Treatment Goals for Plaque Psoriasis: Treat to Target

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Overview of Psoriasis

Chronic inflammatory disease with a prevalence of over 3% of the US population.

Ultimately patients have poor long-term health outcomes, the significance of which we are continuing to realize.\(^1\)

Comorbid diseases associated with psoriasis

- Psoriatic arthritis
- Inflammatory bowel disease
- Uveitis
- Renal disease
- Hepatosteatosis
- COPD
- Sleep apnea
- Depression
- Alcoholism
- Smoking

- Diabetes
- Dyslipidemia
- Obesity
- Myocardial infarction
- Stroke
- Peripheral vascular disease
- Avascular necrosis

Impact of psoriasis compared with other chronic diseases

Physical Component of Psoriasis as Compared to Other Major Diseases¹

Healthy adults
Dermatitis
Cancer
Depression
Hypertension
Arthritis
Myocardial infarction
Chronic lung disease
Type 2 diabetes
Psoriasis
Congestive heart failure

Mental Component of Psoriasis as Compared to Other Major Diseases¹

Healthy adults
Hypertension
Type 2 diabetes
Myocardial infarction
Congestive heart failure
Cancer
Arthritis
Dermatitis
Psoriasis
Chronic lung disease
Depression

317 patients with psoriasis completed the SF-36 Health Survey Compared with 10 other chronic medical or psychiatric chronic conditions reported in the National Survey of Functional Health Status (NSFHS)

SF-36=Short-form 36

# Therapies for psoriasis: Conventional systemic agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing</th>
<th>PASI 75 after wk. 12</th>
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<tbody>
<tr>
<td>Methotrexate</td>
<td>10-25 mg/wk.</td>
<td>40%</td>
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<tr>
<td>Cyclosporine</td>
<td>5 mg/kg/day</td>
<td>70%</td>
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<tr>
<td>Acitretin</td>
<td>50 mg daily</td>
<td>23%</td>
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</tbody>
</table>
Poor risk benefit ratios

Efficacy
- CsA
- MTX
- Acitretin

Side effect risk
- Kidney toxicity
- NMSC
- Liver toxicity
- Bone marrow toxicity
- Lipid abnormalities
Therapies for psoriasis: Biologic and small molecule agents

- TNF inhibitors
  - Etanercept
  - Infliximab
  - Adalimumab
- IL12/23 inhibitor
  - Ustekinumab
- IL17 inhibitors
  - Secukinumab
  - Ixekizumab
- PD4 inhibitor
  - Apremilast
## Currently available biologic agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage frequency</th>
<th>PASI-75 response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>5mg/kg week 0, 2, 6 then q8 weeks IV</td>
<td>76-80% (wk. 10)</td>
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<tr>
<td>Adalimumab</td>
<td>80mg loading dos, 40mg week 1, then q2 weeks SC</td>
<td>71-80% (wk. 12)</td>
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<tr>
<td>Etanercept</td>
<td>50mg twice weekly x 3mo, then 50mg weekly SC</td>
<td>47% (wk. 12)</td>
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<tr>
<td>Ustekinumab</td>
<td>&lt; 100kg: 45mg @ week 0, 4 then q12 weeks SC</td>
<td>66 – 68% (wk. 12)</td>
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<td></td>
<td>≥100kg: 90mg @ week 0, 4 then q12 weeks SC</td>
<td></td>
</tr>
<tr>
<td>Secukinumab</td>
<td>300mg weekly x 5 weeks, then 150-300mg q4</td>
<td>81.6% (wk. 12)</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>160 mg SC, THEN 80 mg SC q2wks at weeks 2, 4, 6, 8, 10, and 12, THEN 80 mg SC q4wks</td>
<td>78-90% (wk. 12)</td>
</tr>
<tr>
<td>Apremilast</td>
<td>30 mg twice daily after taper</td>
<td>29-33% (wk. 16)</td>
</tr>
</tbody>
</table>
A few drugs lost along the way

- PUVA-NMSC (SCC) and melanoma
- Alefacept-efficacy too low
- Efalizumab-toxicity too high
What about the patients?

NPF surveys show that many patients continue to undertreat and are dissatisfied.\(^2\) Factors contributing to this include: access issues, fear of side-effects, and lack of defined treatment goals in the US.

The 4 minute mile
Need for Treatment Targets in the U.S.

