Perspectives and experiences of health care professionals and patients regarding treatments for type 2 diabetes

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ABSTRACT

Background: Several treatment options exist for type 2 diabetes, but little is known about the factors considered by health care providers (HCPs) and patients in Canada in making therapeutic decisions. This study explores perceptions and practices of HCPs and patients related to add-on (i.e., second-line) therapy for type 2 diabetes when initial therapy no longer provides adequate glycemic control.

Methods: HCPs (pharmacists, family physicians, diabetes educators, endocrinologists and nurse practitioners) and patients with type 2 diabetes in Ottawa and Halifax were randomly selected to participate in the study. Phone interviews were conducted with endocrinologists and nurse practitioners and focus groups with the other HCPs and patients.

Results and Interpretation: Sixty HCPs and 14 patients participated in the study. Metformin was consistently reported by prescribers (physicians and nurse practitioners) as the preferred initial therapy. Important factors in choosing second-line therapy (once glycemic control was inadequate with metformin) were antihyperglycemic efficacy, risk of hypoglycemia and weight gain, and long-term safety. Other considerations were cost, insurance coverage and patient preference. There were differences within and between HCP groups in how these other factors were considered and in the perceived advantages and disadvantages of each drug class. Some patients expressed anxiety when second-line agents were prescribed, and others felt poorly informed about treatment options.

Conclusion: In choosing a second-line therapy for type 2 diabetes, most HCPs placed a high priority on antihyperglycemic efficacy, although there was considerable variability in the relative weight placed on other factors. These findings point to an opportunity for pharmacists to collaborate more actively with other HCPs to ensure that treatment decisions are based on the best available evidence and to educate and involve patients in these decisions. *Can Pharm J (Ott)* 2013;147:45-54.

Despite the high and growing prevalence of type 2 diabetes, little is known about the factors that are most important to clinicians and patients when they make choices regarding diabetes therapies. The goal of this study was to gain a better understanding of decision making in this important therapeutic area.

Malgré la prévalence élevée et grandissante du diabète de type 2, nous en savons peu sur les facteurs considérés, par les cliniciens et les patients, comme les plus importants dans le choix d'un traitement. Cette étude vise à mieux comprendre le processus décisionnel derrière cet important domaine thérapeutique.

Introduction

While metformin is generally recommended as the first-line agent for type 2 diabetes patients requiring medications,[1,2] most patients eventually require more than 1 antihyperglycemic agent to achieve target blood glucose levels.[3,4] Numerous options exist for second-line therapy after metformin, including sulfonylureas, alpha-glucosidase inhibitors (AGIs), thiazolidinediones (TZDs), meglitinides, dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide-1 (GLP-1) analogues. Clear guidance on the choice

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KNOWLEDGE INTO PRACTICE

- A large number of treatment options exist for patients with type 2 diabetes for whom metformin no longer provides adequate glycemic control.
- There is considerable variability in how treatments are chosen for patients requiring a second-line agent after metformin.
- By working collaboratively with other health care providers and patients, pharmacists can help promote the use of best available evidence in support of therapeutic decisions related to type 2 diabetes. This could have a positive impact on patient outcomes and help make the best use of limited health care resources.

of second-line therapy is generally not available in treatment guidelines,[1,2,5] which may explain the considerable variability observed in the types of second-line agents used in Canada.[6] Due to the high and increasing prevalence of type 2 diabetes, suboptimal use of second-line antihyperglycemic drugs can have a detrimental effect on health outcomes and health care costs. Hence, an understanding of the beliefs, perceptions and practices of patients and health care providers (HCPs) is necessary to identify gaps between evidence-based and cost-effective use of second-line antidiabetes drugs and real-world practice. To our knowledge, this area has not been previously studied, although prior investigations have assessed attitudes toward antihyperglycemic therapy more generally, particularly in the context of initiating insulin therapy.[7-18] Here, we report the main results of a qualitative study of HCPs and patients designed to explore decision making regarding second-line therapies for type 2 diabetes. Detailed methods and results are reported elsewhere.[19]

Methods

Eight in-person focus groups were conducted during the summer of 2009: 2 each with pharmacists, family physicians, diabetes educators (DEs) (self-identified) and patients from Ottawa, Ontario, and Halifax, Nova Scotia. In addition, one-on-one phone interviews were conducted with endocrinologists and nurse practitioners located across Ontario and Atlantic Canada. HCPs were randomly selected using commercially available lists. Diabetes clinics in the community or affiliated with hospitals were also contacted to recruit diabetes educators. Diabetes patients were identified through random sampling from telephone directories. All potential participants were contacted via telephone to explain the study and screen for eligibility. The study adhered to principles of the Tri-Council Policy Statement (TCPS): Ethical Conduct for Research Involving Humans.[20] Participation was strictly voluntary, and all participants provided written informed consent. An honorarium was offered to all participants.

