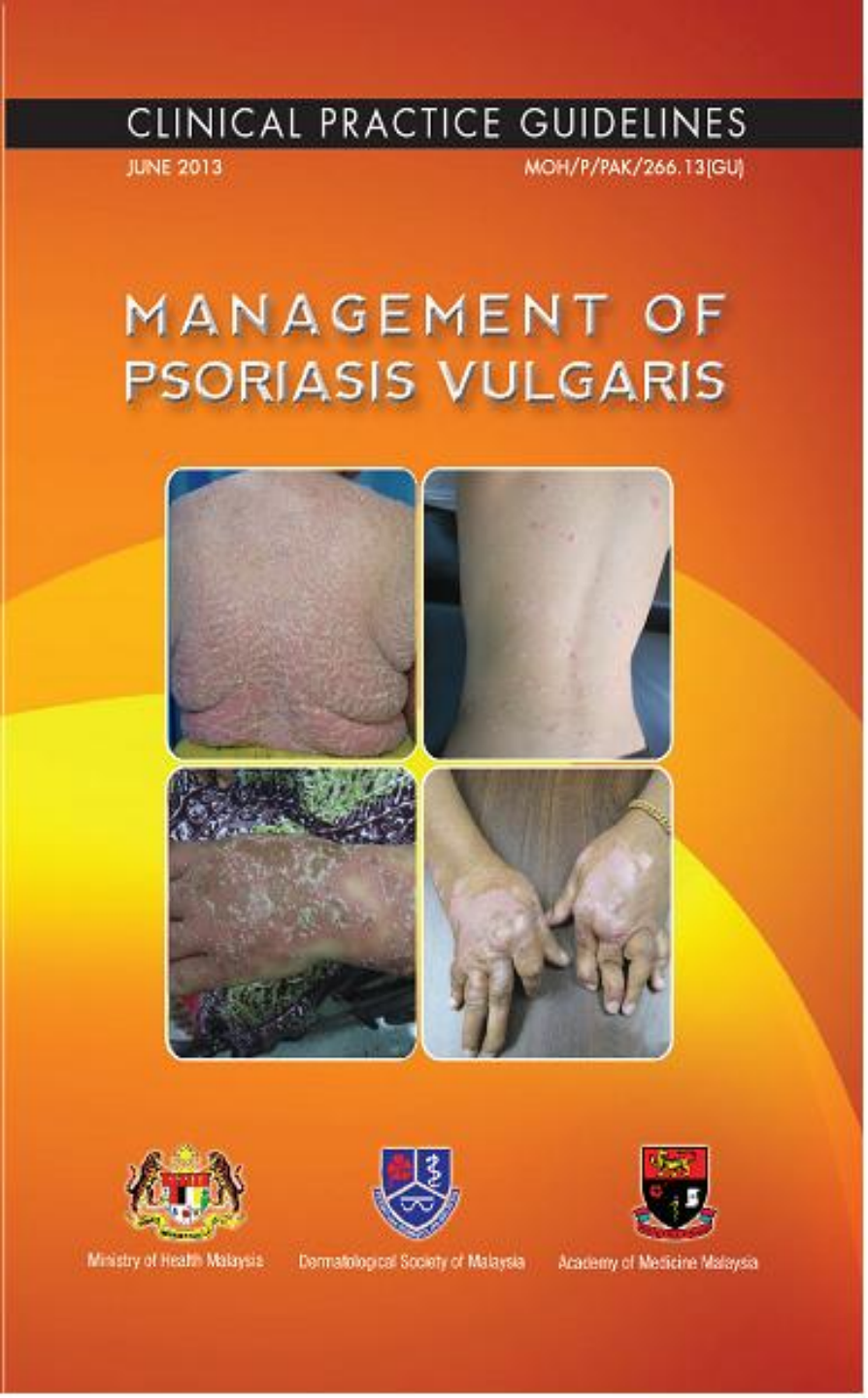


Improving care with Treatment Goals

Clinical Practice Guidelines Management of Psoriasis Development Group

Choon Siew Eng

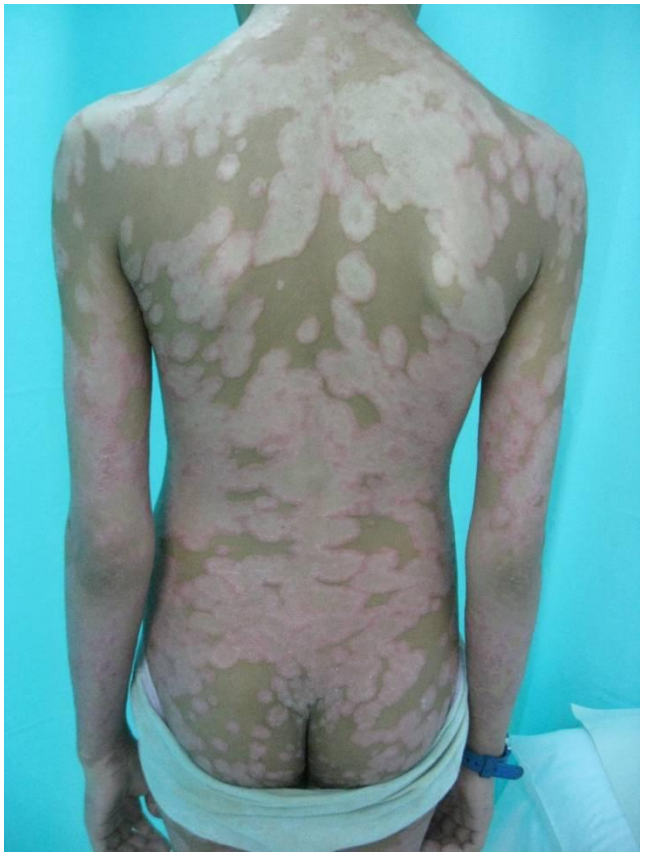
FRCP

Hospital Sultanah Aminah Johor Bahru

Malaysian CPG: Management of psoriasis vulgaris Improving care with treatment goals

