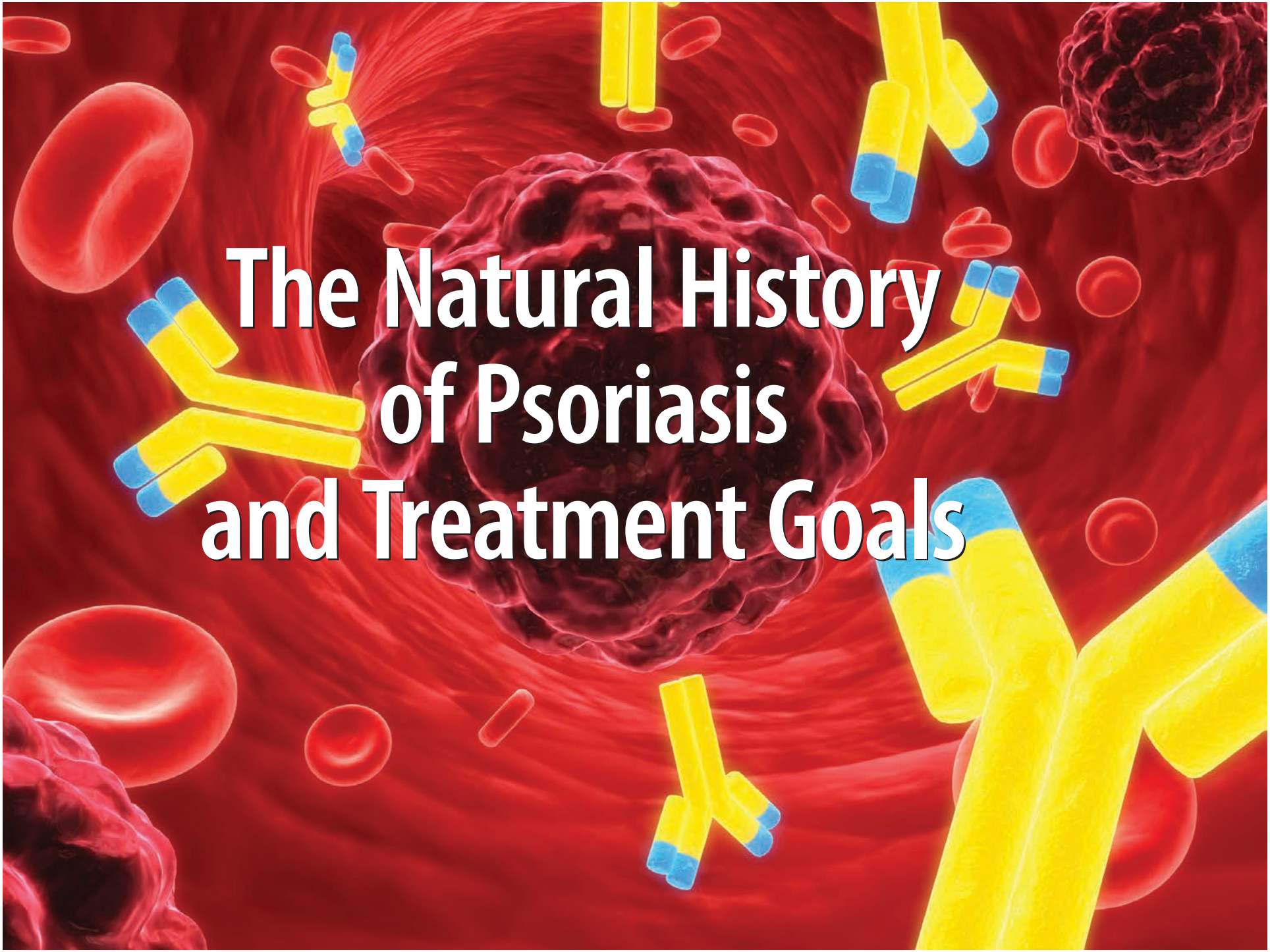
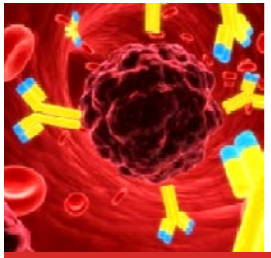

The Natural History
of Psoriasis
and Treatment Goals

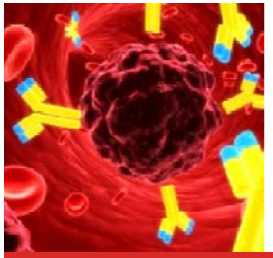


Psoriasis Epidemiology

- Prevalence
  - Affects 2-3% of adult population (>7 million in US)
  - Caucasians: 2.5%
  - African Americans: 1.3% (more likely to have moderate-to-severe disease)
- Disease severity
  - 15% have moderate disease (3-10% BSA)
  - 5% have severe disease (>10% BSA)

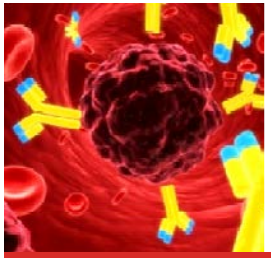
BSA – body surface area

Adapted from Neimann AN, et al. *Expert Rev Dermatol*. 2006;1:63-75. Gelfand JM, et al. *J Am Acad Dermatol*. 2005;52:23-26. Kurd SK, Gelfand JM. *J Am Acad Dermatol.* 2009;60:218-224.

