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Canadian Schizophrenia Guidelines: Introduction and Guideline Development Process

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Tamara Pringsheim, MD[1] and Donald Addington, MD[2]

Abstract

Introduction: The aim of the Canadian Schizophrenia Guidelines is to provide evidence-based recommendations for the treatment of schizophrenia and schizophrenia spectrum disorders. The target users are health care professionals. Recommendations are provided as guidance to physicians and patients, with the goal of improving the overall standard of care of individuals with schizophrenia.

Methods: The guidelines were developed using the ADAPTE process, a systematic approach and alternative to de novo guideline development, in which an existing guideline is customised to suit the local context. We assembled a multidisciplinary team of experts, patients, and family carers from across Canada with the goal of involving individuals with diverse areas of expertise and offering different perspectives.

Results: We identified 6 guidelines that were suitable for adaptation. Recommendations from each guideline were extracted and, based on content, were reviewed by the relevant working group. Each working group examined the evidence from which the recommendation was derived and the acceptability and applicability of the recommendation to the Canadian context. Working groups also made decisions on modifications to recommendations when language or terms differed between the source guideline and the Canadian context. Each working group presented selected recommendations to the guideline panel at an in-person consensus meeting. Once the consensus process was completed, each working group created a manuscript with the recommendations adapted from the included guidelines, with the rationale for each recommendation.

Conclusions: The process yielded an up-to-date list of evidence-based recommendations that are relevant and applicable in Canada.

Keywords
schizophrenia, methodology

Introduction

Scope and Purpose

The aim of the Canadian Schizophrenia Guidelines is to provide evidence-based recommendations for the treatment of schizophrenia and schizophrenia spectrum disorders that are adapted to the Canadian Health Care System. The guideline addresses the treatment of schizophrenia from its onset in youth and includes a section on the emerging field of intervention in those at clinical high risk of developing schizophrenia.

Target Users

The target users of the Canadian Schizophrenia Guidelines are health care professionals. The guidelines may also be useful to individuals with schizophrenia and their families, as well as health policy makers, health administrators, and funding agencies. Recommendations are provided as guidance to physicians and patients, with the goal of improving the overall standard of care of individuals with schizophrenia. It is important to note that it is not possible for these guidelines to cover all possible situations and scenarios. Ultimately, collaborative decisions between health care providers and their patients must be made based on the unique needs and preferences of patients and their families.

[1] Department of Clinical Neurosciences, Psychiatry, Pediatrics and Community Health Sciences, University of Calgary, Calgary, Alberta
[2] Department of Psychiatry, University of Calgary, Calgary, Alberta

Corresponding Author:
Tamara Pringsheim, MD, Mathison Centre for Mental Health Research and Education, 3280, Hospital Drive NW, Calgary AB T2N 4Z6.
Email: tmprings@ucalgary.ca

Process

The last edition of the Canadian Schizophrenia Guidelines was published in 2005. Since then, there have been advances in our conceptualisation of schizophrenia as a spectrum disorder,[1] which has been endorsed in *DSM-5*.[2] This change is supported by studies that find the presence of individual psychotic symptoms in the general population and an increased risk of developing schizophrenia with increasing numbers and duration of individual psychotic symptoms.[1] It also fits with the finding that the presence of attenuated psychotic symptoms can be used to define a population at clinical high risk of developing a psychotic illness over the next 2 years.[3] The concept of a schizophrenia spectrum fits with a growing emphasis on earlier treatment, both in psychotic disorders and in those at clinical high risk of developing a psychosis. There has been a greater attention to the physical care of people with schizophrenia due to the reduced life span in this population. The last guidelines antedated the large government-sponsored "Practical Clinical Trials" that compare antipsychotics in less restrictive studies than typical registration studies. These have led to a focus on pharmacotherapy that minimises both tardive dyskinesia and the metabolic side effects of antipsychotics. There has been increased research to support the benefits of psychosocial treatments, particularly cognitive behaviour therapy. At a broader health system level, there has been a greater emphasis on recovery and personalised care, both of which are important for the treatment of schizophrenia. Our revised guidelines reflect these changes, which are addressed in each section of the guideline.

