Canadian Guidelines for the Management of Plaque Psoriasis: Overview

*Kim Papp, Wayne Gulliver, Charles Lynde, Yves Poulin, and John Ashkenas for the Canadian Psoriasis Guidelines Committee**

New clinical treatment guidelines for plaque psoriasis, written by a panel of 16 Canadian dermatologists, were recently published online. These *Canadian Guidelines for the Management of Plaque Psoriasis* are evidence based and free of any influence from corporate sponsors and have been endorsed by the Canadian Dermatology Association (CDA). The *Guidelines* offer treatment recommendations for mild and moderate to severe body psoriasis, as well as for psoriasis affecting specific areas of the skin, such as the facial, flexural, and genital areas; nails; scalp; and palms and soles. The present overview describes the genesis and contents of the *Guidelines*, which are available in full through the CDA at <http://www.dermatology.ca/guidelines/cdnpsoriasisguidelines.pdf> (English) or <http://www.dermatology.ca/french/psoriasisguidelines.html> (French).

De nouvelles lignes directrices sur le traitement clinique du psoriasis en plaques, rédigées par un groupe de 16 dermatologues du Canada, ont été récemment publiées en ligne. Ces *Lignes directrices canadiennes pour la prise en charge du psoriasis en plaques* sont fondées sur des données probantes et à l'abri de toute influence des sociétés commanditaires; en outre, elles ont été endossées par l'Association canadienne de dermatologie (ACD). Les *Lignes directrices* offrent des recommandations en matière de traitement des formes légères, modérées à graves de psoriasis du corps, ainsi que du psoriasis qui touche des régions particulières de la peau, comme la région faciale, les plis, et la partie génitale ; les ongles ; le cuir chevelu ; et les paumes ainsi que les plantes du pied. Le présent aperçu décrit la genèse et le contenu des *Lignes directrices*, que vous pouvez vous procurer dans leur intégralité auprès de l'Association canadienne de dermatologie à l'adresse <http://www.dermatology.ca/french/psoriasisguidelines.html> (français) et <http://www.dermatology.ca/guidelines/cdnpsoriasisguidelines.pdf> (anglais).

PLAQUE PSORIASIS is a chronic inflammatory skin disease that requires ongoing, lifelong care. Plaque psoriasis is distinguished by the presence of erythematous plaques, usually covered with silver, flaking scales. These plaques may be itchy or painful; depending on their extent and location, they may also be physically debilitating or socially isolating.

Plaque psoriasis imposes a burden of disease that extends far beyond the physical dermatologic symptoms. Psoriasis may lead to stigmatization, high levels of stress, and poor self-esteem,[1–6] with pervasive negative effects on social functioning, interpersonal relationships, and success at school or work.[7,8] Patients with more severe disease or with involvement of a more visible (e.g., face or scalp) or highly used (e.g., hands) area of the body may suffer disproportionately from these problems.[9] Unfortunately, physicians frequently underestimate the degree of psychological and social impact of this disease.[1,10,11]

Psoriasis patients are also at risk for a wide variety of serious clinical comorbidities that add to their burden, complicate management, and increase the risk of premature death. Metabolic syndrome and related cardiovascular diseases are more common in psoriasis patients. Psoriasis per se is a risk factor for cardiovascular disease, conferring an approximately threefold increased relative risk of myocardial infarction in

From K. Papp Clinical Research, Waterloo, ON; Probity Medical Research, Waterloo, ON; Newlab Clinical Research Inc., St. John's, NL; Memorial University, St John's, NL; Lynderm Research Inc., Markham, ON; University of Toronto, Toronto, ON; Centre Dermatologique du Québec, Métropolitain, Québec, QC; Université Laval, Québec, QC; and SCRIPT, Toronto, ON.

**Members of the Psoriasis Guidelines Committee (in alphabetical order): Stewart P. Adams, Lorne Albrecht, Benjamin Barankin, Kirk Barber, Marc Bourcier, Wayne Carey, Lyn C. Guenther, Wayne Gulliver, Vincent C. Ho, Charles W. Lynde, Kim Alexander Papp, Yves Poulin, Neil H. Shear, John Toole, Ronald Vender, and Norman Wasel.*

Address reprint requests to: Kim Papp, MD, PhD, FRCPC, 135 Union St. E, Waterloo, ON N2J 1C4; E-mail: kapapp@probitymedical.com.