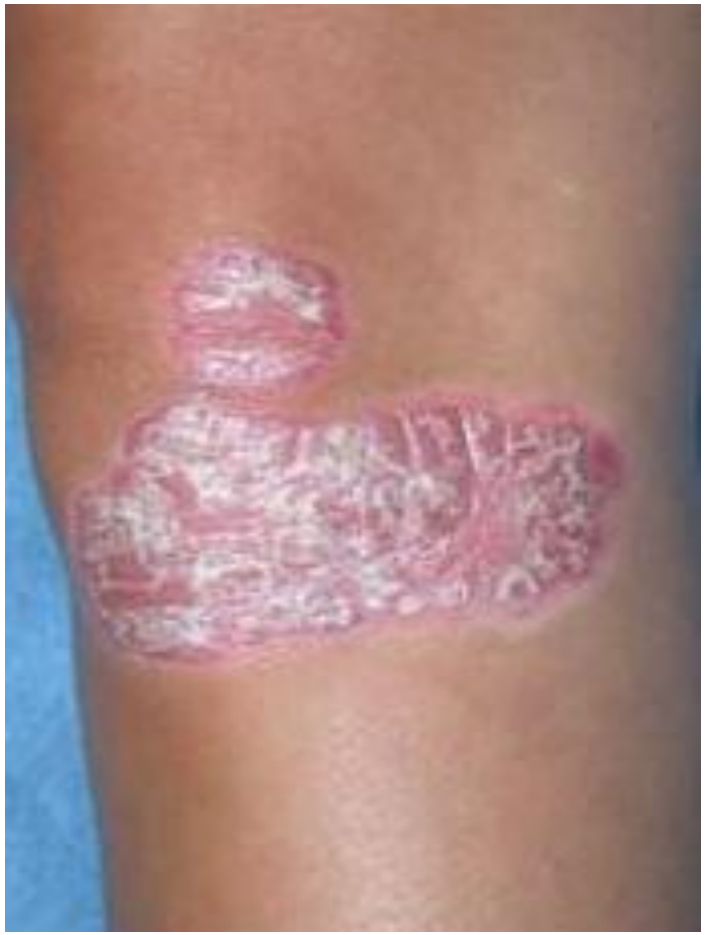
Outline of talk

- Burden of Disease
- Rationale and objective for developing our own CPG
- Tools to assess psoriasis severity
- Treatment goals
- Algorithms summarising key generic recommendations



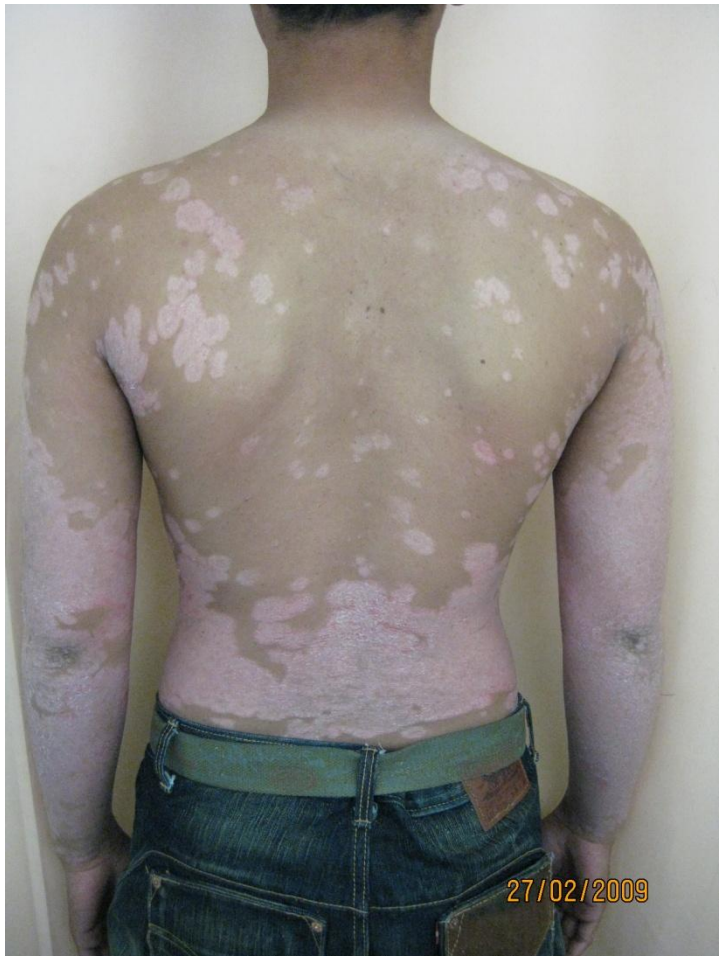
PSORIASIS

- Genetically determined
- Immune mediated
- Systemic chronic inflammatory disease
  - predominantly affects the skin and joints
- Chronic plaque psoriasis (Psoriasis vulgaris) is the most common type worldwide



Epidemiology Of Psoriasis

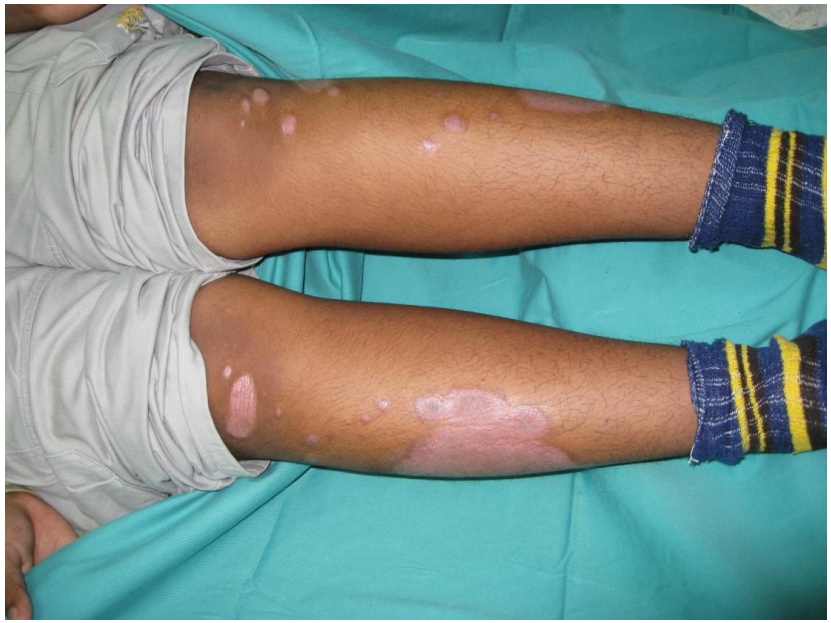
- Psoriasis occurs worldwide
  - 1 - 3% of world population
- Its prevalence varies greatly among different countries and ranges from 0.2% in China to 4.8% in Norway
- There is no population-based prevalence study on psoriasis in Malaysia
  - accounts for 2-6% of yearly dermatology new clinic attendees in Malaysia