We assembled a multidisciplinary team of experts, patients, and family carers from across Canada with the goal of involving individuals with diverse areas of expertise and offering different perspectives on the assessment and management of schizophrenia. The team consisted of child and adult psychiatrists and psychologists specialising in the care of individuals with schizophrenia, psychotic disorders, and clinical high-risk populations; general psychiatrists; a family physician, pharmacist, and evidence-based medicine methodologist; 4 individuals with lived experience with schizophrenia; and a representative from the Schizophrenia Society of Canada. As the guideline team was aware of several recently published international guidelines on the assessment and management of schizophrenia, the team decided to review existing guidelines and determine if adaptation of these guidelines to the Canadian context was appropriate for the creation of the Canadian Schizophrenia Guidelines.

Funding

Funding for the Canadian Schizophrenia Guidelines was provided through a seed grant from the Mathison Centre for Mental Health Research and Education, based at the University of Calgary. All guideline team members donated their time to participate in the creation of the guidelines and were not compensated financially for their participation.

Renewal Process

The guidelines were developed with 2 major organisational collaborators, the Canadian Psychiatric Association (CPA) and the Schizophrenia Society of Canada (SSC). The CPA has a guideline development process and the capacity to support broad dissemination through from publication to conferences and workshops. The SSC provided members of the writing group and will work on developing a lay version of the guideline for its members. The CPA Clinical Practice Guidelines are maintained by the CPA Professional Standards and Practices Committee. The committee can request changes to the guideline at any time in response to new information. It is the policy of the CPA to review each position paper, policy statement, and clinical practice guideline every 5 years after publication or last review. Any such document on the CPA website that has been published more than 5 years ago and does not explicitly state it has been reviewed and retained as an official document of the CPA, either with revisions or as originally published, should be considered as a historical reference document only.

Guideline Development Process

The Canadian Schizophrenia Guidelines were developed using the ADAPTE process,[4] under the guidance of Dr. T. Pringsheim (evidence-based medicine methodologist, American Academy of Neurology and associate professor, University of Calgary). Recognising that the development of guidelines requires substantial resources, the ADAPTE process was created to take advantage of existing guidelines and reduce duplication of effort. The ADAPTE process uses a systematic approach for adapting guidelines produced in one setting for use in a different cultural and organisational context. The ADAPTE process has been used by many other organisations to develop guidelines, such as the Canadian Neurological Sciences Federation and Parkinson Society Canada to create the Canadian Guidelines on Parkinson's Disease.[5] International groups have also utilised that ADAPTE methodology, including the Asian Pacific League of Associations for Rheumatology[6] and Cancer Council Australia.[7] A challenge with adapting guidelines in Canada is that each province is responsible for health care delivery. Despite this localised accountability, all provinces operate under the Canada Health Act, which provides funding for hospital and medical services. The Mental Health Commission of Canada, a federally funded organisation, has partnered with the provinces to develop a mental health strategy that has broad national consensus. Furthermore, a complex funding formula provides federal funding for a proportion of the costs of provincial health care delivery. Thus, many national organisations have developed Canadian Clinical Practice Guidelines. The ADAPTE Collaboration has published a manual and resource toolkit to assist guideline developers following the ADAPTE process.

The first phase of the ADAPTE process, the setup phase, involved preparing for the ADAPTE process. These steps