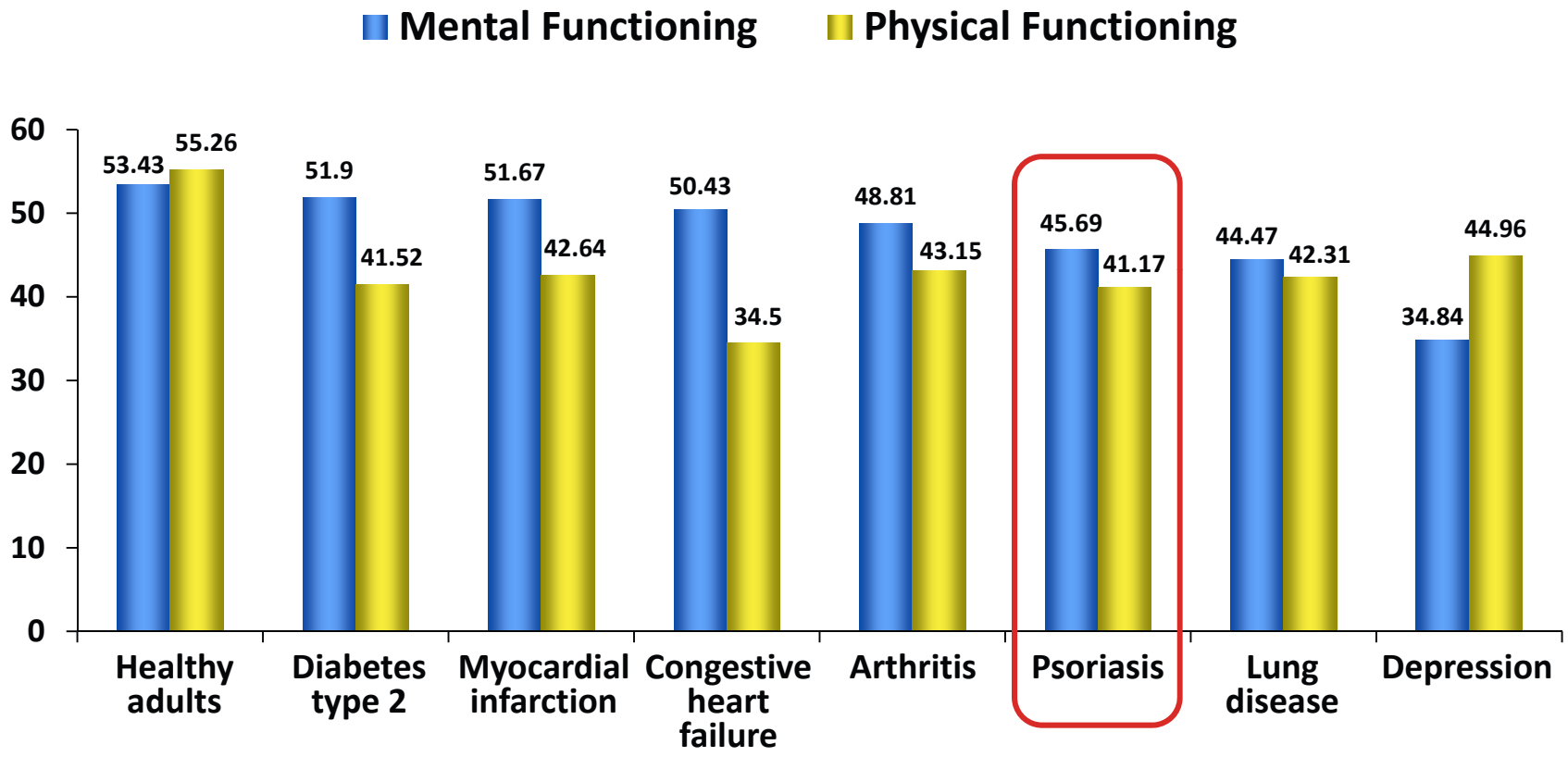


Psoriasis Natural History

- Chronic disease with typical onset in 20s to 30s
- Genetic susceptibility
  - 40% have + family history
  - *HLA-Cw6* most commonly implicated
  - >40 genes implicated
- Any part of skin can be affected, including face, scalp, nails, genitals
- Majority of patients with more severe psoriasis remain poorly controlled for decades