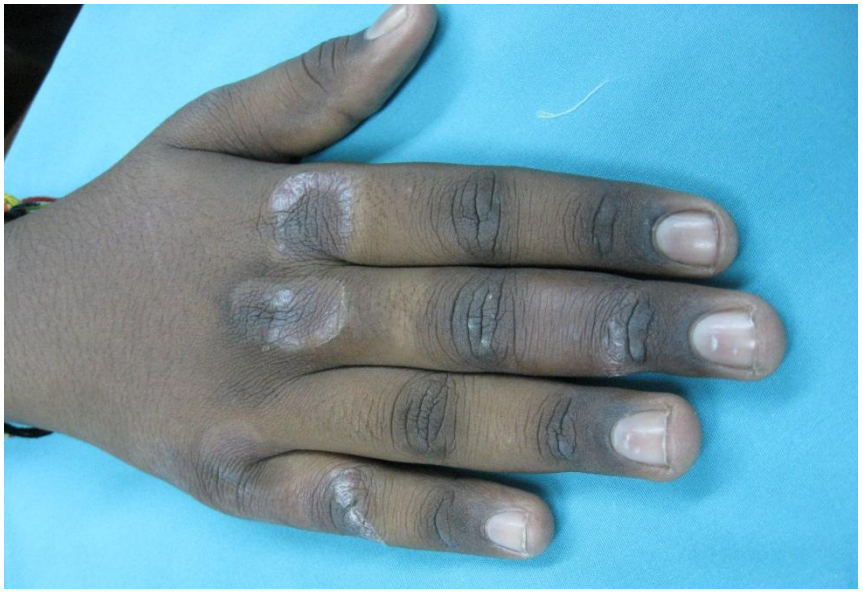


- Gudjonsson JE et.al, Clin Dermatol.2007;25:535-546.
- Tsai TF et.al J Dermatol Sci.2011 63(1):40-46.
- Choon SE et.al International J Dermatol.2013
- Siow KY et al. MJM.2004 59(3):330 - 334.

PSORIASIS

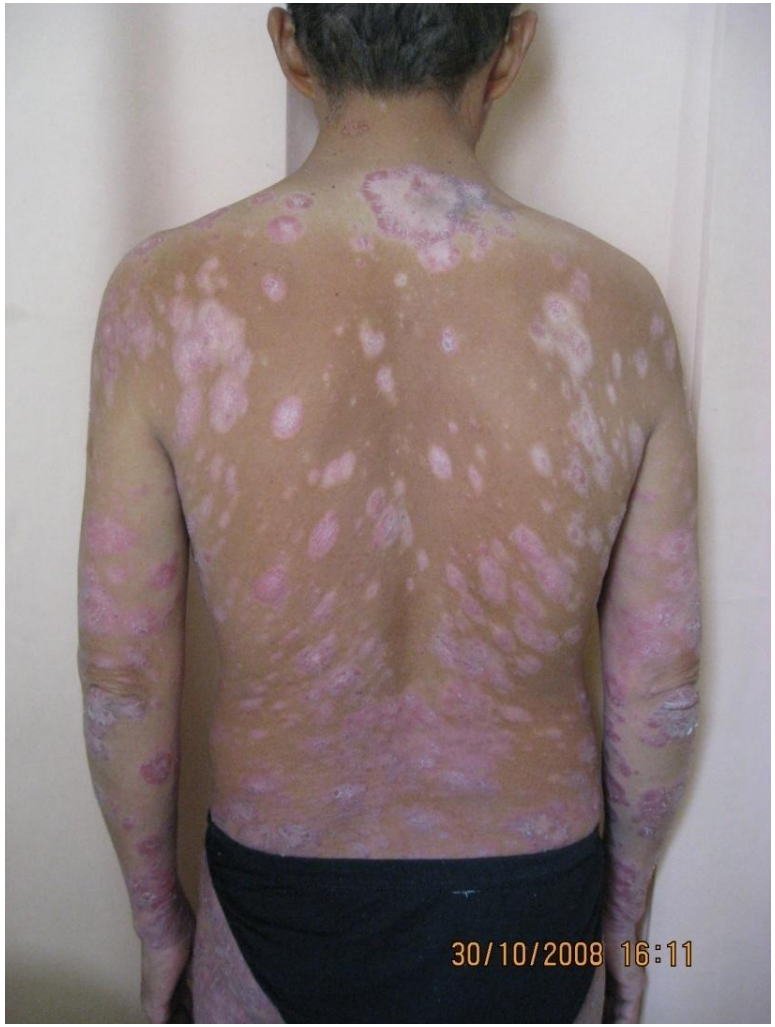
- Disease expression
  - Due to complex interactions between **genetic** and **environmental** factors