consisted of 1) determining if adaptation is feasible, 2) establishing an organisation committee and multidisciplinary group panel, 3) identifying necessary resources and skills, 4) development of terms of reference, 5) declaration of conflict of interest, 6) identification of potential endorsement bodies, and 7) creation of an adaptation plan. The organisation committee for the project included Dr. Donald Addington, psychiatrist, content and methodology expert; Dr. Tamara Pringsheim, neurologist and methodology expert; Dr. Ross Norman, psychologist and content expert; and Dr. Gary Remington, psychopharmacologist and content expert. We assembled a national multidisciplinary panel from across Canada, including stakeholders with expertise in schizophrenia and mental health, health policy, patient advocacy, and lived experience with schizophrenia. All panel members committed to 1 face-to-face meeting and conference calls and to reviewing all documents related to guideline adaptation. Endorsement bodies for the guidelines include the Canadian Psychiatric Association and the Schizophrenia Society of Canada, which were also heavily involved in the dissemination and implementation strategy. The CPA is the national voluntary professional association for Canada's 4000 psychiatrists. The CPA advocates for the professional needs of its members and promotes excellence in education, research, and clinical practice. The SSC is a national registered charity. The SSC is committed to improving the quality of life for those affected by schizophrenia and psychosis through education, support programs, public policy, and research. It works with 10 provincial societies to help individuals with schizophrenia and their families. Declaration of conflict of interest for all guideline panel members can be found in the Appendix below.

The second phase of the ADAPTE process, the adaptation phase, involves the process of identifying specific health questions; searching for and retrieving guidelines; assessing guideline quality, currency, content, consistency, and applicability; decision making around adaptation; and preparing the draft adapted guideline. Our specific health questions are centred on the following interventions:

- Access and engagement to early intervention services and community treatment services
- Pharmacological therapy
- Psychological therapy

The populations of interest include the following:

- Adults with psychosis and schizophrenia
- Children and young people with psychosis and schizophrenia
- Individuals with psychosis and comorbid substance misuse

The guideline was divided into 9 separate sections with their own working groups (see Table of Contents).

The next step of the adaptation phase was to search for existing guidelines and evaluate their quality. We searched for guidelines in guideline clearinghouses, including the US National Guideline Clearinghouse and the Guidelines International Network. We also searched the websites of well-established guideline developers for mental health disorders, including the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), the American Psychiatric Association, the American Academy of Child and Adolescent Psychiatry, and the European Psychiatric Association. A MEDLINE search was also performed using the term *guideline* as the publication type and *schizophrenia* as the title or clinical topic. Inclusion criteria were that the guideline needed to be published after 2010, be written in English, and that recommendations had to be developed using a defined and systematic process. We chose 2010 as our cutoff date to include guidelines based on more recent systematic reviews of the literature. We identified 8 current guidelines that were potentially suitable for adaptation. These guidelines were reviewed and evaluated in duplicate using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) tool,[8] an instrument to evaluate the methodological rigour and transparency in which a guideline is developed (see online Supplemental Appendix). Based on this evaluation, we determined that the 6 guidelines in Table 1 were of suitable quality and content for adaptation. While there was no minimum specified score for inclusion of a guideline, the guidelines we chose for adaptation scored between 75% and 92% in the AGREE II overall guideline assessment, whereas the guidelines we chose not to use scored between 58% and 67%.

Once we determined which guidelines would be included for adaptation, recommendations from each guideline were extracted and divided based on content and reviewed by the relevant working group. For example, the Working Group on Pharmacotherapy of Schizophrenia in Adults reviewed recommendations from all included guidelines pertaining to pharmacotherapy in adults. Following the ADAPTE process, working groups selected between guidelines and recommendations to create an adapted guideline. Each working group carefully examined each recommendation, the evidence from which the recommendation was derived, and the acceptability and applicability of the recommendation to the Canadian context. After reviewing the recommendations from the guidelines, the working groups decided which recommendations to accept and which to reject, as well as which recommendations were acceptable but needed to be modified (e.g., new data may be added to the original recommendation, or the wording might be changed to better reflect the Canadian context). Care was taken when modifying existing recommendations not to change the recommendations to such an extent that they were no longer in keeping with the evidence upon which they were based. Each chapter includes an appendix of how and why recommendations were modified from their original form. Common reasons for modification included when terminology or referral resources differed between the United Kingdom and Canada.

Table 1. Clinical Practice Guidelines Used for the Canadian Schizophrenia Guidelines.

