (UMR 1016 Institut Cochin), Université de Paris, Paris, France
- Rupani, Hitasha
 - Portsmouth Severe Asthma Service, Queen Alexandra Hospital, Southwick Hill Road, Portsmouth, Hampshire, PO6 5LY, United Kingdom
- Sabroe, Ian
 - Sheffield Teaching Hospitals NHS Foundation Trust, Royal Hallamshire Hospital, Glossop Road, Sheffield, S10 2JF, United Kingdom
- Samitas, Konstantinos
 - Athens Chest Hospital "SOTIRIA", Mesogion 152 Ave, Athens, Attiki 11527, Greece
- Santus, Pierachille
 - Department of Biomedical and Clinical Sciences, University of Milan, Via GB Grassi, 74, Milano, 20157, Italy
- Schleich, Florence
 - Rue Hubert Delvenne 1, Hody, 4172, Belgium
- Selmi, Carlo
 - Division of Rheumatology and Clinical Immunology, Humanitas Clinical and Research Center – IRCCS, Humanitas University, Via A. Manzoni 113, Rozzano, Milano, 20089, Italy
- Senna, Gianenrico
 - Allergy Unit Asthma Center, University of Verona, Italy
- Sherlock, Mark
 - Department of Endocrinology, Beaumont Hospital, Beaumont, Dublin D9 and Royal College of Surgeons, Ireland
- Siddiqui, Salman
 - University of Leicester and Leicester NIHR Biomedical Research Centre (Respiratory Theme), Glenfield Hospital, Leicester, LE3 9QP, England, United Kingdom
- Smith, Andrew
 - NHS Lanarkshire, University Hospital Wishaw, 50 Netherton Street, Wishaw, Lanarkshire, ML2 0DP, Scotland, United Kingdom
- Spanevello, Antonio
 - Dipartimento di Medicina e Chirurgia, Malattie dell'Apparato Respiratorio, Università degli Studi dell'Insubria, Varese – Como; Dipartimento di Medicina e Riabilitazione Cardio Respiratoria, U.O. di Pneumologia Riabilitativa, Istituti Clinici Scientifici Maugeri, IRCCS Tradate, Italia

- Taillé, Camille
 - Assistance Publique-Hôpitaux de Paris and Université de Paris, 46 rue Henri Huchard, F-75018 Paris Cedex, France
- Taube, Christian
 - Universitätsmedizin Essen- Ruhrlnadklinik, Tüschener Weg 40, Essen, 45239, Germany
- ten Brinke, Anneke
 - Medical Centre Leeuwarden, H Dunantweg 2, Leeuwarden, 8934AD, Netherlands
- Tudoric, Neven
 - Clinical Hospital Dubrava, Avenija Gojka Suska 6, Zagreb, 10000, Croatia
- Tunsäter, Alf
 - Department of Respiratory Medicine & Allergology, Skane University Hospital, Lund, 221 85, Sweden
- Ulrik, Charlotte
 - Head of Respiratory Research Unit & Severe Asthma Clinic Hvidovre, Department Of Respiratory Medicine, Hvidovre University Hospital, DK-2650 Hvidovre, Denmark
 - Upham, John
 - Princess Alexandra Hospital, 199 Ipswich Road, Woolloongabba, Brisbane, Qld 4102, Australia
 - Van Ganse, Eric
 - PharmacoEpidemiology Lyon (PELyon), Faculté d'Odontologie; HESPER, Claude Bernard Lyon1 University, Respiratory Medicine; Croix Rousse University Hospital, 69008 Lyon, France
 - Walker, Brandie
 - Canada Division of Respirology, Department of Medicine, University of Calgary; Calgary COPD and Asthma Program, Alberta Health Services; Airways Working Group, Respiratory Health Strategic Clinical Network; 1007 Health Sciences Centre, 3330 Hospital Drive NW, Calgary, AB, T2N 4N1, Canada
 - Wang, Eileen
 - National Jewish Health, 1400 Jackson Street, K624a, Denver, CO, 80238; University of Colorado, 13001 East 17th Place, Aurora, CO, 80045, United States of America
 - Wark, Peter
 - Priority Research Centre for Healthy Lungs, Respiratory Medicine HMRI, Lookout Road, New Lambton, New South Wales 2305, Australia
 - Wechsler, Michael
 - NJH Cohen Family Asthma Institute, Department of Medicine, National Jewish Health, 1400 Jackson St, Denver, CO 80206, United States of America
 - Winders, Tonya
 - Allergy & Asthma Network, 8229 Boone Blvd, Ste 260, Vienna, VA, 22182, United States of America
 - Zervas, Eleftherios
 - 7th Resp. Department and Asthma Centre, Athens Chest Hospital, Mesogion Ave. 152, Athens, Attica 11527, Greece