Psoriasis is a strongly inherited trait

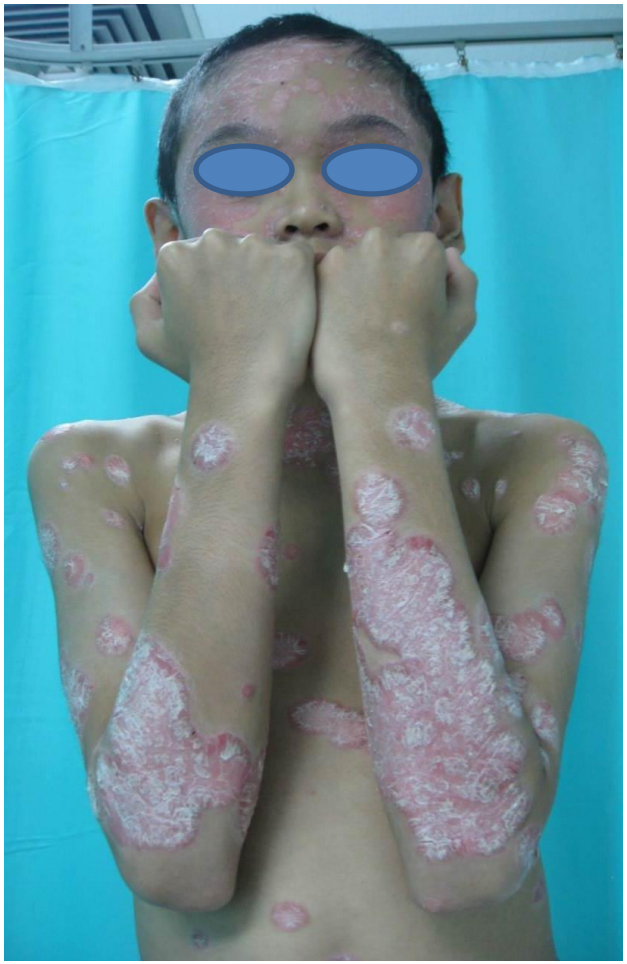
- Concordance rate
  - monozygotic twins 65%
  - dizygotic twins 20%
- Family history
  - 30% positive family history
  - 70% with childhood psoriasis has a positive family history



1. Lomholt G. Ph.D Thesis. Copenhagen, 1963. 2. Farber EM, et al. Arch Dermatol. 1974;109(2):207-11. 3. Tiilikainen A et al. Br J Dermatol. 1980; 102:179-84. 4. Trembath RC et al. Hum Mol Genet. 1997; 6:813-20. 5. Nair RP et al. Hum Mol Genet. 1997; 6:1349-56. 6. Liu Y et al. Genes Immun. 2007; 8:1-12. (REVIEW). 7. Cargill M et al. Am J Hum Genet. 2007; 80:273-90. 8. Capon F et al. Hum Genet. 2007; 122:201-6. 9. Duerr RH et al. Science. 2006; 314:1461-3. 10 Becker KG, et al. Proc Natl Acad Sci U S A. 1998;95:9979-84.

Posriasis is genetically determined

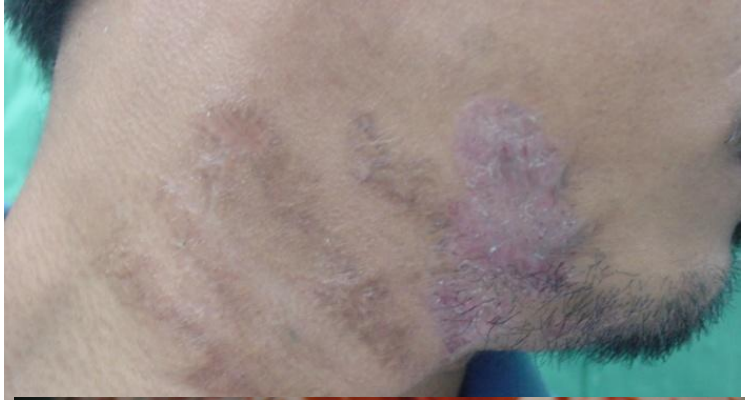
- 40 susceptibility loci
  - HLA-cw6 located on PSOR1 locus
    - 50-60 % susceptibility
  - CARD4
    - 80%
- Polymorphism at IL12B or IL23R also a risk factor
  - Polymorphism at IL23R also in Crohn's disease
  - Prevalence of Crohn's disease is 3.8-7.5 folds higher in psoriasis