- Disease burden remains high among U.S. psoriasis patients.
- Establishment of treatment targets helps providers and patients work towards a set of goals.
- Without treatment targets, it is difficult to determine what to aim for during treatment course.
Case for treatment targets: hypertension


Different systolic blood pressure targets for people with history of stroke or transient ischaemic attack: PAST-BP (Prevention After Stroke--Blood Pressure) randomised controlled trial.


Abstract
OBJECTIVE: To assess whether using intensive blood pressure targets leads to lower blood pressure in a community population of people with prevalent cerebrovascular disease.

DESIGN: Open label randomised controlled trial.


PARTICIPANTS: People with a history of stroke or transient ischaemic attack whose systolic blood pressure was 125 mm Hg or above.

INTERVENTIONS: Intensive systolic blood pressure target (<130 mm Hg or 10 mm Hg reduction from baseline if this was <140 mm Hg) or standard target (<140 mm Hg). Apart from the different target, patients in both arms were actively managed in the same way with regular reviews by the primary care team.

MAIN OUTCOME MEASURE: Change in systolic blood pressure between baseline and 12 months.

RESULTS: 529 patients (mean age 72) were enrolled, 266 to the intensive target arm and 263 to the standard target arm, of whom 379 were included in the primary analysis (182 (68%) intensive arm; 197 (75%) standard arm). 84 patients withdrew from the study during the follow-up period (52 intensive arm; 32 standard arm). Mean systolic blood pressure dropped by 16.1 mm Hg to 127.4 mm Hg in the intensive target arm and by 12.8 mm Hg to 129.4 mm Hg in the standard arm (difference between groups 2.9 (95% confidence interval 0.2 to 5.7) mm Hg; P=0.03).

CONCLUSIONS: Aiming for target below 130 mm Hg rather than 140 mm Hg for systolic blood pressure in people with cerebrovascular disease in primary care led to a small additional reduction in blood pressure. Active management of systolic blood pressure in this population using a <140 mm Hg target led to a clinically important reduction in blood pressure. Trial registration Current Controlled Trials ISRCTN29062286.
Case for treatment targets: diabetes

**Optimal home SBP targets for preventing the progression of diabetic nephropathy in patients with type 2 diabetes mellitus.**


**Abstract**

**OBJECTIVES:** Home blood pressure control can reduce the risk of increased urinary albumin excretion in patients with diabetes mellitus. However, the optimal home blood pressure targets to prevent the onset or progression of diabetic nephropathy are not well defined.

**METHODS:** We performed a retrospective cohort study of 851 patients with type 2 diabetes mellitus. Logistic regression models were used to evaluate the correlations of home SBP levels with progression of diabetic nephropathy.

**RESULTS:** During the follow-up of 2 years, 86 patients had progression of diabetic nephropathy. Adjusted odds ratios (95% confidence interval) for progression of diabetic nephropathy in patients with morning SBP of 120-129 mmHg [2.725 (1.074-6.917), P=0.035], 130-139 mmHg [3.703 (1.519-9.031), P=0.004] and in those with morning SBP equal or more than 140 mmHg [2.994 (1.182-7.581), P=0.021] were significantly higher than that in those with morning SBP less than 120 mmHg in multiple logistic analyses.

**CONCLUSION:** The preferable morning SBP targets might be less than 120 mmHg for preventing the onset or progression of diabetic nephropathy in patients with type 2 diabetes mellitus.
Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial

Catriona Grigor, Hilary Capell, Anne Stirling, Alex D McMahon, Peter Lock, Ramsay Vallance, Wilma Kincaid, Duncan Porter

Summary
Background Present treatment strategies for rheumatoid arthritis include use of disease-modifying antirheumatic drugs, but a minority of patients achieve a good response. We aimed to test the hypothesis that an improved outcome can be achieved by employing a strategy of intensive outpatient management of patients with rheumatoid arthritis—for sustained, tight control of disease activity—compared with routine outpatient care.

Methods We designed a single-blind, randomised controlled trial in two teaching hospitals. We screened 183 patients for inclusion. 111 were randomly allocated either intensive management or routine care. Primary outcome measures were mean fall in disease activity score and proportion of patients with a good response (defined as a disease activity score <2.4 and a fall in this score from baseline by >1.2). Analysis was by intention-to-treat.