Guideline Developer	Guideline Title	Year Published
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence (NICE)	NICE National Clinical Guideline Number 178. Psychosis and Schizophrenia in Adults: Treatment and Management[9]	2014
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence (NICE)	NICE National Clinical Guideline Number 155. Psychosis and Schizophrenia in Children and Young People: Recognition and Management[10]	2013
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence (NICE)	NICE National Clinical Guideline Number 120. Psychosis with Coexisting Substance Misuse: Assessment and Management in Adults and Young People[11]	2011
Scottish Intercollegiate Guidelines Network (SIGN)	SIGN 131. Management of Schizophrenia[12]	2013
European Psychiatric Association	European Psychiatric Association Guidance on the Early Intervention in Clinical High Risk States of Psychoses[13]	2015
American Psychiatric Association	American Psychiatric Association Practice Guidelines for Psychiatric Assessment of Adults[14]	2016

The working groups also created de novo recommendations in situations where it was felt a recommendation was needed but none of the existing guidelines provided recommendations addressing the situation or topic. When de novo recommendations were created, the SIGN methodology was followed for the levels of evidence and the grades of recommendation (see Table 2).

Each working group developed a final list of recommendations from the included guidelines that were presented to the entire guideline panel at an in-person consensus meeting at the University of Calgary. Working group leaders presented each recommendation and its rationale to the panel. Anonymous voting by the entire panel using clicker technology was performed for each recommendation. Recommendations required agreement by 80% of the group to be included in the Canadian guidelines. Panel members were allowed to abstain from voting if they felt they did not have the necessary expertise to vote on a recommendation. If a recommendation did not receive 80% agreement, the group discussed the recommendation and if minor modifications to the recommendation would alter the likelihood that the recommendation would pass. In these situations, recommendations were modified (as described above) and the group revoted at a later date using an online anonymous survey. Whenever modifications in wording were made to original recommendations, the text "modified recommendation from" appears in the Canadian Schizophrenia Guidelines. In the Canadian Schizophrenia Guidelines, the source of each recommendation is written beside the recommendation statement. The strength or grade of the recommendation is provided in brackets if applicable, using the system from which the recommendation came. The grades of recommendation for each reference guideline and their meaning are explained in Table 2.

Once voting and consensus process was completed, each working group created a separate manuscript that contains all the recommendations adapted from the included guidelines, with accompanying text explaining the rationale for each recommendation.

During the finalisation phase, the Canadian Schizophrenia Guidelines were externally reviewed by those who will be affected by its uptake: practitioners, policy makers, health administrators, and patients and their families. The external review asked questions about whether the users approve of the draft guideline, strengths and weaknesses, and suggested modifications. The process was facilitated through the *Canadian Journal of Psychiatry* and the Schizophrenia Society of Canada. The Canadian Psychiatric Association Clinical Practice Guidelines Committee reviewed and approved the guideline methodology process. The final product was reviewed using the AGREE II instrument to assess how the adapted guideline rates with respect to quality criteria.

The main advantage of using the ADAPTE methodology is financial. Creating clinical practice guidelines requires the use of substantial resources to perform the evidence review, which can take several years to complete. The ADAPTE process takes advantage of existing guidelines and reduces reduplication of effort. Weaknesses of the ADAPTE process include issues with currency; even adapted guidelines take time to create, and the evidence upon which the original recommendations were based may be increasingly out of date by the time the adapted guideline is published.

Dissemination and Implementation

The guidelines will be published by the Canadian Psychiatric Association following its normal peer review process and launched at an annual meeting of the Canadian Psychiatric Association. It will be submitted to CPG Infobase: the Canadian Medical Association Clinical Practice Guideline Database. It will be disseminated more broadly through the CPA CPD Institutes, which provide specialists with the latest advances in neuroscience and its practical application to improving clinical decision-making skills through workshops offered across the country. Members of the writing group will present focused components of the guidelines at other national meetings of professional associations and local workshops and conferences.