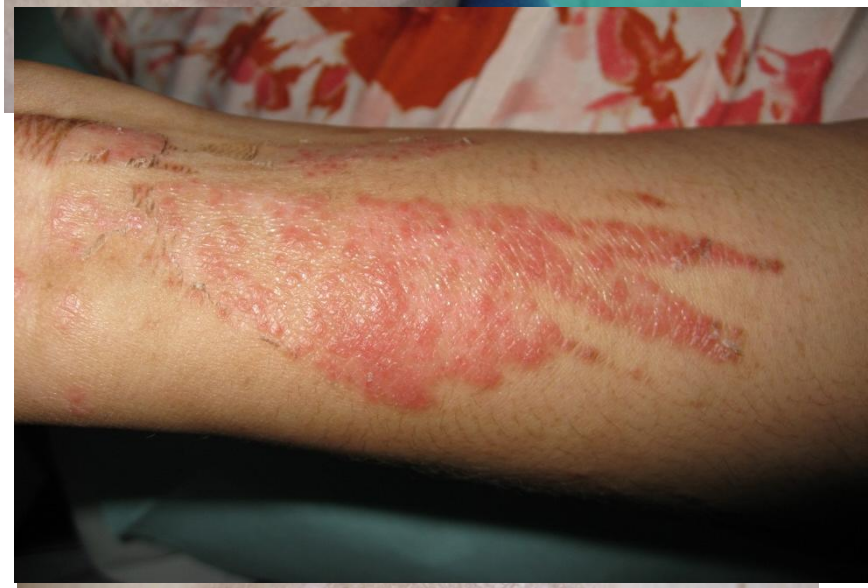


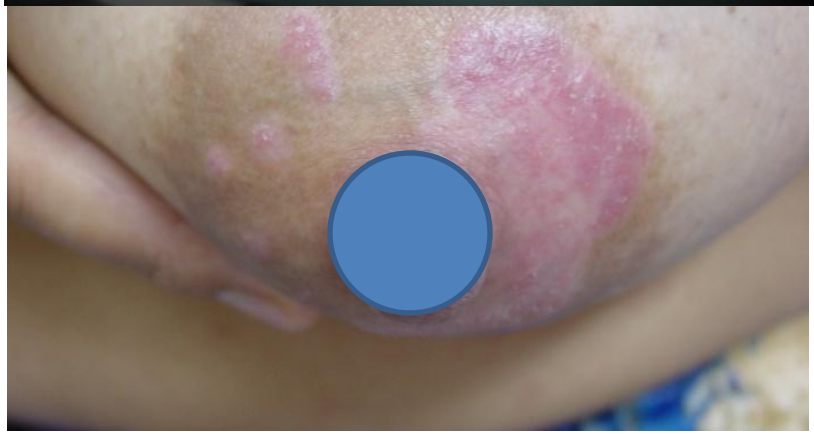
Psoriasis

Risks and aggravating Factors

- Trauma
  - Koebner's phenomenon
- Infection
    - Streptococcus, HIV, chikungunya
- Drugs
    - Lithium, beta-blockers, antimalarials, NSAIDs, ACE inhibitors, gemfibrosil, interferon, IL2, G- CSF
- Lifestyle (Smoking, Alcohol)
- Psychogenic-Stress
- Pregnancy
- Obesity

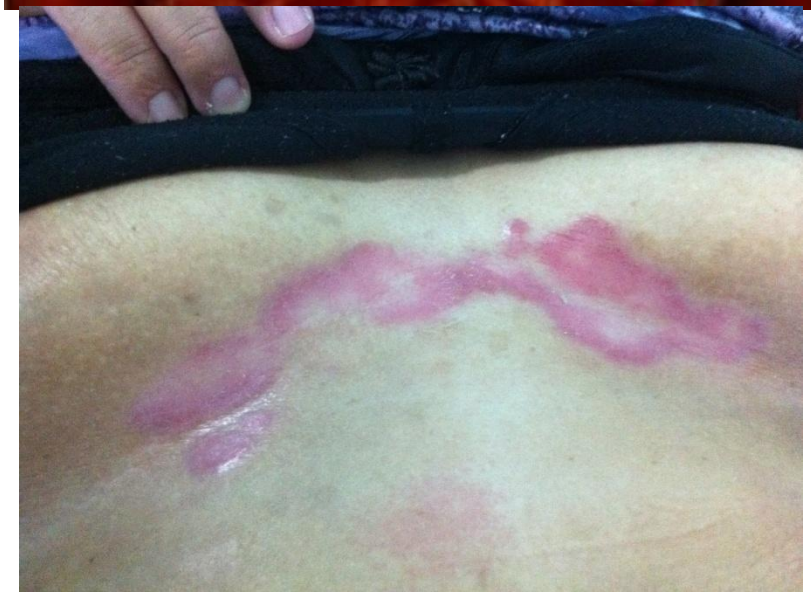






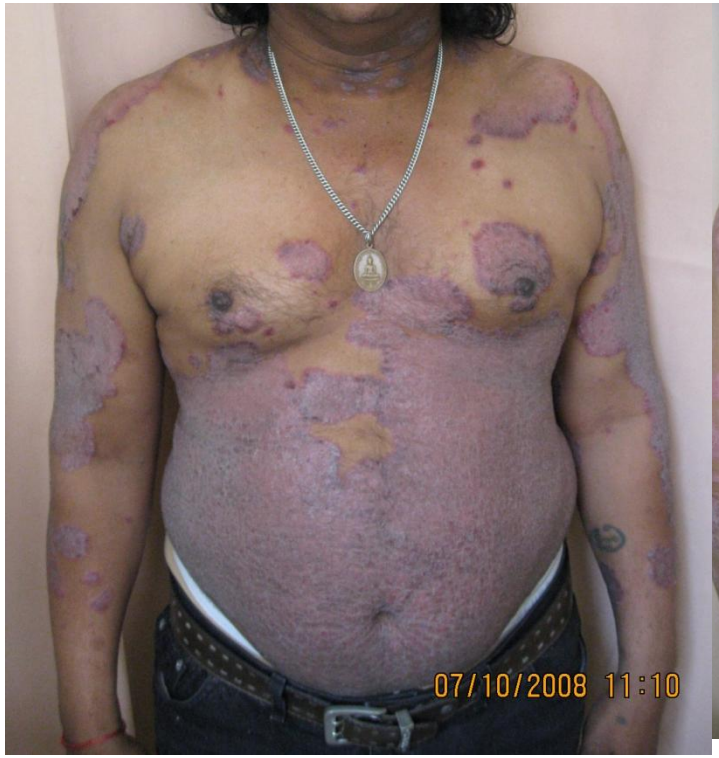
Psoriasis -clinical types

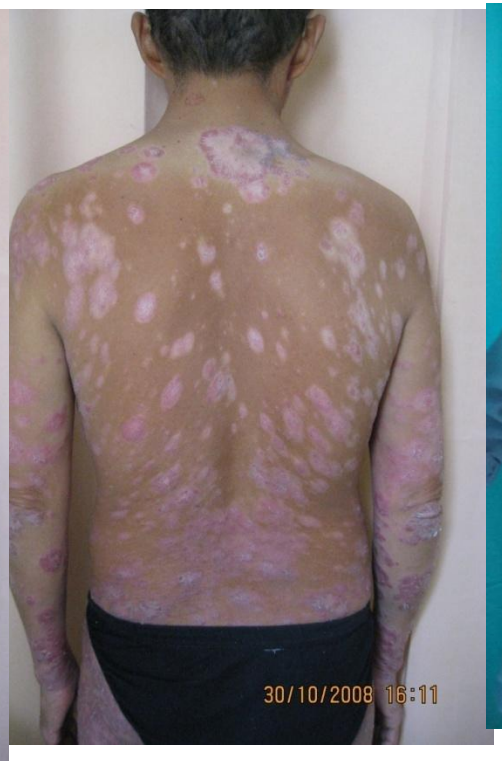
1. Classic plaque psoriasis
2. Guttate psoriasis
3. Inverse psoriasis
4. Erythrodermic psoriasis
5. Pustular psoriasis
    - Localised pustular psoriasis
        - Of palms and soles
        - Acrodermatitsi continua suppurativa
    - Generalised pustular psoriasis of von Zumbusch