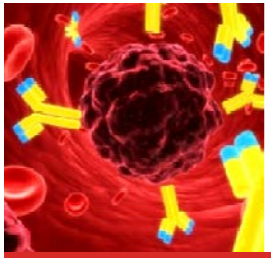


Psoriasis Impact on Quality of Life (QoL) Compared to Other Major Morbidities

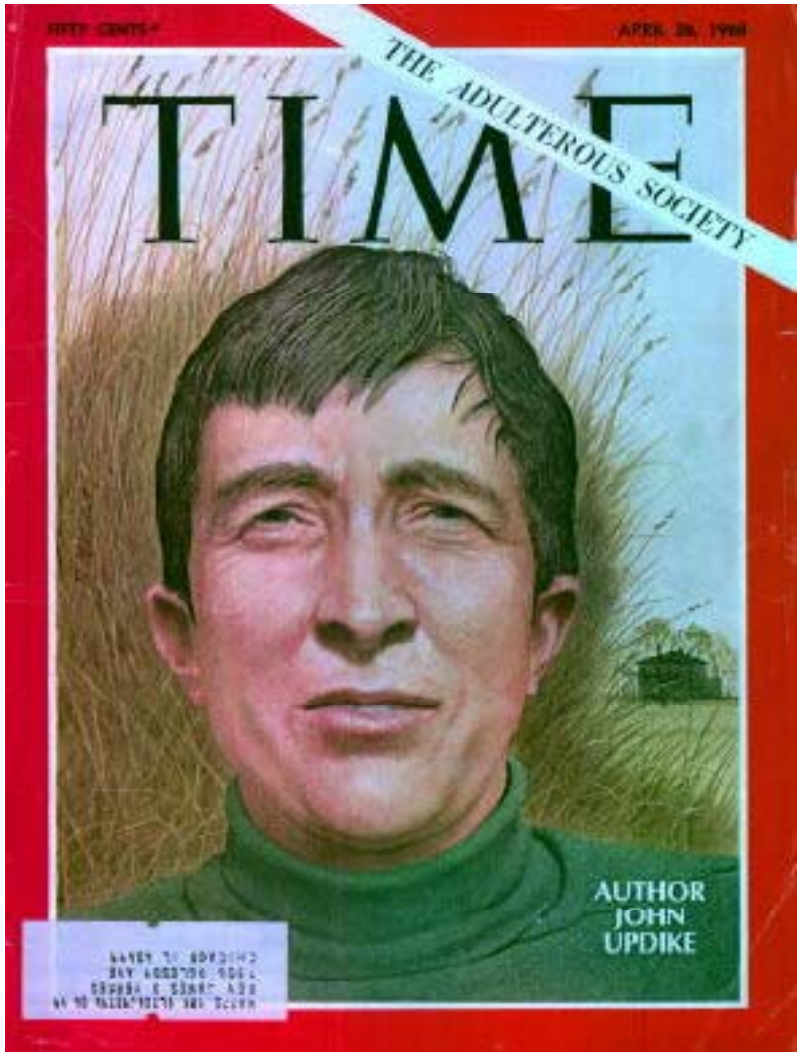


QoL outcome was SF-36 physical and mental health domains

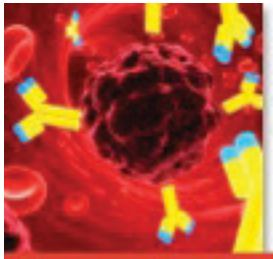
Adapted from Rapp SR, et al. *J Am Acad Dermatol.* 1999;41:401-407.



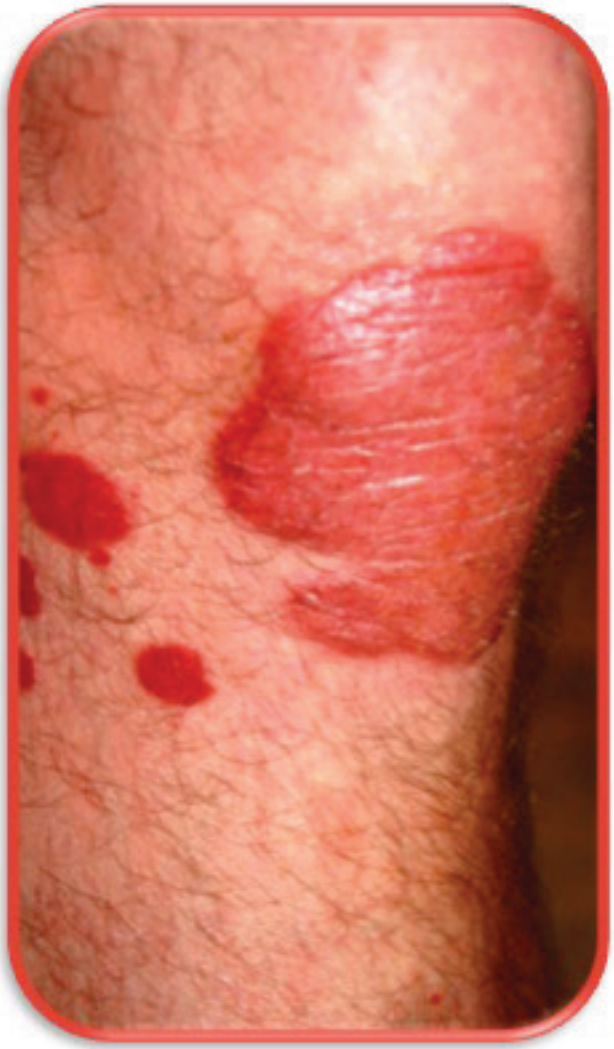
"Only psoriasis could have taken a very average boy…and made him into a prolific, adaptable, ruthless-enough writer"