Table 2. Grade/Strength of Recommendation Classification Systems for Included Guidelines.[a]

Guideline Developer	Grade/Strength of Recommendation System
NICE	**Strength of recommendations** Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation). For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions and their values and preferences. This discussion aims to help them to reach a fully informed decision. **Interventions that must (or must not) be used** We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening. **Interventions that should (or should not) be used—a 'strong' recommendation** We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm and be cost-effective. We use similar forms of words (for example, 'Do not offer . . . ') when we are confident that an intervention will not be of benefit for most patients. **Interventions that could be used** We use 'consider' when we are confident that an intervention will do more good than harm for most patients and be cost-effective, but other options may be similarly cost-effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the health care professional should spend more time considering and discussing the options with the patient.
SIGN	**Levels of Evidence** 1++ High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias 1+ Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias 1– Meta-analyses, systematic reviews, or RCTs with a high risk of bias 2++ High-quality systematic reviews of case control or cohort studies, or high-quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal 2+ Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal 2– Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal 3 Nonanalytic studies (e.g., case reports, case series) 4 Expert opinion **Grades of Recommendation** A: At least 1 meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population, or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results B: A body of evidence including studies rated as 2++, directly applicable to the target population and demonstrating overall consistency of results, or extrapolated evidence from studies rated as 1++ or 1+ C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, or extrapolated evidence from studies rated as 2++ D: Evidence level 3 or 4 or extrapolated evidence from studies rated as 2+ Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group
European Psychiatric Association	Uses same system as SIGN (see row above)
American Psychiatric Association	**Rating the Strength of Supporting Research Evidence** In accordance with the Methods Guide of the Agency for Healthcare Research and Quality, the ratings are defined as follows: High (denoted by the letter *A*) = High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect. Moderate (denoted by the letter *B*) = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate. Low (denoted by the letter *C*) = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.

(continued)

Table 2. (continued)

Guideline Developer	Grade/Strength of Recommendation System
	Rating the Strength of Recommendations Each guideline statement is separately rated to indicate strength of recommendation and strength of supporting research evidence. "Strength of recommendation" describes the level of confidence that potential benefits of an intervention outweigh potential harms. This level of confidence is informed by available evidence, which includes evidence from clinical trials as well as expert opinion and patient values and preferences. As described under "Guideline Development Process," the rating is a consensus judgment of the authors of the guideline and is endorsed by the APA Board of Trustees. There are two possible ratings: recommendation or suggestion. These correspond to ratings of "strong" or "weak" (also termed "conditional") as defined under the GRADE method for rating recommendations in clinical practice guidelines. "Recommendation" indicates confidence that the benefits of the intervention clearly outweigh harms. "Suggestion" indicates uncertainty (i.e., the balance of benefits and harms is difficult to judge or either the benefits or the harms are unclear).

[a]NICE, National Institute for Health and Care Excellence; RCT, randomised controlled trial; SIGN, Scottish Intercollegiate Guidelines Network.

Appendix 1

Canadian Schizophrenia Guideline Panel

Name	Qualifications	Conflict of Interest
Alain Lesage	MD, FRCPC, MPhil, DFAPA Professor, Department of Psychiatry, University of Montreal Psychiatrist and researcher, Centre de recherche Fernand-Seguin Institut universitaire en santé mentale de Montréal	No conflict of interest to disclose
Austin Mardon	PhD, CM, LLD (Hon) Assistant Adjunct Professor, John Dossetor Health Ethics Centre, University of Alberta, Edmonton, AB	No conflict of interest to disclose
Chris Summerville	D.Min., CPRP Chief Executive Officer Schizophrenia Society of Canada / Societe Canadienne de la Schizophrenie	No conflict of interest to disclose
Donald Addington	MBBS, MRCPsych, FRCPC Professor, Department of Psychiatry, University of Calgary Mathison Centre for Research & Education Department of Psychiatry	No conflict of interest to disclose
Doug Urness	MD, LMCC, FRCPC Clinical Department Head, Addiction and Mental Health Program, Central Zone, Alberta Health Services	No conflict of interest to disclose
Gary Remington	Schizophrenia Program Director Centre for Addiction and Mental Health University of Toronto	Participated in the development of one of the selected guidelines (Optimal Use Recommendations for Atypical Antipsychotics: Combination and High-Dose. Presenting the results at the CPA 2013 and CAMH Grand rounds – 2013. Has worked as a consultant for Novartis and Laboratorios Farmaceuticos Rovi Has worked as consultant and Speaker's honoraria for Novartis
Iliana Garcia-Ortega	MD, Psychiatrist Research Associate	No conflict of interest to disclose
Jean Addington	Professor, University of Calgary Mathison Centre for Mental Health Research and Education	No conflict of interest to disclose