DOI 10.2310/7750.2011.10066

younger psoriasis patients.[12] Severe psoriasis is also associated with an increased risk of mortality, leading to a 3.5- and 4.4-year reduction in life expectancy for males and females, respectively, relative to individuals without psoriasis.[13]

Unbiased clinical treatment guidelines for psoriasis have been lacking in Canada. We therefore undertook to develop clinically relevant, patient-focused, evidence-based guidelines with recommendation for the management of plaque psoriasis. The resulting document is available online at <http://www.dermatology.ca/psoriasisguidelines>.[14]

Here we offer an overview of the development and the findings of the *Canadian Guidelines for the Management of Plaque Psoriasis*. We emphasize the treatment options discussed in the chapter on moderate to severe body psoriasis. The reader is referred directly to the *Guidelines*[14] for evidence-based management recommendations on other aspects of psoriasis care. These can be found in chapters on mild body psoriasis; facial, flexural, and genital psoriasis; nail psoriasis; scalp psoriasis; palmoplantar psoriasis; psoriatic flares; psoriasis treatment in special populations and circumstances (including pediatric and elderly patients, pregnant and lactating women, and individuals with hepatitis, human immunodeficiency virus [HIV], or a history of cancer); psoriasis comorbidities; and social and psychological aspects of psoriasis.

Methods

The *Guidelines* development process endeavored to meet the standards of the international AGREE (Appraisal of Guidelines for Research & Evaluation) Instrument[15] and the Canadian Medical Association's *Handbook on Clinical Practice Guidelines*.[16]

Guidelines Committee Structure

The Guidelines Committee was subdivided into four groups: the Steering Committee, the Section Heads, the Evidence Committee, and the Recommendations Committee.

The Steering Committee set the parameters for the *Guidelines* and monitored the progress of the manuscript. The Section Heads worked with a team of professional medical writers to produce the first draft of the manuscript. The Evidence Committee ratified the assigned level of evidence for each recommendation, and the Recommendations Committee did the same for the assigned grade of each recommendation.

Evaluation of Evidence

Section Heads identified key terms that were used to search *PubMed* and *EMBASE* for papers on psoriasis and antipsoriatic therapies, published in 1980 or later. All peer-reviewed literature was considered. In all, 5,439 peer-reviewed research articles were judged to be relevant to Canadian practice.

A modified version of the Scottish Intercollegiate Guidelines Network (SIGN) system[17] was used to assign levels of evidence and grade the treatment recommendations (Table 1). SIGN assigns levels of evidence according to the type and quality of the study. A grade of recommendation (A, B, C, D) was then applied according to the level of evidence, with ''considered judgment'' allowing some flexibility in converting level of evidence (LoE) into a recommendation grade.

Roles of Industry Sponsors and Community Reviewers

After a complete draft of the *Guidelines* had been revised to the satisfaction of Committee members and all treatment recommendations were approved, the document was circulated to 17 Canadian or international authorities on psoriasis care or family practice. These community reviewers' comments were incorporated to produce a final draft.

Ten Canadian pharmaceutical companies supported the development of the *Guidelines* through unrestricted grants. The sponsors were encouraged to submit unpublished manuscripts for the Committee's consideration during the drafting of the document; for the corresponding information to remain in the final document, these manuscripts had to be accepted for publication by February 15, 2008.

Sponsors received regular progress reports but were not informed of the identity of Guidelines Committee members. Sponsors were not party to discussions of the *Guidelines*' content and did not see the manuscript until the final draft was completed.

Findings

Prevalence of Plaque Psoriaisis

Large-scale population studies in the United Kingdom[18] and the United States[1] found that 1.5% and 2.6% of individuals, respectively, had been diagnosed with psoriasis. As shown in Table 2, application of age-specific psoriasis prevalence rates from the United Kingdom to the Canadian population suggests that more than 500,000 Canadians (approximately 1.7% of the population) have

Table 1. Modified SIGN System Used by the Evidence and Recommendations Committees

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 of RCTs, or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2–	Case-control or cohort studies with a high risk of confounding, bias, or chance 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 one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population or A systematic review of RCTs 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 1−, 2−, or 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+

RCT = randomized, controlled trial; SIGN = Scottish Intercollegiate Guidelines Network.

psoriasis. This affected population includes approximately 40,000 older individuals (≥ 70 years) and 20,000 children (≤ 10 years). Given the prevalence of plaque psoriasis, all physicians are likely to confront this burdensome chronic disease in the course of routine care.

Patient-Centered Psoriasis Care

According to the guiding principle of patient-centered care, as developed in the *Guidelines*, treatment adequacy should be judged on the basis of the patient's perception of the disease and its burdens.

Table 2. Estimated Prevalence of Psoriasis in Canada

Age Group (yr)	*Canadian Population**	*Estimated Psoriasis Prevalence by Age Group (per 10,000)†*	*Estimated Number of Canadians with Psoriasis by Age Group*
0–9	3,499,915	55.02	19,257
10–19	4,220,415	137.37	57,976
20–29	4,065,965	151.04	61,412
30–39	4,228,500	178.01	75,272
40–49	5,231,055	203.43	106,415
50–59	4,441,920	222.78	98,957
60–69	2,824,445	225.95	63,818
70–79	1,933,360	161.39	31,202
80–89	989,390	88.44	8750
Over 90	177,925	47.33	842
Total	31,612,895		523,902

*Data from Canadian 2006 census.[32]
†Based on published age-specific prevalence rates in the United Kingdom.[18]

Physicians caring for patients with plaque psoriasis face two tasks. First, they must identify therapies that are effective, safe, and suited to the symptoms that the patient presents. Second, and no less important, they must choose from among the appropriate options the one that the patient is most likely to use consistently, over the long term, to achieve and maintain control of his or her condition. In the *Guidelines*, we therefore emphasize the broad range of therapeutic options that the physician should consider, deferring as much as possible to the patient's preferences and priorities.