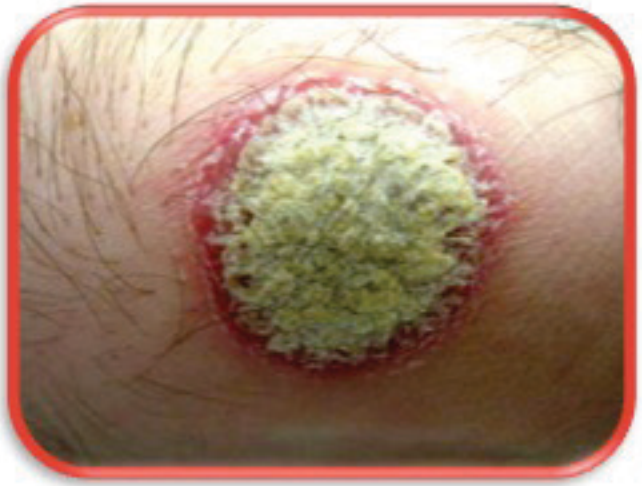


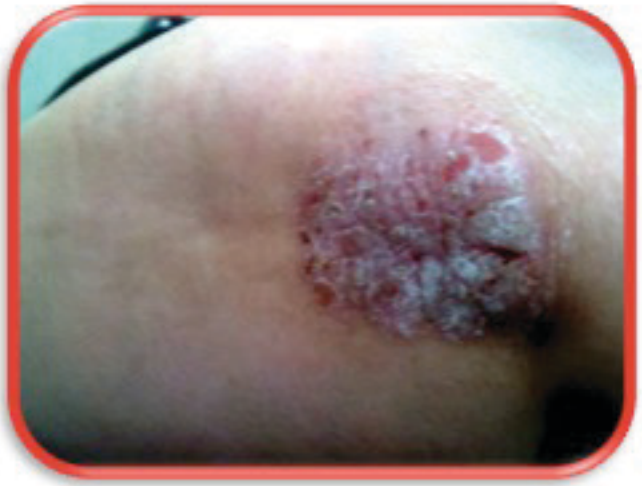
"At war with my skin" in Self-Consciousness by John Updike