The interviews were semi-structured through the use of predetermined moderator guides. Information elicited from HCPs included feedback on the merits of different oral agents and insulin, factors considered when recommending second-line therapy and resources accessed for information. In addition, prescribers (family physicians, nurse practitioners and endocrinologists) were asked about their current practice patterns in prescribing second-line therapy. Patients were asked about current antihyperglycemic therapy, perceptions about second-line therapy options, resources accessed when seeking information on diabetes and ease of access to diabetes medications.

All focus group sessions were led by the same moderator (BG) and lasted approximately 90 minutes. Interviews lasted about 40 minutes and were conducted by BG and 1 additional interviewer. All focus group sessions and phone interviews were audio-recorded and transcribed with prior participant consent. Confidentiality was maintained for all original recordings and transcripts.

In analyzing the data, we focused on both the variety and frequency of responses, identifying where participant responses converged and diverged. In addition, thematic analysis was used to identify common themes within and between groups.

Findings

A total of 74 individuals participated in this study (Table 1). Supplementary materials for this article are available at www.cpjournal.ca.

Prescribers

Prescribers unanimously identified metformin as first-line therapy for most patients with type 2 diabetes, unless there were contraindications or very elevated HbA1c levels (e.g., >10%), which were thought to require either 2 oral agents or insulin. Metformin's effectiveness, modest side effect profile, neutral effects on weight or even modest weight-loss and low cost were seen as benefits.

Inability to achieve HbA1c targets despite maximal or near-maximal doses of metformin was cited by most prescribers as a trigger to progress to second-line therapy. There was unanimous preference for adding an agent to metformin rather than switching to another therapy, unless metformin was not well tolerated. However, there was variation in the timing (from "a couple of weeks" to 6 months) for instituting second-line therapy. Prescribers also considered adverse effects (especially gastrointestinal) and the presence of comorbid conditions (i.e., cardiovascular disease, hypertension) when considering whether and when to move to a second-line agent. Patient financial resources, drug insurance and cognitive ability were also considered by some prescribers.

Prescribers described a multifaceted process for selecting a second-line agent. The primary consideration was overall efficacy in achieving glycemic control. A related concern was durability of effect, particularly the perception that sulfonylurea efficacy may be less durable than that of other drug classes. Acute adverse effects such as hypoglycemia (with sulfonylureas or insulin) and weight gain (with sulfonylureas, TZDs or insulin) were also important considerations. In terms of long-term risks, many prescribers expressed concerns about the impact on the pancreas from chronic stimulation of insulin secretion by sulfonylureas and a corresponding preference for agents thought to increase insulin sensitivity (e.g., TZDs). Others were concerned about the risks of cardiovascular disease and reduced bone mineral density associated with TZDs, although this concern was not shared by all participants. Concern about unknown long-term adverse effects was also cited as a rationale for exercising caution with newer agents, such as the DPP-4 inhibitors.

Many prescribers considered drug coverage status and affordability in selecting therapies. Newer classes of second-line agents, such as TZDs and DPP-4 inhibitors, were thought to be more expensive and less likely to be covered by public drug plans. Finally, some prescribers pointed to convenience, patient preference and patients' ability to manage complex regimens as important factors; once-daily insulin, meglitinides or combination products were cited as favourable in this regard.