Our emphasis on treatment acceptability reflects evidence that treatment adherence is often inadequate in the chronic management of psoriasis.[19–21] Nonadherence[22] can create a vicious cycle, leading to poor outcomes. The patient, disappointed or frustrated because the therapy is not working as well as expected, stops following it or does not use it appropriately, further lowering the chances of treatment success. Poor adherence is commonplace, even in patients who characterize their own disease, and its impact on their lives, as severe.[23]

The *Guidelines* therefore distinguish between therapies that work (i.e., treatment options that are supported by strong clinical evidence) and therapies that the patient will work with (i.e., those that an individual patient will continue to adhere to over the long term). In treating mild body psoriasis, for example, three topical options receive Grade A recommendations for first-line use: corticosteroids, calcipotriol, and calcipotriol–betamethasone dipropionate combination therapy (LoE 1++ for all).[24–26] However, the *Guidelines* also note that other agents are superior to placebo in managing mild psoriasis and suggest (LoE 4, Grade D) that individual treatment considerations could supersede these recommendations. The *Guidelines* further recommend (LoE 4, Grade D) that physicians consider the vehicle used in topical agents and select formulations that will be acceptable to the patient.

Locus of Psoriasis Care

The *Guidelines* recommend (LoE 4, Grade D) that patients with mild, uncomplicated plaque psoriasis who respond to first- or second-line therapy be managed by their primary care providers. Conditions for dermatologic referral are given in Table 3.

Goals and Options for Managing Moderate to Severe Plaque Psoriasis

In the *Guidelines*, moderate to severe psoriasis is distinguished from milder disease in that it is, or would be expected to be, refractory to topical monotherapy (Table 4).

Table 3. Specialist versus Primary Care of Plaque Psoriasis

Dermatologic referral may be indicated:
• For patients with more severe disease, as judged by the extent of the disease or the distress it causes the patient
• For those requiring in-depth counseling or education outside the scope of primary care practice
• To assess an uncertain diagnosis
• To assess or help establish an appropriate therapeutic regimen
• On request from a patient
• For patients failing to respond to therapy or becoming unresponsive to a previously successful treatment
• For patients with involvement of the face, scalp, hands/feet, or intertriginous areas
• For patients with complicated psoriasis (pustular, guttate, erythrodermic) or concomitant psoriatic arthritis

For some patients with moderate to severe psoriasis, amelioration (i.e., short-term improvement and limited long-term disease control[27]) may be an adequate treatment goal. Indeed, many therapeutic tools are available that can be used as monotherapy to achieve some degree of control. However, the literature also shows that clearance represents an achievable and appropriate goal in treating many patients.

Although many antipsoriatic therapies are ameliorative, fewer of them can be used to achieve complete or nearly complete clearance of symptoms. This more ambitious clinical goal is also more difficult to document because only rarely (and only in the most recent publications) are 90 or 100% reduction in Psoriasis Area and Severity score (PASI-90/100) included as clinical end points.

Table 5 identifies therapeutic options that may be considered for management of moderate to severe

Table 4. Criteria for Assessing Severity of Plaque Psoriasis

Term	*Definition Applied in the* Guidelines
Mild plaque psoriasis	Disease with a minimal impact on the patient's quality of life (QoL); patient can achieve acceptable symptomatic control by standard topical therapy
Moderate plaque psoriasis	Disease that cannot be, or would not be expected to be, controlled to an acceptable degree by standard topical therapy, and/or Disease that significantly affects the patient's QoL
Severe plaque psoriasis	Disease that cannot be, or would not be expected to be, satisfactorily controlled by topical therapy and that causes severe degradation of the patient's QoL

Table 5. Dermatologist's Toolkit for Managing Moderate to Severe Plaque Psoriasis

*Treatment Option**	*Considerations*	*Evidence for Ameliorative Effect in Monotherapy†*	*Evidence for Disease Clearance/Near Clearance*		
			Within ≈3 mo of Therapy	*At ≈6 mo of Therapy*	*Beyond 1 yr of Therapy*
Topical agent					
Calcipotriol–betamethasone dipropionate combination ointment	Effective in moderate to severe psoriasis (including baseline PASI > 17), as well as in milder disease; should not be used on facial, flexural, and genital areas	LoE 1++[33]			
Oral systemic agents					
Acitretin	Retinoid drug; highly teratogenic and strictly contraindicated in pregnancy Not to be used in women of childbearing age unless they are able and willing to use contraception for 3 yr after discontinuing acitretin Rarely used as monotherapy but often combined with topical agents such as potent corticosteroids or with other therapeutics to allow for more rapid/complete control, with reduced exposure to the other therapeutic	LoE 1−[34,35]			
Cyclosporine	Immunosuppressive drug; leads to cumulative renal toxicity; can exacerbate hypertension and hypertriglyceridemia Can be highly effective in severe disease but best employed intermittently, rather than for continuous long-term use[36–38]	LoE 1++[39]			
Methotrexate	Immunomodulatory and antiproliferative drug, often chosen for long-term management Strictly contraindicated in pregnancy owing to teratogenic and abortifacient effects Use is also limited by risk of liver toxicity and the requirement for ongoing monitoring of liver function[40,41] Generally administered with folate supplement to reduce systemic toxicity[42]	LoE 1+[43,44]			

Table 5. Cont.