(continued)

Appendix 1. (continued)

Name	Qualifications	Conflict of Interest
Kevin Jackson	Family Member	No conflict of interest to disclose
Kim Jackson	Family Member Corporate Secretary and Investor Relations Associate	No conflict of interest to disclose
Martina Ann Kelly	Clerkship Director, Department of Family Medicine University of Calgary Health Sciences Centre	No conflict of interest to disclose
Michael Teehan	Associate Professor Department of Psychiatry Early Psychosis Program Dalhousie University	No conflict of interest to disclose
Ross Norman	Professor, Western University Department of Psychiatry - PEPP Psychosis Program Department of Epidemiology & Biostatistics	No conflict of interest to disclose
Sabina Abidi	MD FRCP Assistant Professor Division Head, Outpatient Services, IWK Mental Health & Addictions Program Head, IWK Youth Psychosis Program	No conflict of interest to disclose
Tamara Milka Pringsheim	MD, FRCPC Neurology Associate Professor, University of Calgary Department of Clinical Neurosciences, Psychiatry, Pediatrics and Community Health Sciences Evidence Based Medicine Methodologist, American Academy of Neurology	No conflict of interest to disclose
William Honer	MD, FRCPC, FCAHS Jack Bell Chair in Schizophrenia Professor and Head, Department of Psychiatry Director, Institute of Mental Health University of British Columbia	Academic/expert consultant on Optimal Use Recommendations for Atypical Antipsychotics: Combination and High-Dose Treatment Strategies in Adolescents and Adults with Schizophrenia (CADTH); presentation of work at Canadian Psychiatric Association meeting. Consultant to Silico Biosciences, Otsuka, Lundbeck, Roche and Lilly. Honoraria from CADTH, Otsuka, Lundbeck, Roche and Lilly.
Zahinoor Ismail	MD FRCPC Clinical Associate Professor, University of Calgary Assistant Professor, University of Toronto Hotchkiss Brain Institute, University of Calgary	Has worked as paid consultant for: BMS & Otsuka & Lundbeck; Janssen; Pfizer
Tarek Rajji	MD FRCPC Canada Research Chair in Neurostimulation for Cognitive Disorders Chief, Geriatric Psychiatry Division Centre for Addiction and Mental Health Associate Professor, Department of Psychiatry University of Toronto	No conflict of interest to disclose
Irfan Mian	MD FRCPC, DABPN Assistant Professor, Department of Psychiatry, University of Toronto	No conflict of interest to disclose
David Crockford	MD, FRCPC, DABPBN, FAPA, FCPA Clinical Professor, Department of Psychiatry University of Calgary	No conflict of interest to disclose
Thomas Raedler	MD Associate Professor, Department of Psychiatry, University of Calgary	Honoraria, travel support and/or grant support fro Amgen, AstraZeneca, BMS, Boehringer-Ingelheim, Forum (EnVivo), Janssen, Lundbeck, Otsuka, Pfizer, Purdue, Roche, Sanofi Aventis, Sunovion, Valeant.
Tania Lecomte	PhD Professor, Universite de Montreal	No conflict of interest to disclose

Declaration of Conflicting Interests

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Supplementary Material

Supplementary material is available for this article online.

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