Insulin was rarely chosen as a second-line agent by respondents, except when HbA1c levels remained significantly elevated (i.e., >8%)

MISE EN PRATIQUE DES CONNAISSANCES

- Il existe de nombreux traitements pour les personnes atteintes de diabète de type 2 pour qui la metformine ne permet pas d'atteindre un contrôle glycémique adéquat.
- On observe une grande variabilité dans la manière de choisir le traitement des patients qui ont besoin d'un médicament de deuxième ligne après la metformine.
- En collaborant avec les autres professionnels de la santé et les patients, les pharmaciens peuvent promouvoir l'utilisation des meilleures données probantes disponibles pour appuyer les décisions thérapeutiques en lien avec le diabète de type 2. Cette collaboration pourrait avoir des répercussions favorables sur la santé des patients et les aider à tirer le meilleur parti des ressources limitées du secteur de la santé.

TABLE 1 Study participation by group, location and type of interaction

City	Pharmacists	Family physicians	Diabetes educators*	Patients	Diabetes specialists	Nurse practitioners	Total
Focus groups					**Phone interviews**		
Ottawa/ Ontario	7	7	7	7	6	4	**38** 15 men 23 women
Halifax/ Atlantic Canada	7	8	8	7	2	4	**36** 14 men 22 women
TOTAL	**14**	**15**	**15**	**14**	**8**	**8**	**74**

* Diabetes educators were self-identified and were not required to be certified. None of the diabetes educators identified themselves as pharmacists.

despite the use of oral therapies. If insulin was used, there was a preference for nighttime basal insulin due to convenience and higher likelihood of adherence.

Table 2 summarizes the most common perceived advantages and disadvantages of each class of second-line agent.

Some prescribers indicated a lack of information on specific drugs, particularly newer agents, as a possible barrier to their use. Generally, the most important gaps were felt to be the lack of data on comparative efficacy on important outcomes, such as cardiovascular end points, and on efficacy and safety of combination therapy.

Prescribers listed several different sources for information on diabetes therapies. Physicians identified a preference for live continuing medical education (CME) sessions, while nurse practitioners almost unanimously preferred web-based information. Respondents cited pharmaceutical companies as another potential resource, although the potential for bias was acknowledged.

Pharmacists and diabetes educators

Perceptions of pharmacists and DEs regarding antidiabetic agents are presented in Table 3. These groups expressed many of the same opinions as prescribers. One interesting difference, particularly among DEs, was the greater emphasis on the possible detriment to the pancreas from drugs that chronically stimulate insulin secretion (so-called pancreatic overstimulation). Consequently, earlier initiation of insulin was viewed more positively by DEs.

Drug costs and lack of drug insurance were described as significant barriers to the choice of second-line therapies by nearly all pharmacists and DEs participating in this study. Short-term adverse effects, such as risk of hypoglycemia or weight gain, were also considered important factors. Similar to prescribers, long-term risks of therapy were a concern. Pharmacists and diabetes educators further believed that adherence and convenience were important considerations when recommending a second-line agent.

A number of positive views were expressed regarding insulin therapy. Most pharmacists and DEs agreed that when initiating insulin, a single evening dose of basal insulin was the most desirable choice. Pharmacists mentioned that patients often find that insulin administration is not as difficult or painful as originally feared. Several DEs also felt that insulin empowers patients and encourages them to "take control" of their condition. They suggested that physicians should refrain from framing insulin as a "last resort" or using the "threat" of insulin as a negative motivator to increase adherence to lifestyle interventions or oral antihyperglycemic treatments. Some perceived limitations of insulin included the cost of needles, the need for continual dose adjustments and risk of hypoglycemia.

Unlike DEs who felt that there were barriers in accessing some second-line agents, pharmacists believed that most patients could access appropriate therapies. Pharmacists and DEs agreed that psychological barriers—both a patient's willingness to adhere to a medication and a physician's comfort level in prescribing it—can prevent patients from accessing appropriate second-line therapies. Lack of education on the part of patients or their physicians about the range of options available was also identified as a possible barrier.

Similar to prescribers, pharmacists and DEs identified the lack of long-term safety data for newer agents as a significant knowledge gap. Several different resources for information were suggested by pharmacists and educators as being reliable; these included workshops, Canadian Diabetes Association (CDA) clinical practice guidelines, professional and scientific publications and professional websites. DEs also pointed to endocrinologists as influential sources of information.

Patients

Patients with diabetes described a range of personal experiences with oral agents and insulin. Nearly all began treatment with metformin, followed by the addition of another agent for improved blood glycemic control.