*Treatment Option**	*Considerations*	*Evidence for Ameliorative Effect in Monotherapy†*	*Evidence for Disease Clearance/Near Clearance*		
			Within ≈3 mo of Therapy	*At ≈6 mo of Therapy*	*Beyond 1 yr of Therapy*
Biologic agents‡					
Adalimumab	Targets TNF-α Safety profile, primarily based on record of use in rheumatoid and psoriatic arthritis, suggests some overlap in adverse events (e.g., reactivation of latent TB and melanoma) seen with other TNF-α antagonists[45] Approved for use in psoriatic arthritis as well as psoriasis Appears to be appropriate for long-term continuous use	LoE 1++[46,47]	Some patients may achieve 100% PASI reduction within 16 wk of treatment (LoE 1++[46])	Some additional patients achieve/ maintain 100% PASI reduction by 24 wk of treatment (LoE 2++[46])	
Etanercept (50 mg BIW, stepped down to 25 mg BIW)§	Targets TNF-α; may be associated with risk of infections, demyelinating disorders,[48] and reactivation of latent TB or melanoma[49] Approved for use in psoriatic arthritis, as well as psoriasis Appropriate for long-term continuous use	LoE 1++[50]	With the standard dosing regimen, some patients may achieve ≥ 90% PASI reduction within the initial 12 wk of treatment, prior to step-down (LoE 1++[50])	Some patients achieve/ maintain ≥ 90% PASI reduction by 24 wk of treatment (LoE 2++[51,52])	
Infliximab	Targets TNF-α Highly effective on initial exposure, even in severe, acute flares Variable efficacy following reinitiation or beyond the first year of continuous treatment[53,54] Associated with infusion reactions and risk of infections, demyelinating disorders,[48] and reactivation of latent TB or tumors[54] Approved for use in psoriatic arthritis as well as psoriasis	LoE 1++[55]	Patients may achieve a ≥ 90% PASI reduction within the initial 6–10 wk of treatment (LoE 1+[55])	Patients may maintain ≥ 90% PASI reduction through the initial 24 wk of treatment (LoE 1+[55])	Patients may achieve/ maintain ≥ 90% PASI reduction through at least 50 wk of treatment (LoE 2++[55,56])

Table 5. Cont.

*Treatment Option**	*Considerations*	*Evidence for Ameliorative Effect in Monotherapy*†	*Evidence for Disease Clearance/Near Clearance*		
			Within ≈3 mo of Therapy	*At ≈6 mo of Therapy*	*Beyond 1 yr of Therapy*
Alefacept	Targets pathogenic T cells Generally benign safety record, but monitoring is required to avoid depletion of CD4 T lymphocytes[57] Relative to the other biologics, alefacept monotherapy provides limited control of psoriasis, but with long periods of complete or incomplete remission in some cases Can be combined with other therapies for fuller and more durable control[58]	LoE 1++[59,60]			
Phototherapeutic methods					
UVA with psoralen (PUVA)‖	Psoralen may be administered orally or by immersion of affected areas in a psoralen solution, prior to UVA exposure (oral vs bath PUVA) Associated with cumulative risk of nonmelanoma skin cancer, primarily squamous cell carcinoma[61] May be combined with other agents in suitable patients to reduce UV exposure[62–64]	LoE¶ 2++[65–67]	Patients may achieve clearance within 4–15 wk (LoE 1+[66,68])	Remission following treatment cessation may be maintained for 6 mo in some patients (LoE 2++[66,68])	
UVB#	Broadband UVB has been used for decades; now often applied using narrowband (NB) irradiation at 311 nm, a more effective option Less durable remission than with PUVA[66,68] but believed to have a more benign safety profile May be combined with topical, systemic, or biologic agents for more rapid and more complete control, potentially reducing exposure to both UV light and other therapeutic agents	LoE¶ 2++[65–67]	Patients may achieve clearance within 4–15 wk with TIW treatment with NB-UVB (LoE 1+[67])	Remission following treatment cessation may be maintained for 6 mo in some patients with TIW NB-UVB treatment (LoE 2++[67])	Remission following treatment cessation may be maintained for at least 12 mo in some patients with TIW NB-UVB treatment (LoE 2++[67])

BIW = twice per week; LoE = level of evidence; PASI = Psoriasis Area and Severity Index; TB = tuberculosis; TIW = three times per week; TNF-α = tumor necrosis factor α; UV = ultraviolet; UVA = ultraviolet A; UVB = ultraviolet B.