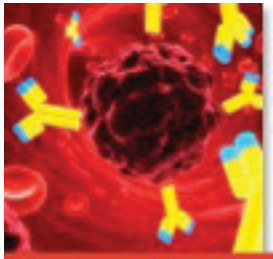


Psoriasis Vulgaris – Clinical Features



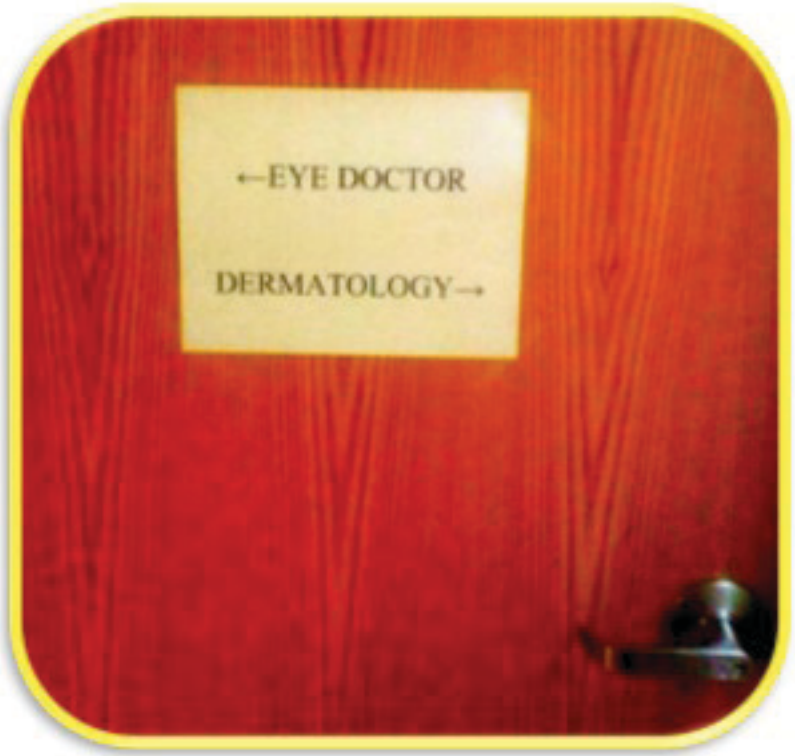


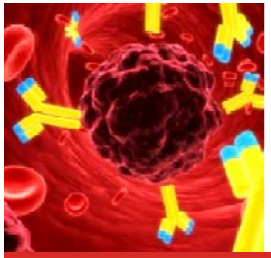




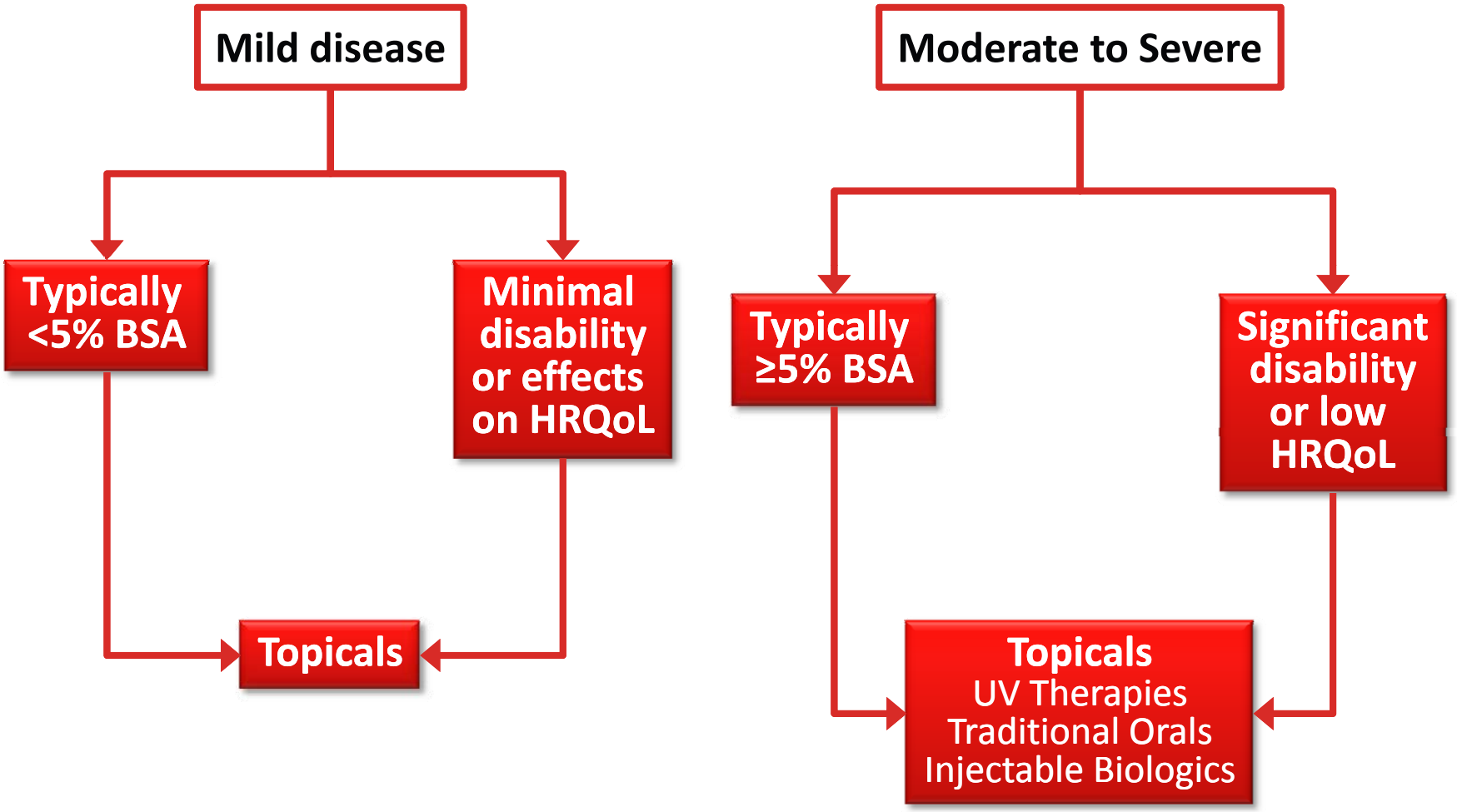
Differential Diagnosis of Psoriasis

- Autoimmune diseases
  - Subacute cutaneous lupus, dermatomyositis
- Cancer
  - Mycosis fungoides, squamous cell, basal cell carcinoma
- Infection
  - Tinea, scabies, syphilis
- Other skin diseases
  - Eczema, pityriasis rubra pilaris, lichen planus
- Drug reaction



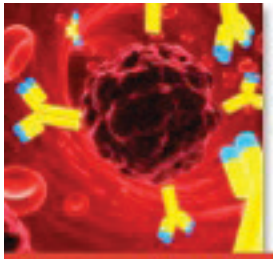


Psoriasis Treatment Paradigm



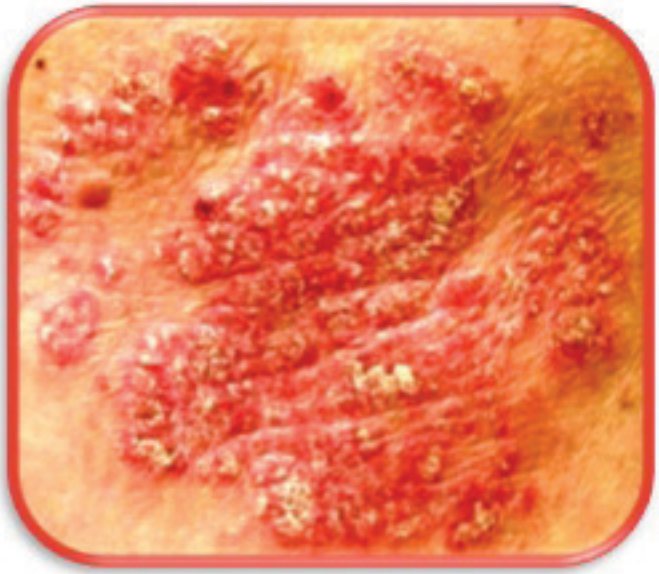
BSA – Body Surface Area, HRQoL – Health-Related Quality of Life, UV – Ultraviolet

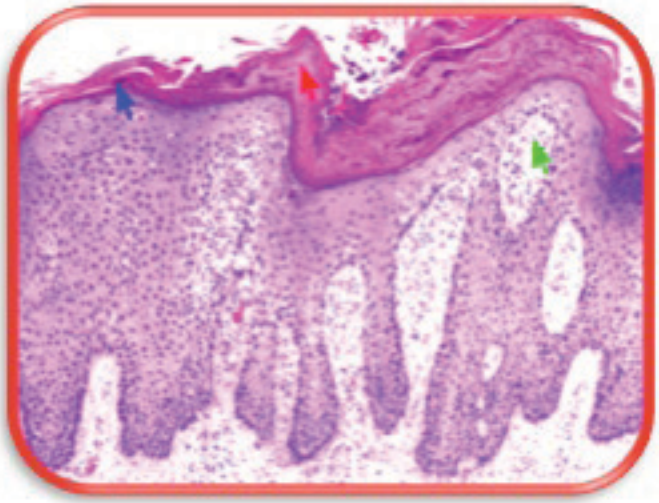
Adapted from Pariser DM, et al. *Arch Dermatol*. 2007;143:239-242.