Patients experienced a range of sentiments when prescribed a second-line agent. Some expressed disappointment and anxiety, perceiving the need to add another agent as a personal failure. Other patients expressed confidence in their prescriber and were more accepting of the need for augmented therapy. About one-third of patients expressed concerns about the possible side effects of the second agent, particularly hypoglycemia and weight gain. There was little to no discussion about differences in efficacy between drug

TABLE 2 Advantages and disadvantages of second-line antihyperglycemic agents commonly cited by prescribers, by drug class*

Class	Perceived advantages	Perceived disadvantages
Sulfonylureas	• Efficacious (% drop in A1c) • Work faster to lower A1c • Well-known side effect profile • Low cost	• Weight gain • Effects not as durable as other agents • Risk of hypoglycemia—may be especially problematic for geriatric patients • Risk of pancreatic overstimulation that may speed the decline of insulin secretory capacity
Thiazolidinediones	• Efficacy • No risk of hypoglycemia • Lack of pancreatic overstimulation • Work well with other drugs • Work well in combination with sulfonylureas	• Slower reduction in A1c • Risk of heart failure • Patient fear, preference and lack of adherence due to negative media coverage • Lack of coverage by publicly funded drug plans • Weight gain • Fluid retention • Risk of fracture • Contraindicated in patients with congestive heart failure • High cost
Incretin agents	• Less risk of hypoglycemia • Less risk of pancreatic overstimulation; preserve pancreatic function • Complement metformin and thiazolidinediones well • Help patients maintain or lose weight through increased postprandial satiety • Popular with patients based on what they hear from friends, family and media • Good at controlling postmeal blood glucose	• Limited effect on A1c • Relatively new—lack of data on long-term risks • High cost • Not covered by publicly funded drug plans • Gastrointestinal side effects
Meglitinides	• Convenience and patient adherence • Act quickly so can be taken with meals	• Not as efficacious as other agents • Not covered by publicly funded drug plans
α-Glucosidase inhibitors	• Good in early diabetes • Weight neutral or may cause some weight loss	• Less than 1% drop in A1c • Gastrointestinal side effects
Insulins	• Efficacious (more than 2% drop in A1c)—recommended when A1c is very high (i.e., above 9%). • No "highest dosage" • Once-a-day dosing of basal insulins improves patient adherence • A "natural" way to control blood glucose • Many insulins covered by insurance plans • Effective when oral agents are not	• Patient fear (especially of needles) and sense of failure—insulin as "the last resort" • Weight gain • Some prescribers feel the need for a specialist consult to initiate insulin • Newer insulins not covered • Multiple doses of insulin require a "sophisticated" patient • Require self-monitoring of blood glucose • Risk of hypoglycemia

* Prescribers included family physicians, nurse practitioners and endocrinologists.

TABLE 3 Advantages and disadvantages of second-line antihyperglycemic agents commonly cited by diabetes educators and pharmacists, by drug class

Class	Perceived advantages	Perceived disadvantages
Sulfonylureas	• Low cost • Newer versions (e.g., modified-release gliclazide) are released more slowly and can lessen the risk of hypoglycemia • Once-daily dosage for some agents • Well-known adverse effect profile • Long-term safety is backed by ample research	• Pancreatic overstimulation and possibility of more rapid reduction in insulin secretory ability • Risk of hypoglycemia • Not recommended for elderly patients or those with congestive heart failure
Thiazolidinediones	• Efficacy • More user-friendly in terms of timing and other requirements • Reduce dosage of insulin required	• Long-term risk of adverse effects such as heart failure • Edema • Expensive
Incretin agents	• No risk of hypoglycemia • Convenience—once-daily dosage • Less risk of weight gain	• Expensive • No data on long-term health risks • Many physicians not yet familiar with or comfortable with this class
Meglitinides	• Convenience—take with the meal	• Not covered by public drug plans
α-Glucosidase inhibitors	• None cited	• Gastrointestinal side effects
Insulins	• Patients feel "in control" as they can adjust dosage and timing • Give the pancreas a break—help to preserve it • No need to take multiple oral agents • No risk of gastrointestinal side effects • No risk of kidney or liver side effects • Maximum effect on lowering A1c levels	• Patient fear of needles • Perception that insulin is the "treatment of last resort" • Cost of needles • Need to continually increase dosage • Complexity of calculating dosages • Fear reduces adherence • Doses continually need to be increased due to progressive insulin resistance

classes, including long-term efficacy against diabetes-related complications.