*Outcome data are shown for the various treatment options applied as monotherapies. Some ameliorative therapies may be safer or more effective when applied in a combination regimen. Consult the *Guidelines* chapter on moderate to severe psoriasis for a discussion of various combination approaches, such as topical or systemic agents with phototherapies (photochemotherapeutic regimens).

†Efficacy reflects at least a 75% improvement in PASI score, as determined by a statistically significant difference from placebo in studies of moderate to severe plaque psoriasis.

‡Additional biologics were approved for use in psoriasis or psoriatic arthritis subsequent to the evidence review and publication of the *Guidelines*. These include ustekinumab and golimumab.[31]

§As discussed in the *Guidelines*, continued 50 mg BIW dosing of etanercept (i.e., with no step-down) has also been explored.

‖Phototherapy with PUVA should be restricted to a lifetime total of 200 treatment sessions unless clinically indicated, using UV-sparing combination regimens as appropriate (LoE 2++, Grade B).

¶Therapy not well suited to placebo control.

#Phototherapy with UVB should be conducted to minimize cumulative lifetime exposure to UV light, using UV-sparing combination regimens as appropriate (LoE 4, Grade D).

psoriasis. This table describes the level of evidence available to support the use of different possible monotherapies to achieve any of several possible outcomes. The reader may consult the *Guidelines* for a fuller description of evidence supporting antipsoriatic combination therapies.

Physicians should explore all appropriate choices to identify ones that patients will adhere to and be satisfied with over the long term.

Outlook

The recommendations in the *Guidelines* reflect good dermatologic practice at the time they were written and published. However, even in the brief period since the *Guidelines* became available, several potentially important changes have occurred in the landscape of Canadian psoriasis care.

First is the publication of three independent surveys of Canadians with moderate to severe plaque psoriasis.[28–30] Taken together, these surveys confirm our speculation, as stated in the *Guidelines*, that psoriasis is widely undertreated in this country.[29,30] They also highlight the substantial psychological and emotional burden of psoriasis,[28–30] particularly for patients who report joint discomfort (with or without a physician's diagnosis of psoriatic arthritis).[28] The survey data also suggest that satisfaction with traditional psoriasis care is low and that use of biologics, which patients consider more satisfactory, is limited by such financial considerations as personal income and insured status.[30]

Second, several new therapeutic agents have appeared on the Canadian market, including two biologics, one with a novel mechanism of action (ustekinumab) and one targeting tumor necrosis factor (golimumab, approved only for psoriatic arthritis).[31] Newly approved topical treatments include a fixed-dose combination of calcipotriol and betamethasone dipropionate, formulated as a gel for use in scalp psoriasis, and a vitamin D (calcitriol) ointment that is already commonly prescribed in Europe and elsewhere. Evidence supporting use of these agents will be considered when the *Guidelines* are updated.

Finally, a trend toward higher-quality studies in the psoriasis literature continues, including studies with ambitious clinical end points and, in some cases, active comparator design.[31] With this welcome trend, the physician's task of choosing appropriate therapeutics for patients with plaque psoriasis should be considerably simplified.

Acknowledgment

Financial disclosure of authors and reviewers: None reported.

References

1. Koo J. Population-based epidemiologic study of psoriasis with emphasis on quality of life assessment. Dermatol Clin 1996;14:485–96, doi:10.1016/S0733-8635(05)70376-4.
2. Krueger G, Koo J, Lebwohl M, et al. The impact of psoriasis on quality of life: results of a 1998 National Psoriasis Foundation Patient-Membership Survey. Arch Dermatol 2001;137:280–4.
3. Wahl AK, Gjengedal E, Hanestad BR. The bodily suffering of living with severe psoriasis: in-depth interviews with 22 hospitalized patients with psoriasis. Qual Health Res 2002;12:250–61, doi:10.1177/104973202129119874.
4. Ginsburg IH, Link BG. Feelings of stigmatization in patients with psoriasis. J Am Acad Dermatol 1989;20:53–63, doi:10.1016/S0190-9622(89)70007-4.
5. Vardy D, Besser A, Amir M, et al. Experiences of stigmatization play a role in mediating the impact of disease severity on quality of life in psoriasis patients. Br J Dermatol 2002;147:736–42, doi:10.1046/j.1365-2133.2002.04899.x.
6. Schmid-Ott G, Kuensebeck HW, Jaeger B, et al. Validity study for the stigmatization experience in atopic dermatitis and psoriatic patients. Acta Derm Venereol 1999;79:443–7, doi:10.1080/000155599750009870.
7. Eghlileb AM, Davies EEG, Finlay AY. Psoriasis has a major secondary impact on the lives of family members and partners. Br J Dermatol 2007;156:1245–50, doi:10.1111/j.1365-2133.2007.07881.x.
8. Pearce DJ, Singh S, Balkrishnan R, et al. The negative impact of psoriasis on the workplace. J Dermatolog Treat 2006;17:24–8, doi:10.1080/09546630500482886.
9. Heydendael VM, de Borgie CA, Spuls PI, et al. The burden of psoriasis is not determined by disease severity only. J Investig Dermatol Symp Proc 2004;9:131–5, doi:10.1111/j.1087-0024.2004.09115.x.
10. Richards HL, Fortune DG, Weidmann A, et al. Detection of psychological distress in patients with psoriasis: low consensus between dermatologist and patient. Br J Dermatol 2004;151:1227–33, doi:10.1111/j.1365-2133.2004.06221.x.
11. Jobling RG. Psoriasis—a preliminary questionnaire study of sufferers' subjective experience. Clin Exp Dermatol 1976;1:233–6, doi:10.1111/j.1365-2230.1976.tb01424.x.
12. Gelfand JM, Neimann AL, Shin DB, et al. Risk of myocardial infarction in patients with psoriasis. JAMA 2006;296:1735–41, doi:10.1001/jama.296.14.1735.
13. Gelfand JM, Troxel AB, Lewis JD, et al. The risk of mortality in patients with psoriasis: results from a population-based study. Arch Dermatol 2007;143:1493–9, doi:10.1001/archderm.143.12.1493.
14. Canadian Psoriasis Guidelines Committee. Canadian guidelines for the management of plaque psoriasis. June 2009. Available at: http://www.dermatology.ca/guidelines/cdnpsoriasisguidelines.pdf or http://www.dermatology.ca/guidelines/LignesdirectricespsoriasisCAN.pdf (accessed on April 2011).