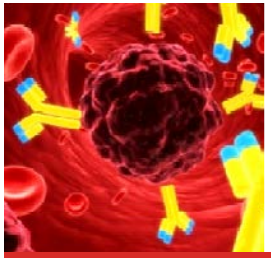


Psoriasis Pathophysiology

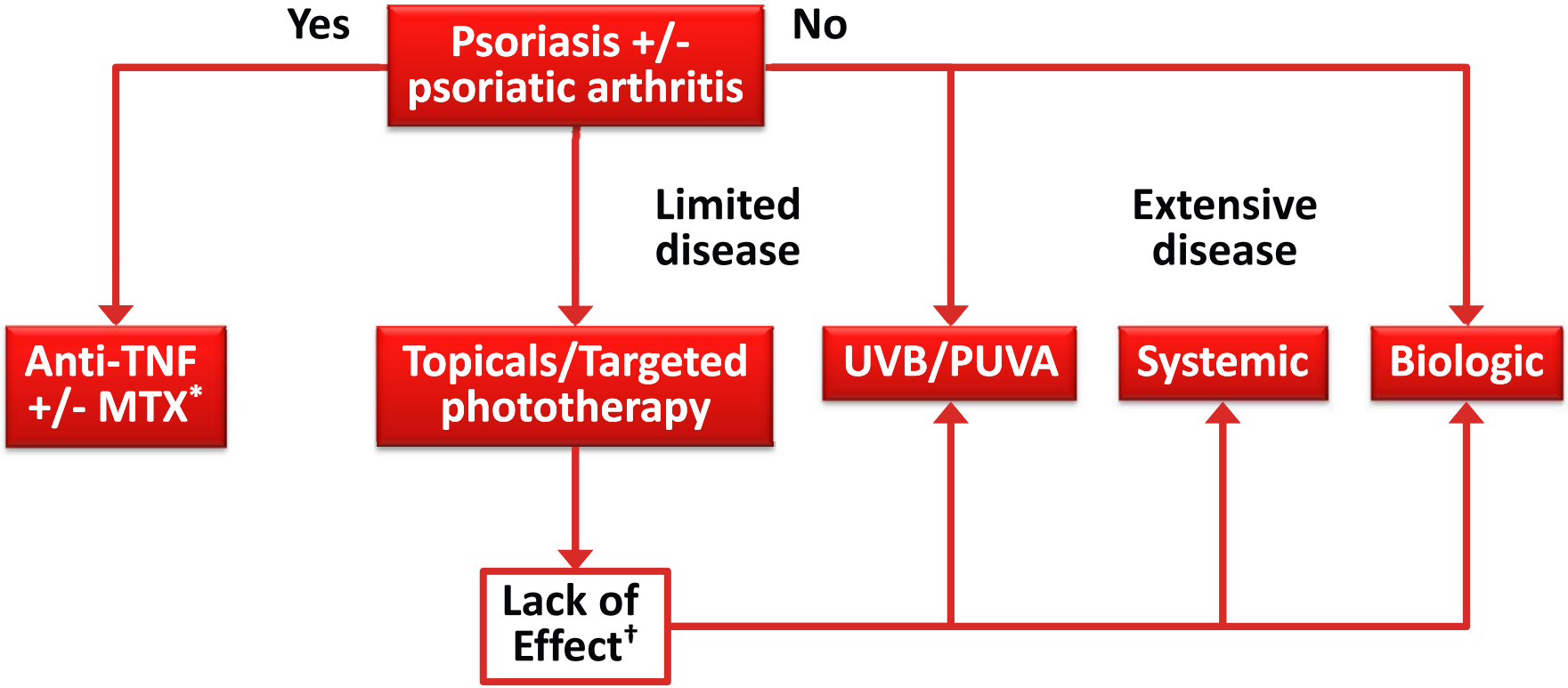
- Localized and systemic inflammation
  - Defects in T regs
  - Upregulation of Th1 and Th17 cells, APCs, and cytokines
  - Associated with increased CRP and other markers of inflammation
- Epidermal Hyperproliferation
  - Clinically appreciated as scaling, cracking
  - Associated with elevated uric acid and oxidative stress
- Angiogenesis
  - Clinically appreciated as “Auspitz” sign
  - Associated with increased circulating VEG-F
- Genes
  - >40 susceptibility loci







Presence of Psoriatic Arthritis Alters Treatment Recommendations (AAD Guidelines)

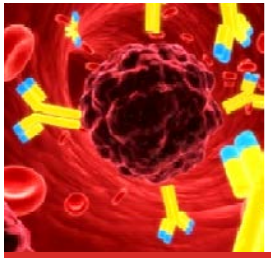


- Patients with nondeforming PsA without any radiographic changes, loss of range of motion, or interference with tasks of daily living should not automatically be treated with TNF inhibitors.

† Patients with limited skin disease should not automatically be treated with systemic treatment if they do not improve; such treatment may carry more risk than the disease itself.