Findings One patient withdrew after randomisation and seven dropped out during the study. Mean fall in disease activity score was greater in the intensive group than in the routine group (−3.5 vs −1.9, difference 1.6 [95% CI 1.1–2.1], p<0.0001). Compared with routine care, patients treated intensively were more likely to have a good response (definition, 45/55 [82%] vs 24/55 [44%], odds ratio 5.8 [95% CI 2.4–13.9], p<0.0001) or be in remission (disease activity score <1.6: 36/55 [65%] vs 9/55 [16%], 9.7 [3.9–23.9], p<0.0001). Three patients assigned routine care and one allocated intensive management died during the study; none was judged attributable to treatment.

Interpretation A strategy of intensive outpatient management of rheumatoid arthritis substantially improves disease activity, radiographic disease progression, physical function, and quality of life at no additional cost.
T2T approach improves joint outcome

OR of ACR 20 in tight vs standard control 1.91
OR of ACR 50 in tight control was 2.36
OR of ACR 70 2.64

Table 3: Univariable analysis (χ² test of independence) for the proportion of patients in the evaluable patient population achieving a response at 48 weeks post randomisation for the key secondary endpoints
Treat to Target Approach in PsA: TICOPA Trial

MDA, minimum disease activity; MTX, methotrexate; R, randomisation; StdC, standard care; TC, tight control; T2T, treat to target

Tight Control was Associated with Significantly Greater Improvements in Signs and Symptoms and Quality of Life at Week 48

Intention to treat (ITT) with multiple imputations
ACR, American College of Rheumatology

Definition of treatment goals for moderate to severe psoriasis: a European consensus

U. Mrowietz · K. Kragballe · K. Reich · P. Spuls · C. E. M. Griffiths · A. Nast · J. Franke · C. Antoniou · P. Arenberger · F. Balieva · M. Bylaite · O. Correia · E. Daudén · P. Gisondi · L. Iversen · L. Kemény · M. Lahfa · T. Nijsten · T. Rantanen · A. Reich · T. Rosenbach · S. Segaert · C. Smith · T. Talme · B. Vole-Platzer · N. Yawalkar

Think beyond the Skin: 2014 Canadian Expert Opinion Paper on Treating to Target in Plaque Psoriasis

Wayne Gulliver, Charles Lynde, Jan P. Dutz, Ronald B. Vender, Jensen Yeung, Marc Bourcier, Pierre-Luc Dion, Chi-Ho Hong, Gordon Searles, and Yves Poulin
NPF Treat to Target effort

Establish specific goals towards which both clinicians and patients will strive in order to:

1. Aid in treatment decisions in clinical practice
2. Reduce disease burden
3. Improve outcomes

To establish specific goals towards which both clinicians and patients will strive in order to reduce psoriasis disease burden and inform treatment decisions in clinical practice.
Methods

1. Literature Review

2. Patient Focus Group (n = 4)

3. Survey to Practicing Dermatologists (n = 19)

4. Four Rounds of Expert Delphi (n = 25)
NPF treat-to-target process

- Initial survey (Pre-Delphi) to board members and advisors (July 29, 2015)
  - Results collected with feedback collected electronically
  - In-person feedback at summer AAD meeting
  - Telephone conference for feedback
- Patient focus group
- Practicing physician survey
- Delphi round 1 (November 19, 2015)
- Delphi round 2 (February 3, 2016)
- Delphi round 3 (February 24, 2016)
Patient focus group discussion

- Five patients participated in a semi-structured focus group discussion regarding treatment targets.
- Patients provided feedback on:
  - Their preference for treatment targets: as clear as possible using therapies with a good safety profile.
  - Aspects of psoriasis most important to address and impact on quality of life
  - Interactions with practitioners to achieve goals
- Feedback incorporated into Delphi and was incorporated into discussion section on the interpretation of the Delphi results.
What is the Delphi method?

- A structured communication method that relies on a panel of experts.
- The experts answer questionnaires in two or more rounds. After each round, an anonymous summary of the group’s input from the previous round is provided as well as the reasons they provided for their judgments, typically of divergent responses.
- Experts are encouraged to reconsider their earlier answers in light of the replies of other members of their panel.
- It is believed that during this process the range of the answers will decrease and the group will converge towards a consensus answer.
- Ways of conducting Delphi are heterogeneous.
Key features of the Delphi: Why the Delphi process works