15. The AGREE Collaboration. Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument. Available at: www.agreecollaboration.org (accessed November 2006).
16. Canadian Medical Association. Handbook on clinical practice guidelines 2007. Available at: http://www.cma.ca//multimedia/CMA/Content_Images/CMAInfobase/EN/handbook.pdf (accessed June 2007).
17. Scottish Intercollegiate Guidelines Network. SIGN 50: a guideline developers' handbook. Available at: www.sign.ac.uk (accessed November 2006).
18. Gelfand JM, Weinstein R, Porter SB, et al. Prevalence and treatment of psoriasis in the United Kingdom: a population-based study. Arch Dermatol 2005;141:1537–41, doi:10.1001/archderm.141.12.1537.
19. Balkrishnan R, Carroll CL, Camacho FT, Feldman SR. Electronic monitoring of medication adherence in skin disease: results of a pilot study. J Am Acad Dermatol 2003;49:651–4, doi:10.1067/S0190-9622(03)00912-5.
20. Carroll CL, Feldman SR, Camacho FT, Balkrishnan R. Better medication adherence results in greater improvement in severity of psoriasis. Br J Dermatol 2004;151:895–7, doi:10.1111/j.1365-2133.2004.06174.x.
21. Ali SM, Brodell RT, Balkrishnan R, Feldman SR. Poor adherence to treatments: a fundamental principle of dermatology. Arch Dermatol 2007;143:912–5, doi:10.1001/archderm.143.7.912.
22. Fouere S, Adjadj L, Pawin H. How patients experience psoriasis: results from a European survey. J Eur Acad Dermatol Venereol 2005;19 Suppl 3:2–6, doi:10.1111/j.1468-3083.2005.01329.x.
23. Richards HL, Fortune DG, O'Sullivan TM, et al. Patients with psoriasis and their compliance with medication. J Am Acad Dermatol 1999;41:581–3.
24. Mason J, Mason AR, Cork MJ. Topical preparations for the treatment of psoriasis: a systematic review. Br J Dermatol 2002;146:351–64, doi:10.1046/j.1365-2133.2000.04713.x.
25. Ashcroft DM, Li Wan Po A, Williams HC, Griffiths CEM. Systematic review of comparative efficacy and tolerability of calcipotriol in treating chronic plaque psoriasis. BMJ 2000;320:963–7, doi:10.1136/bmj.320.7240.963.
26. Papp KA, Guenther L, Boyden B, et al. Early onset of action and efficacy of a combination of calcipotriene and betamethasone dipropionate in the treatment of psoriasis. J Am Acad Dermatol 2003;48:48–54, doi:10.1067/mjd.2003.130.
27. Al-Suwaidan SN, Feldman SR. Clearance is not a realistic expectation of psoriasis treatment. J Am Acad Dermatol 2000;42:796–802, doi:10.1067/mjd.2000.103983.
28. Lynde CW, Poulin Y, Guenther L, Jackson C. The burden of psoriasis in Canada: insights from the pSoriasis Knowledge IN Canada (SKIN) survey. J Cutan Med Surg 2009;13:235–52.
29. Mahler R, Jackson C, Ijacu H. The burden of psoriasis and barriers to satisfactory care: results from a Canadian patient survey. J Cutan Med Surg 2009;13:283–93.
30. Wasel N, Poulin Y, Andrew R, et al. A Canadian self-administered online survey to evaluate the impact of moderate-to-severe psoriasis among patients. J Cutan Med Surg 2009;13:294–302.
31. Papp K, Carey W. Psoriasis care: new and emerging pharmacologic trends. J Cutan Med Surg 2010;14:119–29.