Patients differed widely on the extent to which they felt informed about the risks and benefits of second-line agents. Some clearly wanted more information. Others lamented not receiving enough time and attention from their family physician to learn about prescribed medications and to have questions answered.

The group was evenly split in their perceptions of whether they were receiving the medication they needed. Those who felt they were not pointed to barriers such as a lack of knowledge regarding options and insufficient financial resources.

The group was also split on preferred resources for information, with some citing the websites of well-known organizations such as the CDA, while others cited health professionals, notably pharmacists and physicians.

Discussion

Suboptimal therapeutic choices for patients with type 2 diabetes have important implications for patient well-being, population health and health care costs. A total of $563 million was spent on antihyperglycemic drugs in Canada in 2007,[21] and average per prescription costs nearly doubled between 1998 and 2007.[22] The increase in costs is at least partly attributable to the

prescribing of newer, more costly agents. While the numerous drug classes available to treat type 2 diabetes may facilitate individualization of therapy, they can also contribute to uncertainty and undue variability in prescribing decisions. To our knowledge, ours is the first study to assess perceptions, attitudes and beliefs of health care providers and patients in Canada related to therapies for type 2 diabetes.

Overall, we found similar views across health professional groups in a number of areas, but there were also some interesting differences. All professional groups agreed that overall efficacy in reducing blood glucose levels is paramount in selecting a second-line therapy. Interestingly, few participants discussed efficacy in terms of clinically meaningful outcomes such as reduced risk of diabetes complications or mortality. Efficacy in terms of glycemic control was closely followed in importance by cost and insurance coverage; risk of hypoglycemia, weight gain and other short-term adverse effects; the potential for long-term adverse effects; and the impact of therapy on quality of life.

Reports regarding the potential cardiovascular risks of rosiglitazone were available at the time of our study.[23,24] However, some providers (mostly physicians) questioned the validity of the evidence, continuing to selectively prescribe this agent and the TZDs more generally for their other perceived advantages such as their effects on insulin sensitivity and a lower risk of hypoglycemia. Of course, it is likely that current views regarding TZDs differ substantially from those in 2009, given the more stringent restrictions placed by regulators on the prescribing of rosiglitazone based on the available data regarding cardiovascular safety,[25,26] as well as the emerging evidence of an increased risk of bladder cancer associated with pioglitazone.[27,28]

DEs and, to a lesser extent, other health care professionals tended to express concerns about "pancreatic overstimulation" from the use of insulin secretagogues such as sulfonylureas, as well as the perception that the antihyperglycemic effect of these agents was not as durable as other drug classes. These concepts are not well supported by the available evidence, and the basis of this perception was not clear from the focus group discussions. It is possible that results from ADOPT (A Diabetes Outcome Progression Trial), which showed somewhat more durable antihyperglycemic effects with a TZD compared with a sulfonylurea, or discussion in the literature regarding the possible benefits of non-secretagogue agents on pancreatic islet cell function, underlie some of these beliefs.[29-31] Promotional materials from the pharmaceutical industry may also be a contributing factor.

Most participants considered hypoglycemia and weight gain as important barriers to using sulfonylureas. We were unable to assess the perceived frequency and severity of these adverse effects; however, it is possible that the risk and magnitude of these effects are overestimated. In a systematic review of second-line therapies, the average weight gain with sulfonylureas used as second-line therapy was approximately 2 kg or a 2.5% change from baseline for a patient weighing 80 kg.[32] Similarly, the annual absolute risk of severe hypoglycemia (requiring assistance of another person) when sulfonylureas are used as second-line therapy was estimated at only 1 in 175.[33]

Despite the relative consistency within and across provider groups with respect to the major factors underlying therapeutic decision making in type 2 diabetes, our results reveal considerable variability in the relative weight assigned to each factor, as well as in perceived risks and benefits of each class of therapy. This was the case both between and within provider groups. Hence, our results reveal that a consistently applied prescribing model for the treatment of type 2 diabetes is lacking. Perhaps this is not surprising, given the finding that sources of information varied widely across and within professional groups. The CDA clinical practice guidelines were commonly described as an important source of information on antihyperglycemic treatments. However, these guidelines may themselves contribute to variability in decision making since they recommend individualized therapy based on the properties of each drug class, without consideration of cost-effectiveness. In contrast, the Canadian Agency for Drugs and Technologies in Health (CADTH) has issued recommendations regarding optimal sequential therapy for patients with type 2 diabetes based on a systematic review and meta-analysis of the available evidence and cost-effectiveness analyses.[34-36] The recommendations indicate that a sulfonylurea is the optimal choice for second-line therapy for most patients with inadequate glycemic control on metformin and

that insulin neutral protamine Hagedorn is the optimal third-line therapy for most patients with inadequate glycemic control on metformin and a sulfonylurea.[36]

