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**Consensus on Diagnosis and Management of Cushing’s Disease:
A Guideline Update**

APPENDIX

Methods

Workshop co-chairs and steering committee members identified 28 discrete topics related to CD diagnosis, complications, and treatment to be addressed, and invited experts to summarize key data on their assigned topics in 15-minute, fully referenced slide-lecture presentations recorded approximately one month prior to the meeting. Speakers critically reviewed literature indexed in PubMed and published in English before October 2020. Search terms included “cushing’s disease,” “ectopic Cushing’s,” and terms associated with each topic: “diagnosis,” “urinary free cortisol,” “salivary cortisol,” “screening tests,” “confirmatory testing,” “differential diagnosis,” “localization testing,” “genetics,” “surgery,” “radiation therapy,” “medical therapy,” “biochemical treatment goals,” “tumor shrinkage,” “clinical outcomes,” “adrenal steroidogenesis inhibitors,” “glucocorticoid receptor blockers,” “somatostatin receptor ligands,” “dopamine agonists,” “mortality,” “comorbidities,” “quality of life,” “preoperative treatment,” “combination therapy,” and “guidelines.” All participants were invited to watch the lectures and offer comments in advance of the meeting. More than 50 academic researchers and clinical experts from 13 countries across 5 continents participated in the Workshop.

During the 2-day meeting, speakers provided 5-minute highlight summaries of their assigned topics. Participants were then divided into 4 small groups for extended discussions of each topic during 6 breakout sessions. Session moderators were provided with a set of key questions to

prompt discussion. One person in each group was designated in advance to take notes and assist in recording key discussion comments and consensus statements based on majority opinion.

After the meeting, speakers prepared detailed précis and literature reviews on their assigned topics. The fully referenced slide-lecture presentations, précis, and literature reviews were collated to prepare a draft manuscript, along with more recent data identified in a second literature review using the same keywords performed by the first and senior author in April 2021. Consensus recommendations for managing CD complications and use of medical therapy shown in Panels 1 and 2 were based on written reports from breakout sessions.

Speakers were asked to verify for accuracy manuscript sections related to their assigned topics, and the draft manuscript and consensus recommendations was circulated to all Workshop participants for review.

Speakers were also asked to suggest topics for future research that they consider most important. The full list of suggestions was sent to all participants, who were asked to vote for their top 5 choices. The senior author tabulated responses; topics with more than 10 votes are shown in Panel 3. After incorporating edits and comments, the final manuscript was again circulated for review and approval.

Panel. Grading of Evidence and Recommendations

Evidence	<ul style="list-style-type: none">• Very low quality (VLQ): expert opinion supported by one or few small uncontrolled studies• Low quality (LQ): supported by large series of small uncontrolled studies• Moderate quality (MQ): supported by one or few large uncontrolled studies or meta-analyses• High quality (HQ): supported by controlled studies or large series of large uncontrolled studies with sufficiently long follow-up
Recommendations	<ul style="list-style-type: none">• Discretionary recommendation (DR): based on VLQ or LQ evidence• Strong recommendation (SR): based on MQ or HQ evidence

Based on Guyatt et al *BMJ* 2008 and Giustina et al *Nat Rev Endocrinol* 2014.