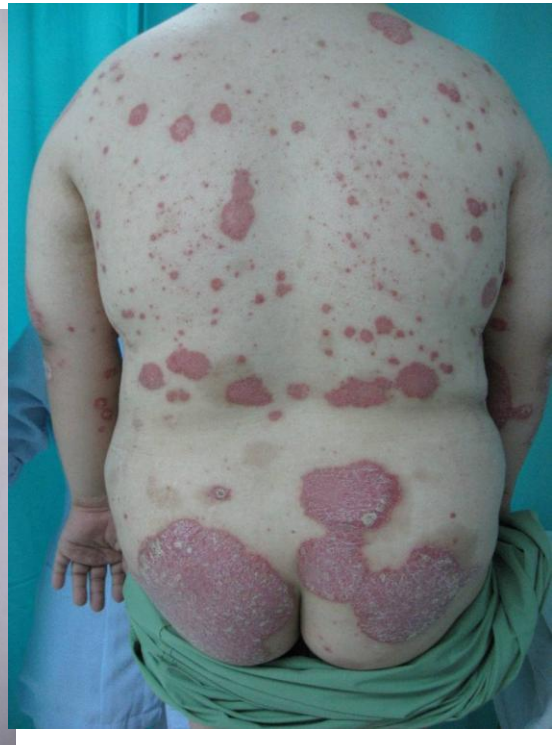


PSORIASIS VULGARIS

- 8664 patients in our National psoriasis registry till June 2013
  - 85% with psoriasis vulgaris
- Physically and mentally disabling