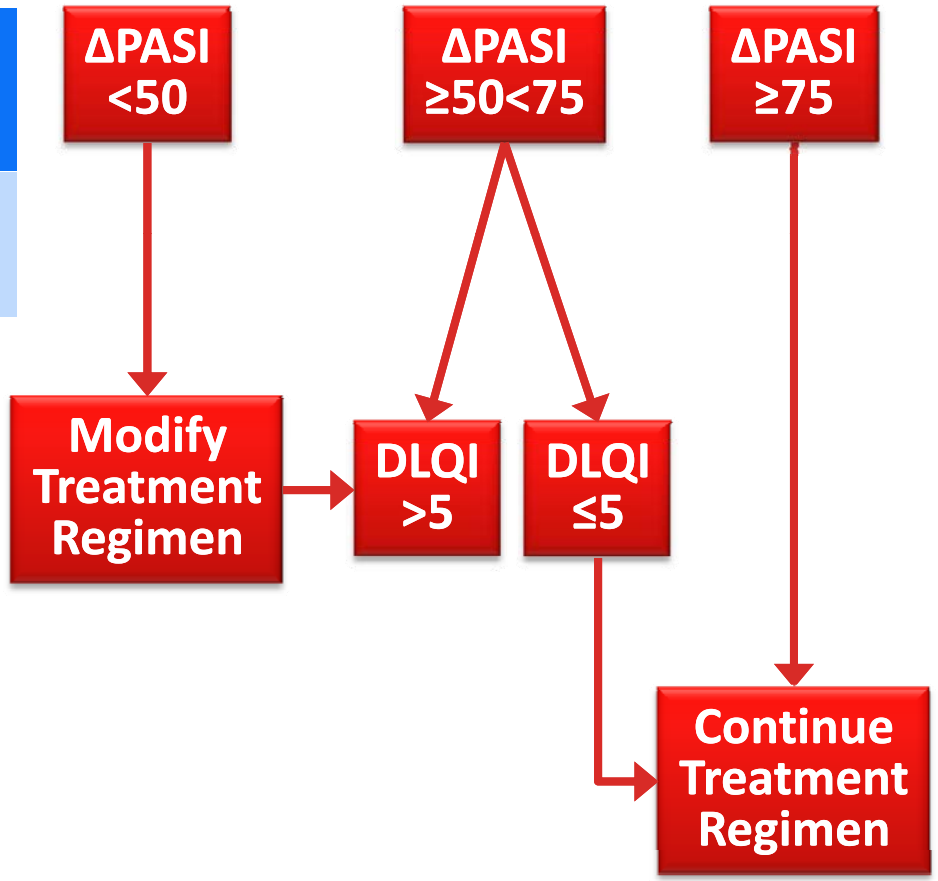
MTX, Methotrexate; PUVA; psoralen plus ultraviolet (UV)-A.

Adapted from Menter A, et al. *J Am Acad Dermatol*. 2008;58:826-850.



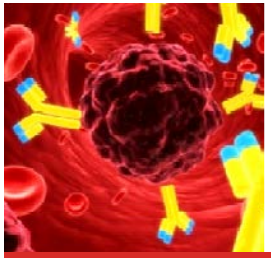
20% of Almost Clear Patients Meet DLQI Criteria for Treatment Change

DLQI	Clear	Almost Clear	*P* value
≥Moderate effect, N (%)	2 (2)	85 (20)	<0.001



DLQI – dermatology life quality index

Adapted from Mrowietz U, et al. *Arch Dermatol Res.* 2011;303:1-10.
Takeshita J, et al. *J Am Acad Dermatol*. 2014 Jun 10. [Epub ahead of print]

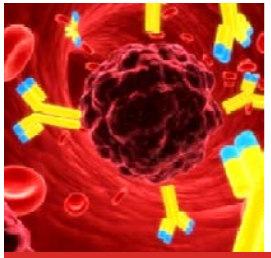


Moderate-to-Severe Psoriasis Outcomes: Clinical Trials

- Clinical-trials primary endpoints focus on PASI 75 and Physician's Global Assessment (PGA) of clear/almost clear
- Increasingly PASI 90 and 100 reported

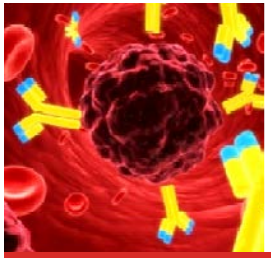
PASI – psoriasis area severity index

Adapted from Robinson A, et al. *J Am Acad Dermatol*. 2012;66:369-375. Revicki DA, et al. *Dermatology.* 2008;216:260-270. Torii H, et al. *J Dermatol*. 2012;39:253-259.