32. Statistics Canada. Age (123) and sex (3) for the population of Canada, 2006 census. Available at: http://www12.statcan.ca/english/census06/data/topics/RetrieveProductTable.cfm?Temporal=2006&APATH=3&PID=88989&THEME=66&PTYPE=88971&VID=0&GK=NA&GC=99&FL=0&RL=0&FREE=0&METH=0&S=1 (accessed January 2008).
33. Anstey AV, Kragballe K. Retrospective assessment of PASI 50 and PASI 75 attainment with a calcipotriol/betamethasone dipropionate ointment. Int J Dermatol 2006;45:970–5, doi:10.1111/j.1365-4632.2006.02939.x.
34. Van De Kerkhof PCM. Update on retinoid therapy of psoriasis in: an update on the use of retinoids in dermatology. Dermatolog Ther 2006;19:252–63, doi:10.1111/j.1529-8019.2006.00082.x.
35. Olsen EA, Weed WW, Meyer CJ, Cobo LM. A double-blind, placebo-controlled trial of acitretin for the treatment of psoriasis. J Am Acad Dermatol 1989;21:681–6, doi:10.1016/S0190-9622(89)70236-X.
36. Ho VC, Griffiths CE, Albrecht G, et al. Intermittent short courses of cyclosporin (Neoral(R)) for psoriasis unresponsive to topical therapy: a 1-year multicentre, randomized study. The PISCES Study Group. Br J Dermatol 1999;141:283–91, doi:10.1046/j.1365-2133.1999.02977.x.
37. Ho VCY, Griffiths CEM, Berth-Jones J, et al. Intermittent short courses of cyclosporine microemulsion for the long-term management of psoriasis: a 2-year cohort study. J Am Acad Dermatol 2001;44:643–51, doi:10.1067/mjd.2001.112400.
38. Grossman RM, Chevret S, Abi-Rached J, et al. Long-term safety of cyclosporine in the treatment of psoriasis. Arch Dermatol 1996;132:623–9, doi:10.1001/archderm.132.6.623.
39. Faerber L, Braeutigam M, Weidinger G, et al. Cyclosporine in severe psoriasis: results of a meta-analysis in 579 patients. Am J Clin Dermatol 2001;2:41–7, doi:10.2165/00128071-200102010-00007.
40. Zachariae H, Kragballe K, Sogaard H. Methotrexate induced liver cirrhosis. Studies including serial liver biopsies during continued treatment. Br J Dermatol 1980;102:407–12, doi:10.1111/j.1365-2133.1980.tb06553.x.
41. Malatjalian DA, Ross JB, Williams CN, et al. Methotrexate hepatotoxicity in psoriatics: report of 104 patients from Nova Scotia, with analysis of risks from obesity, diabetes and alcohol consumption during long term follow-up. Can J Gastroenterol 1996;10:369–75.
42. Salim A, Tan E, Ilchyshyn A, Berth-Jones J. Folic acid supplementation during treatment of psoriasis with methotrexate: a randomized, double-blind, placebo-controlled trial. Br J Dermatol 2006;154:1169–74, doi:10.1111/j.1365-2133.2006.07289.x.
43. Heydendael VMR, Spuls PI, Opmeer BC, et al. Methotrexate versus cyclosporine in moderate-to-severe chronic plaque psoriasis. N Engl J Med 2003;349:658–65, doi:10.1056/NEJMoa021359.
44. Van Dooren-Greebe RJ, Kuijpers ALA, Mulder J, et al. Methotrexate revisited: effects of long-term treatment in psoriasis. Br J Dermatol 1994;130:204–10, doi:10.1111/j.1365-2133.1994.tb02901.x.
45. Schiff MH, Burmester GR, Kent JD, et al. Safety analyses of adalimumab (HUMIRA) in global clinical trials and US post-marketing surveillance of patients with rheumatoid arthritis. Ann Rheum Dis 2006;65:889–94, doi:10.1136/ard.2005.043166.
46. Menter A, Tyring SK, Gordon K, et al. Adalimumab therapy for moderate to severe psoriasis: a randomized, controlled phase III trial. J Am Acad Dermatol 2008;58:106–15, doi:10.1016/j.jaad.2007.09.010.