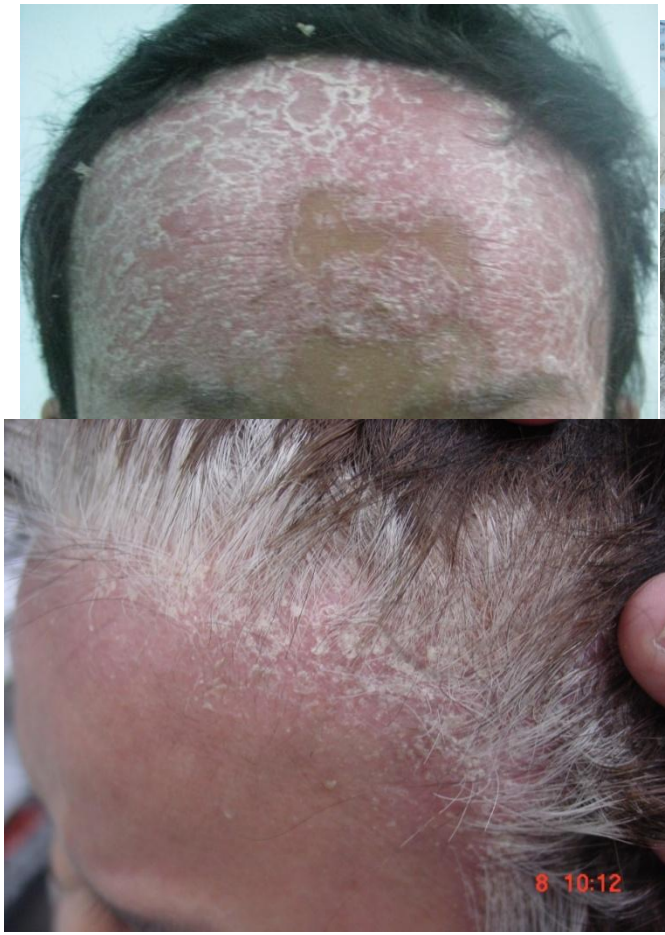




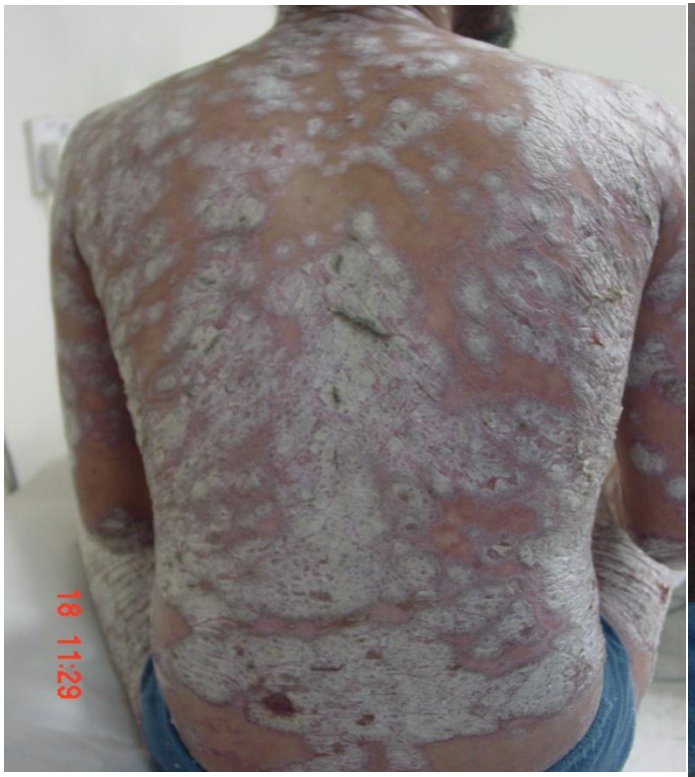


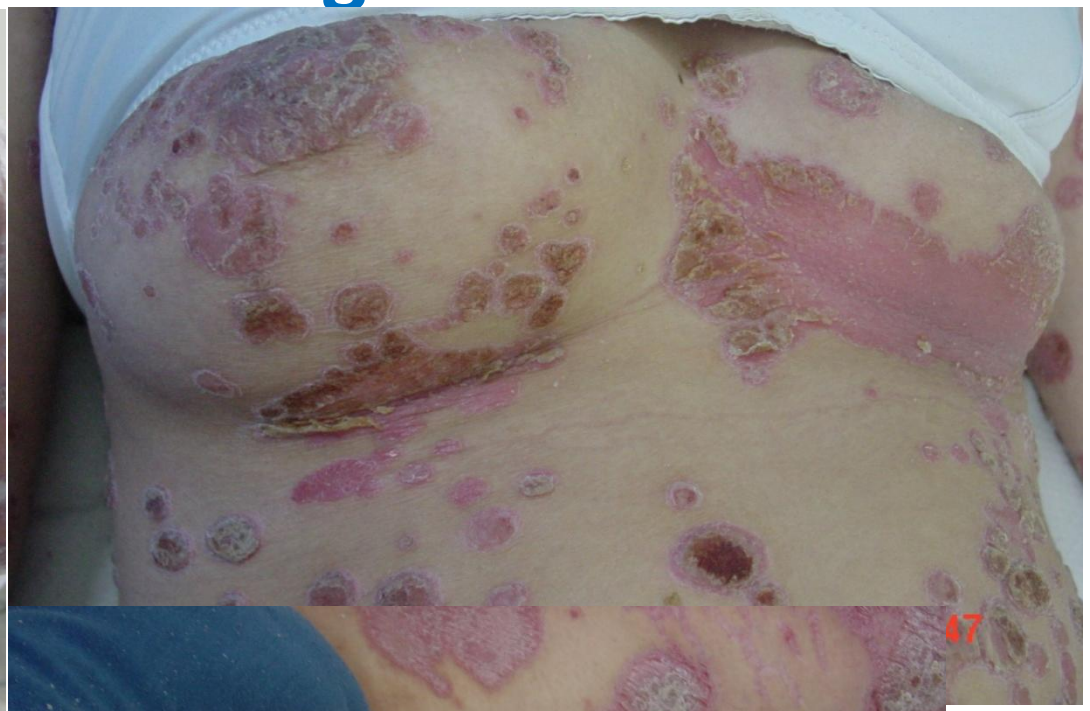
Psoriasis vulgaris

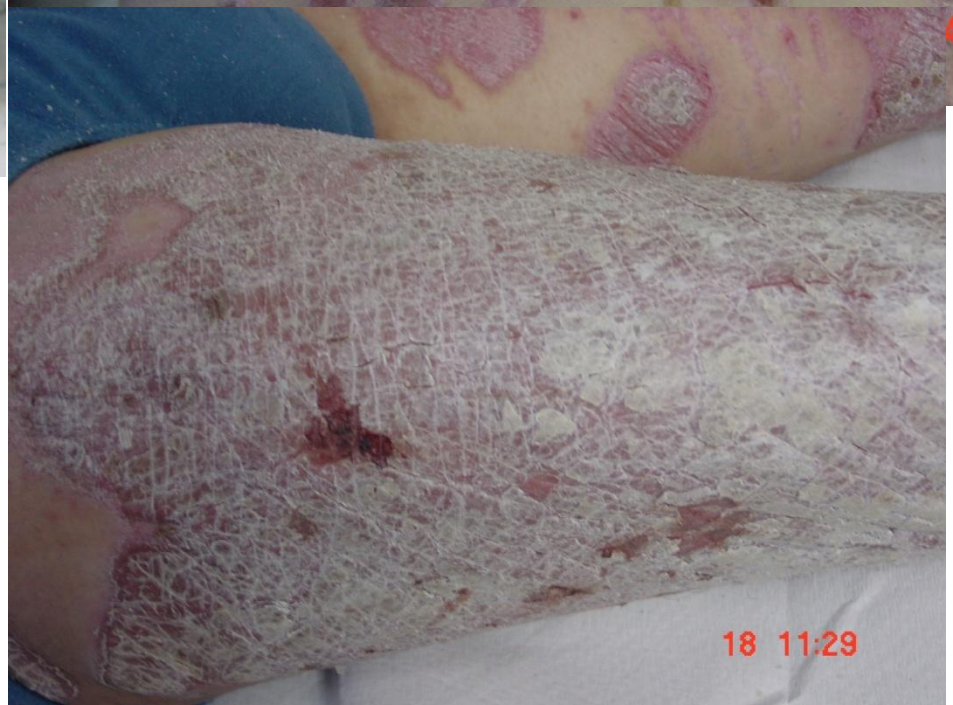
A highly visible disease