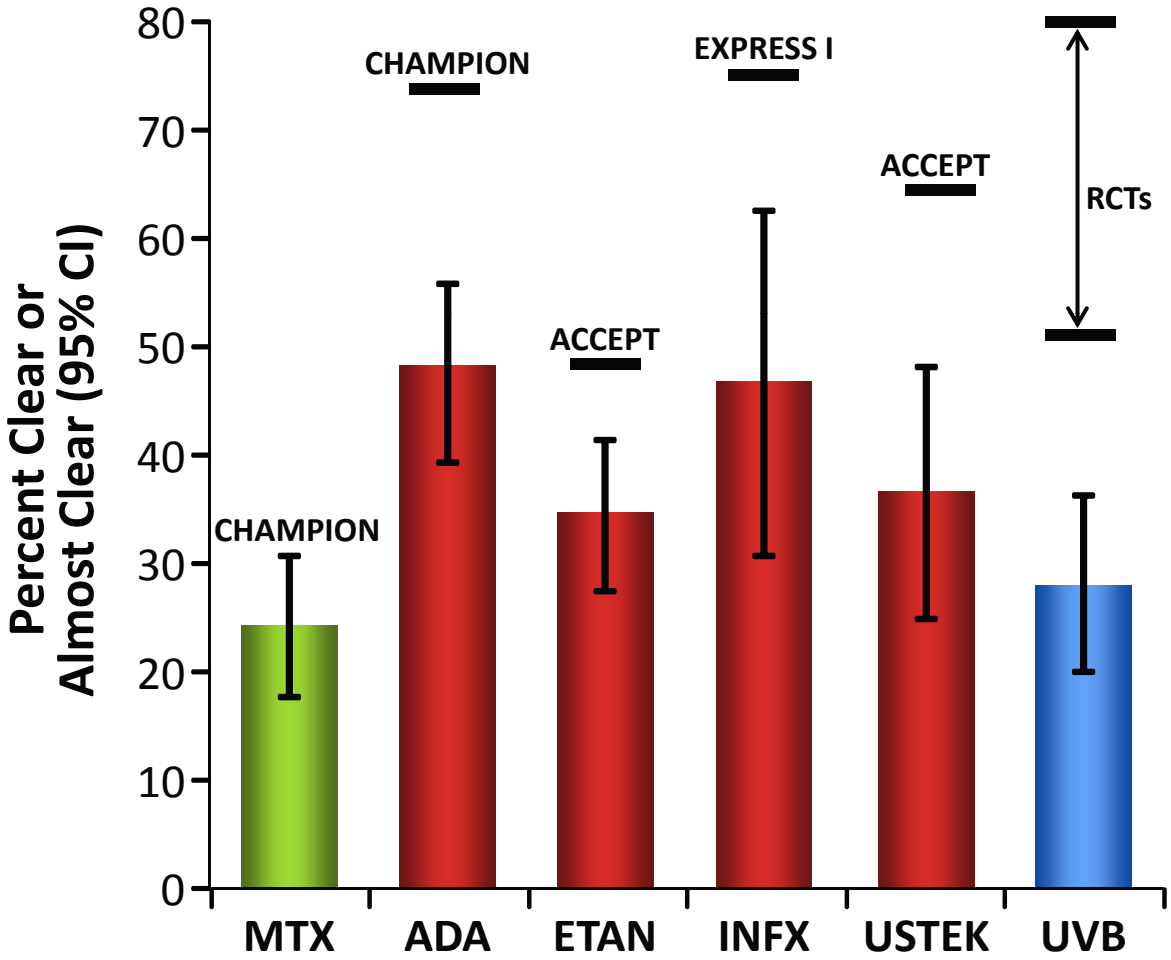
PGA: Physician's Global Assessment (Averaged Over All Lesions)

	Induration (I) or Pustulation	Erythema (E)	Scaling (S)	Physician's Static Global Assessment based upon total average (I+E+S)/3
0	no plaque elevation	no erythema or hyper-pigmentation is present	no evidence of scaling	clear; except for residual discoloration
1	minimal elevation, 0.25mm	faint erythema	minimal; fine scale on <5% of lesion	minimal; majority of lesions have individual scores for (I+E+S)/3 that average 1
2	mild elevation, 0.5mm	light red coloration	mild; fine scale predominates	mild; majority of lesions have individual scores for (I+E+S)/3 that average 2
3	moderate elevation, 0.75mm	moderate red coloration	moderate; coarse scale predominates	moderate; majority of lesions have individual scores for (I+E+S)/3 that average 3
4	marked elevation, 1mm	bright red coloration	marked; thick, nontenacious scale predominates	marked; majority of lesions have individual scores for (I+E+S)/3 that average 4
5	severe elevation, >1.25mm	dusky to deep red coloration	severe; very thick tenacious scale predominates	severe; majority of lesions have individual scores for (I+E+S)/3 that average 5



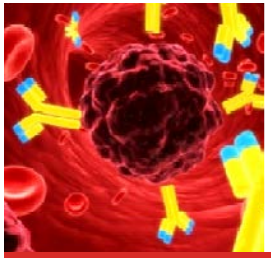
PGA Clearance: Real World vs. RCT

- Most patients fail to achieve long-term disease control
- Durable response rates are much lower in clinical practice compared to short-term RCTs



$P < 0.001$

MTX, Methotrexate; ADA, Adalimumab; Etan, Etanercept; INFX, Infliximab; USTEK, Ustekinumab; UVB, ultraviolet B.
Adapted from Gelfand JM, et al. *Arch Dermatol.* 2012;148:487. Takeshita J, et al. *J Invest Dermatol.* 2013;133:S92.



Moderate-to-Severe Psoriasis Outcomes: Clinical Practice

- Treatment goals in clinical practice remain largely undefined
- Guideline goals:
  - European: PASI 75 and DLQI ≤1 (no effect)
  - Australasian: PASI 75 and DLQI ≤5 (small effect)
- In context of PsA, minimal disease activity defined as PASI ≤1 or BSA ≤3%
- Psoriasis nontreatment, undertreatment, and treatment dissatisfaction remain significant problems in the US

Adapted from Canadian Guidelines for Management of Plaque Psoriasis 2009. Pathirana D, et al. *J Eur Acad Dermatol Venereol*. 2009;23:1-70. Smith CH, et al. *Br J Dermatol*. 2009;161:987-1019. Baker C, et al. *Australas J Dermatol*. 2013;54:148-154. Armstrong AW, et al. *JAMA Dermatol*. 2013;149:1180-1185. Kavanaugh A. *Exp Rheumatol*. 2012;30:s123-s125.