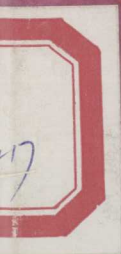


EVIDENCE-BASED

Endocrinology

SECOND EDITION

Pauline M. Camacho
Hossein Gharib
Glen W. Sizemore



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EVIDENCE-BASED ENDOCRINOLOGY

Second Edition

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*The book is dedicated to our spouses—
Francis, Minoo, and Juliet; our families;
the teachers who inspired us; and our
fellows, who taught us so much.*

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Preface

In 2004, we asked, “Why is there no evidence-based handbook in endocrinology?” Clearly, endocrine disorders lend themselves to evidence-based medicine. They encompass large patient populations: an estimated 14 million persons have diabetes mellitus, an estimated 44 million have osteoporosis or low bone mineral density, and 127 million U.S. citizens are overweight. These diseases are associated with high morbidity and mortality rates, a considerable social price, and high treatment costs.

The endocrine literature is huge and can be overwhelmingly so to a busy clinician. For some disease states, large controlled studies of quantifiable treatment regimens with quantifiable results have been undertaken and published; for other disorders, no such trials are found in the literature, but case studies or small trials of drug therapies or diagnostic measures are available. In the contemporary health care environment, some physicians treating endocrine patients may have little specialized training or experience in endocrine disease and only minimal appreciation of the quality of its vast literature. A manual encapsulating the best available evidence-based information in endocrinology was needed. We therefore set out to publish the first concise handbook that contained the latest clinical trials and evidence. We were gratified that the book was very well received in the United States and internationally, and the readers’ feedback was most rewarding.

Given the rapidity and extent of new developments in endocrinology, another edition of the book was warranted. In the second edition of *Evidence-Based Endocrinology*, we have added a new chapter on genetics and expanded chapters on lipids, obesity, and nutrition. All chapters received a fresh look from the authors, and hundreds of new references were added. Diabetes and osteoporosis are perhaps the most rapidly growing fields, and the authors present a comprehensive update of new therapies for these diseases. Finally, a minor but notable change has been the omission of the possessive ending on eponyms, in keeping with the prevailing trend in healthcare publications.

Why should clinicians benefit from this book? At its most basic, it frees them from having to find and digest the huge volume of endocrine literature. The latest and best publications have been sought out and summarized here. At its most useful, *Evidence-Based Endocrinology* may improve diagnosis and treatment of endocrine disorders. Applying a modification of the McMaster criteria (see Introduction), the contributors have critically assessed and graded studies, assisting the readers in quickly evaluating the articles that have led to practice recommendations. This should allow them to apply the latest and, it is hoped, the best science to the diagnostic and therapeutic aspects of their practice.

The text is organized into the traditional clinical areas in endocrinology—hypothalamic–pituitary, thyroid, adrenal, metabolic bone, reproductive, diabetes, lipid disorders, obesity and nutrition, unusual endocrine malignancies, and genetics. Within this framework, our goals were multiple. First, we wished to present a concise, reference-based handbook to students, residents, physicians who provide primary care, and specialists who seek information about endocrine management. Second, we used a modification of the McMaster grading system to evaluate the quality of the references and provide practice recommendations based on summarized and graded references chosen by knowledgeable authors. Third, where possible, we wanted to provide estimates of the cost-effectiveness of clinical choices. With the limited studies available to date in some areas, the final goal has been the most elusive.

It is our hope that readers find the second edition of *Evidence-Based Endocrinology* to be a worthwhile addition to office libraries, to medical reference areas, and, as primarily intended, to the pockets of their lab coats.

Pauline M. Camacho, MD, FACE
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Introduction

In the early years of medicine, patient management was generally based on oral or written strategies gleaned from the interpretation of existing literature or first-hand observation of patients. The results were handed down from “seasoned” or senior authorities to their juniors. Although not uniformly difficult, this form of education certainly had problems. It suffered from the empiric attitudes of some clinicians and their lack of ability or failure to assess current, “best” literature; a bias inherent in the overweighting of the results of limited observations in few patients; often a lack of systematic outcome observation, with failure to include measurements of benefit or harm to patients; and a lack of formal rules to evaluate clinical evidence.