The apparent absence of a consistent prescribing model for selecting treatments for patients with type 2 diabetes presents an opportunity for pharmacists to participate more actively in therapeutic decision making in collaboration with other health care providers and patients with type 2 diabetes. The pharmaceutical care model[37] provides a rational and explicit process to identify therapeutic goals in collaboration with the patient and other health care providers, select and monitor drug therapy and identify drug-related problems. Application of the pharmaceutical care model to the treatment of type 2 diabetes, in combination with the best available evidence, may result in more consistency in prescribing decisions, improved health outcomes and more efficient use of limited health care resources.

Analysis of patient responses also revealed important insights. Patients described the disappointment and sense of failure they feel following the addition of second-line agents. Hypoglycemia and weight gain were cited most frequently as important concerns when choosing antihyperglycemic therapy, even greater than glucose-lowering efficacy. Patients also described the importance of having a provider who can take the time to listen and answer questions. Those without such a provider expressed frustration and anxiety over the choice of the medications prescribed to them. These findings demonstrate the importance of appropriate education and shared decision making as changes to diabetes treatment are made. The fears and misconceptions associated with insulin require particular focus. Pharmacists are in an excellent position to educate patients about diabetes and its available treatments and, above all, to provide reassurance when therapy needs to be augmented.

A strength of this study was that saturation was achieved on the key questions of interest. Furthermore, our findings on HCP and patient perceptions related to the available drugs for type 2 diabetes generally aligned with previous studies, although none of these specifically assessed decision making for second-line therapy.[8-17] In terms of limitations, findings from 2 provinces may not be entirely generalizable to other jurisdictions in Canada due to differences in formulary coverage or practice patterns. Furthermore, it is possible that participants may have tended to describe ideal, rather than actual, perceptions and behaviours.

This study was performed in 2009, and the therapeutic landscape for type 2 diabetes has changed considerably since then. In particular, prescribing restrictions have been placed on rosiglitazone, and the TZD class has generally fallen out of favour. Focus has shifted instead to DPP-4 inhibitors and GLP-1 analogues, a number of which have been introduced to the Canadian market since the study was completed. While we were able to capture some early perceptions regarding these agents, it is likely that a similar study conducted today would yield considerably more experiences and insights regarding these drug classes. Nevertheless, we believe that many of the findings of this study are still pertinent to current clinical practice, particularly the key factors underlying the therapeutic decisions made by HCPs and patients.

Conclusion

Most HCPs assessed antihyperglycemic efficacy, safety, cost, patient acceptance and drug insurance coverage when choosing second-line therapy for patients with type 2 diabetes. However, the relative emphasis placed on these considerations varied widely, as did perceptions surrounding the various drug classes and preferred sources of information on diabetes therapies. In contrast to HCPs, patients were most concerned about weight gain and hypoglycemia. The need for therapy intensification was often perceived by patients as a personal failure. In general, patients wished to be engaged in therapeutic decisions and were frustrated when this did not occur.

Our findings point to the need for a rational prescribing model for type 2 diabetes, one that supports therapeutic decision making based on evidence. In partnership with patients and other health care providers, pharmacists are in an excellent position to promote optimal treatment decisions in the management of type 2 diabetes and to ensure that patients are engaged in these decisions. ■

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References

1. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2013;37(Suppl 1):S1-S212. Available: http://guidelines.diabetes.ca/App_Themes/CDACPG/resources/cpg_2013_full_en.pdf (accessed July 30, 2013).

2. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia* 2012;55:1577-96.

3. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998;352(9131):854-65.

4. Turner RC, Cull CA, Frighi V, Holman RR, UK Prospective Diabetes Study (UKPDS) Group. Glycemic control with diet, sulfonylurea, metformin or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). *JAMA* 1999;281:2005-12.