47. Saurat JH, Stingl G, Dubertret L, et al. Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION). Br J Dermatol 2008;158:558–66.
48. Mohan N, Edwards ET, Cupps TR, et al. Demyelination occurring during anti-tumor necrosis factor alpha therapy for inflammatory arthritides. Arthritis Rheum 2001;44:2862–9, doi:10.1002/1529-0131(200112)44:12<2862::AID-ART474>3.0.CO;2-W.
49. Fulchiero GJ, Jr, Salvaggio H, Drabick JJ, et al. Eruptive latent metastatic melanomas after initiation of antitumor necrosis factor therapies. J Am Acad Dermatol 2007;56(5 Suppl):S65–7, doi:10.1016/j.jaad.2006.12.024.
50. Gordon K, Korman N, Frankel E, et al. Efficacy of etanercept in an integrated multistudy database of patients with psoriasis. J Am Acad Dermatol 2006;54(3 Suppl 2):S101–11, doi:10.1016/j.jaad.2005.11.1088.
51. Leonardi CL, Powers JL, Matheson RT, et al. Etanercept as monotherapy in patients with psoriasis. N Engl J Med 2003;349:2014–22, doi:10.1056/NEJMoa030409.
52. Papp KA, Tyring S, Lahfa M, et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. Br J Dermatol 2005;152:1304–12, doi:10.1111/j.1365-2133.2005.06688.x.
53. Menter A, Feldman SR, Weinstein GD, et al. A randomized comparison of continuous vs. intermittent infliximab maintenance regimens over 1 year in the treatment of moderate-to-severe plaque psoriasis. J Am Acad Dermatol 2007;56(1):31.el–15, doi:10.1016/j.jaad.2006.07.017.
54. Smith CH, Jackson K, Bashir SJ, et al. Infliximab for severe, treatment-resistant psoriasis: a prospective, open-label study Br J Dermatol 2006;155:160–9, doi:10.1111/j.1365-2133.2006.07316.x.
55. Reich K, Nestle FO, Papp K, et al. Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial. Lancet 2005;366:1367–74, doi:10.1016/S0140-6736(05)67566-6.
56. Krathen RA, Berthelot CN, Hsu S. Sustained efficacy and safety of infliximab in psoriasis: a retrospective study of 73 patients. J Drugs Dermatol 2006;5:251–4.
57. Goffe B, Papp K, Gratton D, et al. An integrated analysis of thirteen trials summarizing the long-term safety of alefacept in psoriasis patients who have received up to nine courses of therapy. Clin Ther 2005;27:1912–21, doi:10.1016/j.clinthera.2005.12.007.
58. Legat FJ, Hofer A, Wackernagel A, et al. Narrowband UV-B phototherapy, alefacept, and clearance of psoriasis. Arch Dermatol 2007;143:1016–22, doi:10.1001/archderm.143.8.1016.
59. Gordon KB, Langley RG. Remittive effects of intramuscular alefacept in psoriasis. J Drugs Dermatol 2003;2:624–8.
60. Lebwohl M, Christophers E, Langley R, et al. An international, randomized, double-blind, placebo-controlled phase 3 trial of intramuscular alefacept in patients with chronic plaque psoriasis. Arch Dermatol 2003;139:719–27, doi:10.1001/archderm.139.6.719.
61. Nijsten TEC, Stern RS. The increased risk of skin cancer is persistent after discontinuation of psoralen + ultraviolet A: a cohort study. J Invest Dermatol 2003;121:252–8, doi:10.1046/j.1523-1747.2003.12350.x.
62. Tzaneva S, Honigsmann H, Tanew A, Seeber A. A comparison of psoralen plus ultraviolet A (PUVA) monotherapy, tacalcitol plus PUVA and tazarotene plus PUVA in patients with chronic plaque-type psoriasis. Br J Dermatol 2002;147:748–53, doi:10.1046/j.1365-2133.2002.04896.x.
63. Iest J, Boer J. Combined treatment of psoriasis with acitretin and UVB phototherapy compared with acitretin alone and UVB alone. Br J Dermatol 1989;120:665–70, doi:10.1111/j.1365-2133.1989.tb01354.x.
64. Tanew A, Guggenbichler A, Honigsmann H, et al. Photochemotherapy for severe psoriasis without or in combination with acitretin: a randomized, double-blind comparison study. J Am Acad Dermatol 1991;25:682–4, doi:10.1016/0190-9622(91)70253-X.
65. Schiener R, Brockow T, Franke A, et al. Bath PUVA and saltwater baths followed by UV-B phototherapy as treatments for psoriasis: a randomized controlled trial. Arch Dermatol 2007;143:586–96, doi:10.1001/archderm.143.5.586.
66. Yones SS, Palmer RA, Garibaldinos TT, Hawk JLM. Randomized double-blind trial of the treatment of chronic plaque psoriasis: efficacy of psoralen-UV-A therapy vs narrowband UV-B therapy. Arch Dermatol 2006;142:836–42, doi:10.1001/archderm.142.7.836.
67. Markham T, Rogers S, Collins P. Narrowband UV-B (TL-01) phototherapy vs oral 8-methoxypsoralen psoralen - UV-A for the treatment of chronic plaque psoriasis. Arch Dermatol 2003;139:325–8, doi:10.1001/archderm.139.3.325.
68. Gordon PM, Diffey BL, Matthews JN, Farr PM. A randomized comparison of narrow-band TL-01 phototherapy and PUVA photochemotherapy for psoriasis. J Am Acad Dermatol 1999;41:728–32, doi:10.1016/S0190-9622(99)70008-3.