• All participants’ individual responses remain anonymous.
• This prevents the authority, personality, or reputation of some participants from dominating others in the process.
• It also frees participants (to some extent) from their own personal biases, minimizes the "bandwagon effect" or "halo effect", allows free expression of opinions for all members, encourages open critique, and facilitates admission of errors when revising earlier judgments.
To practicing dermatologists: How familiar are you with these tools? (n=19)
The outcome tool options considered

| Tool types: Static, dynamic, combinations |

<table>
<thead>
<tr>
<th>1= Strongly disagree</th>
<th>2= Disagree</th>
<th>3= Neutral</th>
<th>4= Agree</th>
<th>5= Strongly agree</th>
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<tbody>
<tr>
<td>Dynamic assessment comparing baseline to end of the initiation period</td>
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<td>PASI 75</td>
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<td>PASI 90</td>
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<td>PASI 100</td>
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<td>Static assessment at the end of the initiation period</td>
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<td>PASI=0</td>
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<td>PASI score ≤ 1</td>
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<td>PASI score ≤ 3</td>
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<td>PASI score ≤ 5</td>
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<td>PGA=0 (clear)</td>
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<td>PGA ≤ 1 (clear or almost clear)</td>
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<td>BSA=0%</td>
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<td>BSA ≤ 1%</td>
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<td>BSA ≤ 3%</td>
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<tr>
<td>BSA ≤ 5%</td>
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<td>PGAxBSA =0</td>
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<td>PGAxBSA ≤ 1</td>
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<td>PGAxBSA ≤ 5</td>
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<td>DLQI=0</td>
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<td>PASI or DLQI</td>
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<tr>
<td>PGA or BSA</td>
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<tr>
<td>PASI or PGA</td>
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Treatment Targets

Preferred assessment instrument: **Body Surface Area (BSA)**
Timing of evaluations

2. When a psoriasis patient starts a new treatment, when should the evaluation occur to assess whether the patient has met the “target(s)” at the end of the initiation phase? This decision will impact whether a treatment change needs to be made at the end of the initiation period, such as a dose change, switch, or combination therapy.

   a) 12 weeks post-initiation
   b) 16 weeks post-initiation
   c) 24 weeks post-initiation

Please use the space below to provide any additional comments:

_______________________________________________________________________
_______________________________________________________________________
_______________________________________________________________________

3. During the maintenance phase, how often should the “target” be assessed?

   a) Every 3 months
   b) Every 6 months
   c) Once a year
Treatment Targets

Preferred timing: 3 months after initiation
q 6 month during maintenance
## Treatment Targets

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<thead>
<tr>
<th>Time Post Initiation</th>
<th>Target</th>
<th>Acceptable</th>
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<tbody>
<tr>
<td>3 Months</td>
<td>BSA ≤ 1%</td>
<td>BSA ≤ 3% - or – 75% or greater improvement from baseline BSA</td>
</tr>
</tbody>
</table>
# Treatment Targets

<table>
<thead>
<tr>
<th>Maintenance follow up</th>
<th>Target</th>
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<tbody>
<tr>
<td>Every 6 Months</td>
<td>BSA ≤ 1%</td>
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</table>
Key Take-Aways

• Most preferred treat-to-target instrument: BSA
  • Fulfillment of a single criteria (not multiple criteria) is sufficient for achieving the treatment target.
• Time to initial assessment following therapy initiation: 3 months.
• Treatment target at the end of the initiation phase: BSA ≤ 1%
• Acceptable response at end of initiation phase:
  • 75% reduction from baseline PASI
  • BSA≤ 3 %
• Assessment time interval for maintenance therapy: 6 months
• Treatment target during maintenance phase: BSA ≤ 1%
Psoriasis treat-to-target overview:

Establish treatment targets for clinical practice

- Reduce psoriasis disease burden
  - Inform treatment decisions
  - Enhance patient satisfaction
Upcoming 2017 CME Programs

Online CME
• Managed Care in Psoriatic Disease – April 2017

Early Career Physician Symposium
• June 15 | Hollywood, FL
  In conjunction with Florida Society of Dermatology & Dermatologic Surgery

Allied Healthcare Provider Psoriasis Recognition Program (A-PReP)
• May 19 | Newport Beach, CA
  In conjunction with Real World Dermatology
• Navigators provide ongoing support and guidance to patients coping with the range of issues related to disease management, access to care, and adherence
• Open to all people with psoriatic disease, their families and caregivers
• Communicate via phone, text, email, and instant messaging and Skype

www.psoriasis.org/navigationcenter