5. National Collaborating Centre for Chronic Conditions. *Type 2 diabetes: national clinical guideline for management in primary and secondary care (update)*. London (UK): Royal College of Physicians; 2008. Available: www.nice.org.uk/nicemedia/pdf/CG66diabetesfullguideline.pdf (accessed July 30, 2013).

6. Canadian Agency for Drugs and Technologies in Health. *Current utilization of second- and third-line therapies in patients with type 2 diabetes*. Ottawa (ON): The Agency; 2010. (Optimal therapy report; vol. 4 no. 3.) Available: www.cadth.ca/media/pdf/C1110-CU-Report-2nd-3rd-Line-Agents-final-e.pdf (accessed July 30, 2013).

7. Agarwal G, Nair K, Cosby J, et al. GPs' approach to insulin prescribing in older patients: a qualitative study. *Br J Gen Pract* 2008;58:569-75.

8. Hayes RP, Bowman L, Monahan PO, et al. Understanding diabetes medications from the perspective of patients with type 2 diabetes: prerequisite to medication concordance. *Diabetes Educ* 2006;32:404-14.

9. Nair KM, Levine MAH, Lohfeld LH, Gerstein HC. "I take what I think works for me": a qualitative study to explore patient perception of diabetes treatment benefits and risks. *Can J Clin Pharmacol* 2007;14(2):e251-9.

10. Hayes RP, Fitzgerald JT, Jacober SJ. Primary care physician beliefs about insulin initiation in patients with type 2 diabetes. *Int J Clin Pract* 2008;62(6):860-8.

11. Larkin ME, Capasso VA, Chen CL, et al. Measuring psychological insulin resistance: barriers to insulin use. *Diabetes Educ* 2008;34(3):511-7.

12. Lawton J, Peel E, Parry O, Douglas M. Patients' perceptions and experiences of taking oral glucose-lowering agents: a longitudinal qualitative study. *Diabetes Med* 2008;25(4):491-5.

13. Cefalu WT, Mathieu C, Davidson J, et al. Patients' perceptions of subcutaneous insulin in the OPTIMIZE study: a multicenter follow-up study. *Diabetes Technol Ther* 2008;10:25-38.

14. Tjia J, Givens JL, Karlawish JH, Okoli-Umeweni A, Barg FK. Beneath the surface: discovering the unvoiced concerns of older adults with type 2 diabetes mellitus. *Health Educ Res* 2008;23(1):40-52.

15. Jeavons D, Hungin AP, Cornford CS. Patients with poorly controlled diabetes in primary care: healthcare clinicians' beliefs and attitudes. *Postgrad Med J* 2006;82(967):347-50. Available: www.pubmedcentral.nih.gov/picrender.fcgi?artid=2563795&blobtype=pdf (accessed Nov. 8, 2012).

16. Lai WA, Lew-Ting CY, Chie WC. How diabetic patients think about and manage their illness in Taiwan. *Diabetes Med* 2005;22(3):286-92.

17. Bonneville M, Colgin J, Nalesnick JA, Perez J, Wentz L. Patient perceptions of prandial oral therapy for type 2 diabetes. *Diabetes Educ* 2001;27:669-77.

18. Huang ES, Brown SE, Thakur N, et al. Racial/ethnic differences in concerns about current and future medications among patients with type 2 diabetes. *Diabetes Care* 2009;32:311-6.

19. Canadian Agency for Drugs and Technologies in Health. *Current practice analysis of health care providers and patients: second-line therapy for patients with type 2 diabetes inadequately controlled on metformin*. Ottawa (ON):

The Agency; 2010 Mar. (Optimal therapy report; vol. 4 no. 4.) Available: www.cadth.ca/media/compus/pdf/C1110_Current_Practice_Report_final.pdf. Accessed July 15, 2013.

20. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. *Tri-Council policy statement: ethical conduct for research involving humans,* 1998 (with 2000, 2002, 2005 amendments). Ottawa (ON): Interagency Secretariat on Research Ethics; 2005. Available: www.pre.ethics.gc.ca/eng/archives/tcps-eptc/Default/ (accessed Nov. 8, 2012).