To improve the diagnostic and therapeutic decisions offered in *Evidence-Based Endocrinology*, we have used summarized, graded references based on modifications of the McMaster classification [1]. The evidence-based effort to improve patient care began in the late 1980s at McMaster University [2] and was founded on two ideas: that more emphasis could be placed on the benefits and risks of therapy and that it was best for patients to use the top therapies from pyramids of research information that contained methodologically weak work at the base to outstanding results at the peak. This latter idea recognized that we could separate gold from junk in medical studies [3] and that some results are more certain than others. Although the classification recognizes that validity exists for an initial, intuitive, observational case report or a case-control study, it gives greater weight to placebo-controlled, randomized, double-blind clinical trials.

The grades used in the McMaster classification are 1A, 1B, 1C+, 1C, 2A, 2B, and 2C (Table 1). A grade 1 recommendation suggests that the benefits clearly outweigh harms and cost, whereas grade 2 indicates a weaker recommendation (Table 2). The letter part of the grade denotes the quality of the study. The A grade is given to randomized controlled trials with consistent results. Grade B is applied to randomized trials with less consistent results. Grade C is given to observational studies or the generalization of randomized trial results from one group of patients to a different group. Grade C+ is given to observational studies with compelling results.

The McMaster classification was developed for therapeutic information only. In clinical practice guidelines, recommendations and evidence are usually graded separately. In this book, however, we have asked authors to grade the references and the implied recommendations together. We have also modified its use to include studies of diagnostic tests and, more generally, to use it as a grading system for most types of medical literature. Because many areas remain somewhat controversial, authors have been given broad latitude after reviewing literature in their area to make judgments based on their interpretation of all evidence.

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3. Brody JM. Separating gold from junk in medical studies. *New York Times*, October 22, 2002.

Table 1. McMaster Approach to Grades of Recommendation

Grade ^a	Clarity of Risk/Benefit	Methodologic Strength of Supporting Evidence	Implications
1A	Clear	RCTs without important limitations	Strong recommendation, can apply to most patients in most circumstances without reservation
1B	Clear	RCTs with important limitations (inconsistent results, methodological flaws ^b)	Strong recommendation, likely to apply to most patients
1C+	Clear	No RCTs but RCT results can be unequivocally extrapolated, or overwhelming evidence from observation studies exists	Strong recommendation, can apply to most patients in most circumstances
1C	Clear	Observational studies	Intermediate-strength recommendation; may change when stronger evidence available
2A	Unclear	RCTs without important limitations	Intermediate-strength recommendation; best action may differ depending on circumstances of patients' or societal values
2B	Unclear	RCTs with important limitations (inconsistent results, methodological flaws)	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C	Unclear	Observational studies	Very weak recommendation; other alternatives may be equally reasonable

RCTs = randomized controlled trials.

^a The following considerations will bear on whether the recommendation is grade 1 or 2: the magnitude and precision of the treatment effect, patients' risk of the target event being prevented, the nature of the benefit, and the magnitude of the risk associated with treatment, variability in patient preferences, variability in regional resource availability and health care practices, and cost considerations. Inevitably, weighing these considerations involves subjective judgment. Also, since studies in categories B and C may be flawed, it is likely that most recommendations in these classes will be grade 2.

^b These situations include RCTs with both lack of binding and subjective outcomes, where the risk of bias in measurement of outcomes is high, and with large loss to follow-up. (After Montori VM, Schunemann HJ, Guyatt GH. What is evidence-based medicine? *Endocrinol Clin* 2002;31:521–526.)

Table 2. Factors That May Weaken a Recommendation to Treat, Changing Grade 1 to Grade 2

Less serious outcome
Smaller treatment effect
Imprecise estimate of treatment effect
Lower risk of target event
Higher risk of therapy
Higher costs
Varying values

(After Montori VM, Schunemann HJ, Guyatt GH. What is evidence-based medicine? *Endocrinol Clin* 2002;31:521–526.)

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