21. Morgan S, Raymond C, Mooney D, Martin D. *The Canadian Rx atlas*. 2nd ed. Vancouver (BC): UBC Centre for Health Services and Policy Research; 2008. Available: www.chspr.ubc.ca/pubs/atlas/canadian-rx-atlas-2nd-edition (accessed Nov. 8, 2012).

22. *Utilization of oral antiglycemics in Canada.* Ottawa (ON): Brogan, Inc.; 2008.

23. Psaty BM, Furberg CD. The record on rosiglitazone and the risk of myocardial infarction. *N Engl J Med* 2007;357(1):67-9. Available: www.nejm.org/doi/full/10.1056/NEJMe078116 (accessed Nov. 5, 2012).

24. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *N Engl J Med* 2007;356(24):2457-71.

25. Woodcock J, US Food and Drug Administration, Center for Drug Evaluation and Research. Letter to: NDA 021071. *Decision on continued marketing of rosiglitazone (Avandia, Avandamet, Avandaryl)*. Silver Spring (MD): FDA; 2010 Sep. 22. Available: www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM226959.pdf (accessed Nov. 5, 2012).

26. *Avandia, Avandamet and Avandaryl—important new restrictions on the use of rosiglitazone products due to information on heart-related events*. Ottawa (ON): Health Canada, Marketed Health Products Directorate. 2010 Nov. 10. Available: www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2010/16117a-eng.php (accessed Nov. 5, 2012).

27. Colmers IN, Bowker SL, Majumdar SR, Johnson JA. Use of thiazolidinediones and the risk of bladder cancer among people with type 2 diabetes: a meta-analysis. *CMAJ* 2012;184(12):E675-83.

28. Extended use of thiazolidinediones associated with increased bladder cancer risk in cohort study. *ASCO Daily News*. 2012 Nov 18. Presented at ASCO Annual 2012 Meeting; 2012 Jun 1-5; Chicago. Abstract 1503. Available: http://chicago2012.asco.org/ASCODailyNews/Abstract1503.aspx (accessed May 15, 2013).

29. Kahn SE, Haffner SM, Heise MA, et al. Glycemic durability of rosiglitazone, metformin or glyburide monotherapy. *N Engl J Med* 2006;355(23):2427-43. Available: http://content.nejm.org/cgi/reprint/355/23/2427.pdf (accessed May 15, 2013).

30. Bell DS. Beta-cell rejuvenation with thiazolidinediones. *Am J Med* 2003;115(Suppl 8A):20S-3S.

31. Leiter LA. Can thiazolidinediones delay disease progression in type 2 diabetes? *Curr Med Res Opin* 2006;22:1193-201.

32. McIntosh B, Cameron C, Singh S, et al. Second-line therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed treatment comparisons meta-analysis. *Open Med* 2011;5(1). Available: www.openmedicine.ca/article/view/423/382 (accessed May 5, 2013).

33. Canadian Agency for Drugs and Technologies in Health. Type 2 diabetes—second- and third-line therapies. *CADTH Optimal Therapy Newsletter*. Ottawa (ON): The Agency; 2013. Available: www.cadth.ca/media/pdf/Type_2_Diabetes_2nd_and_3rd_Line_Therapies_Newsletter_e.pdf (accessed Aug. 20, 2013).

34. Canadian Agency for Drugs and Technologies in Health. Second-line pharmacotherapy for type 2 diabetes: update. *CADTH Optimal Use Report* 2013;3:iss. 1A. Available: www.cadth.ca/media/pdf/OP0512_DiabetesUpdate_Second-line_e.pdf (accessed July 30, 2013).

35. Canadian Agency for Drugs and Technologies in Health. Third-line pharmacotherapy for type 2 diabetes: update. *CADTH Optimal Use Report* 2013;3:iss. 1B. Available: www.cadth.ca/media/pdf/OP0512_Diabetes%20Update_Third-line_e.pdf (accessed July 30, 2013).

36. Canadian Agency for Drugs and Technologies in Health. Optimal use recommendations for second-line and third-line pharmacotherapy for patients with type 2 diabetes. *CADTH Optimal Use Report* 2013;3:iss. 1D. Available: www.cadth.ca/media/pdf/OP0512_Diabetes_RecsReport_2nd_3rd-line_e.pdf (accessed July 30, 2013).

37. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm* 1990;47:533-43.