Psoriasis Vulgaris



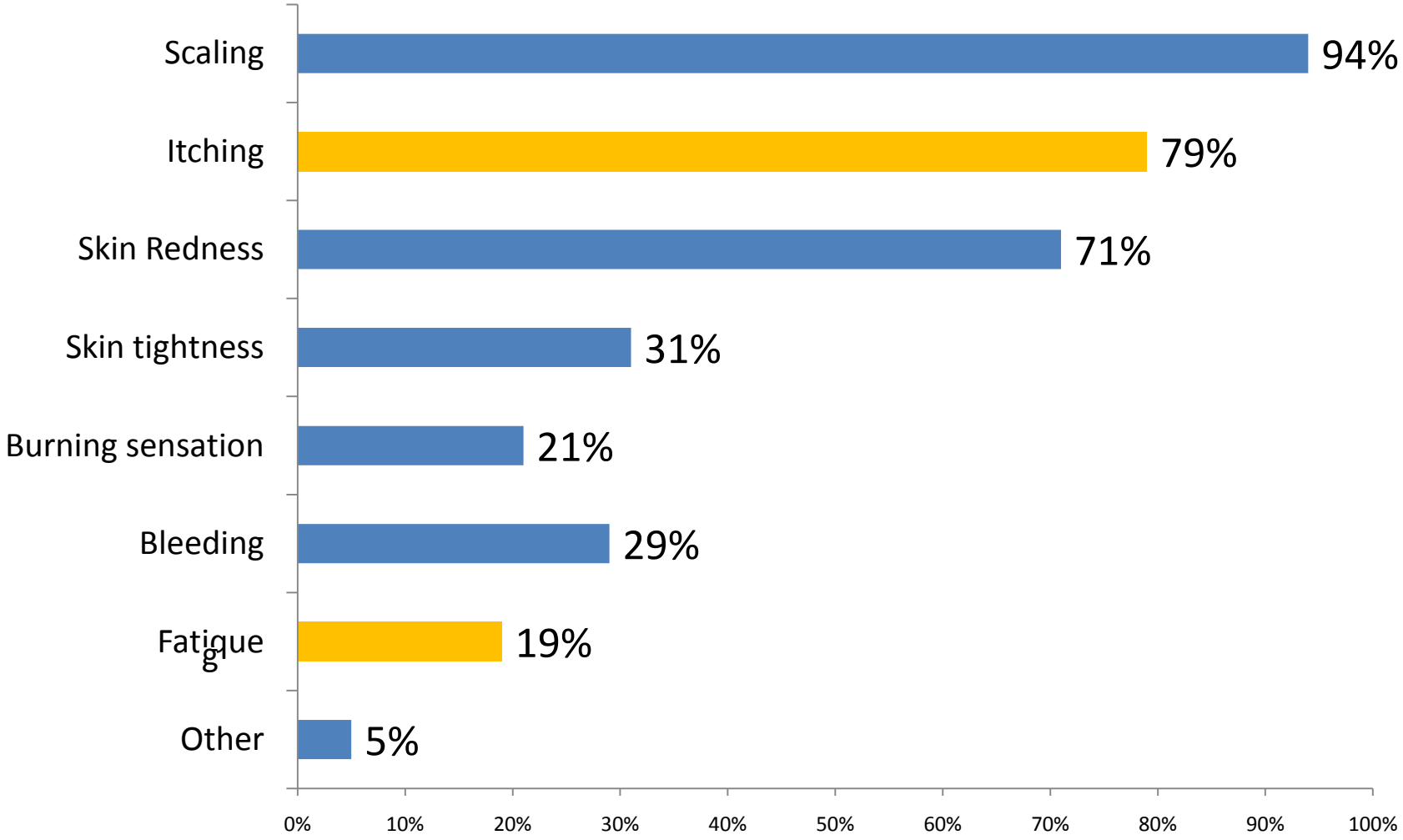




- Physical discomfort
  - Pruritus
  - Scaling
  - Tightness
  - Pain
  - Bleeding

Psoriasis symptoms

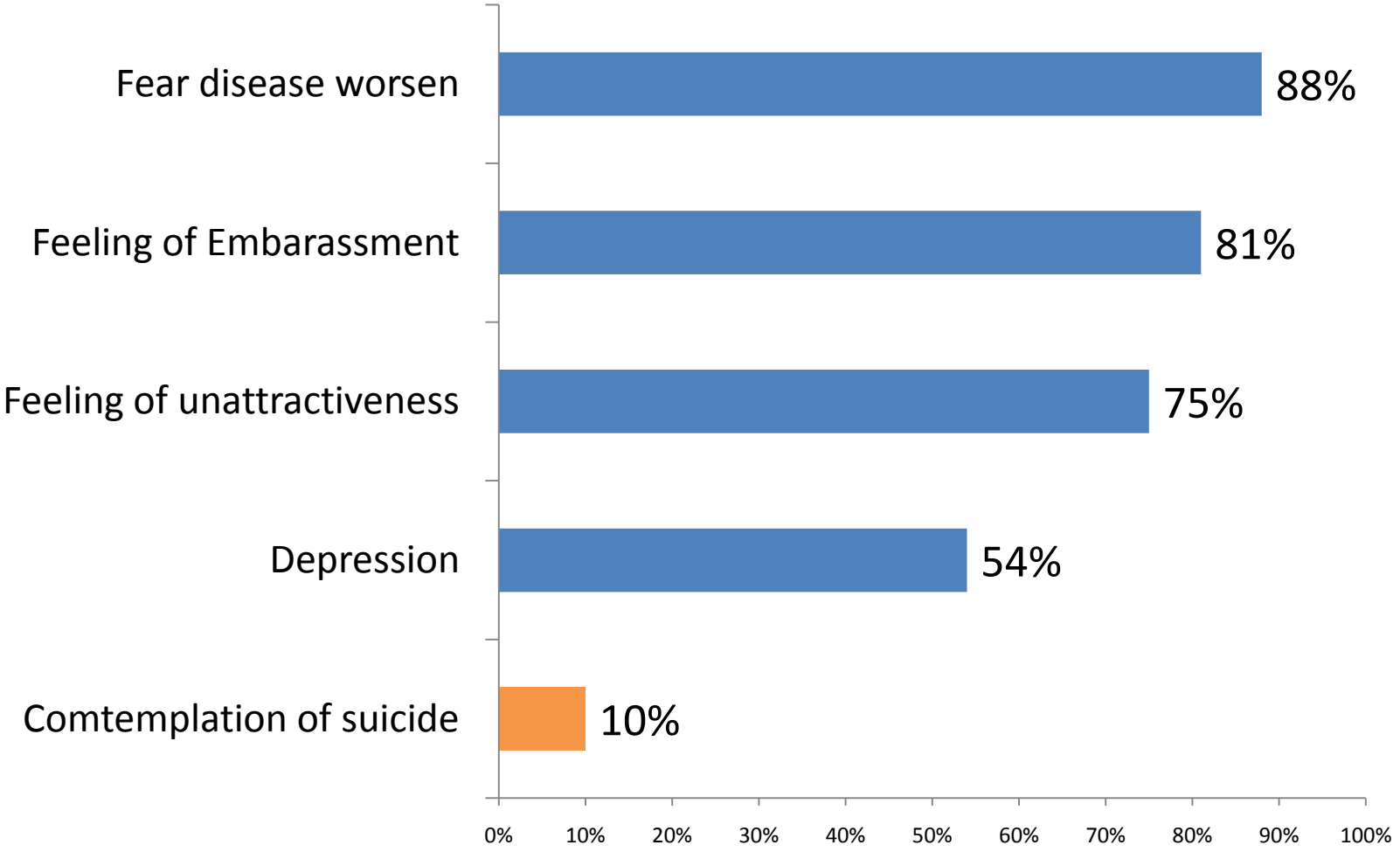
17 425 respondents



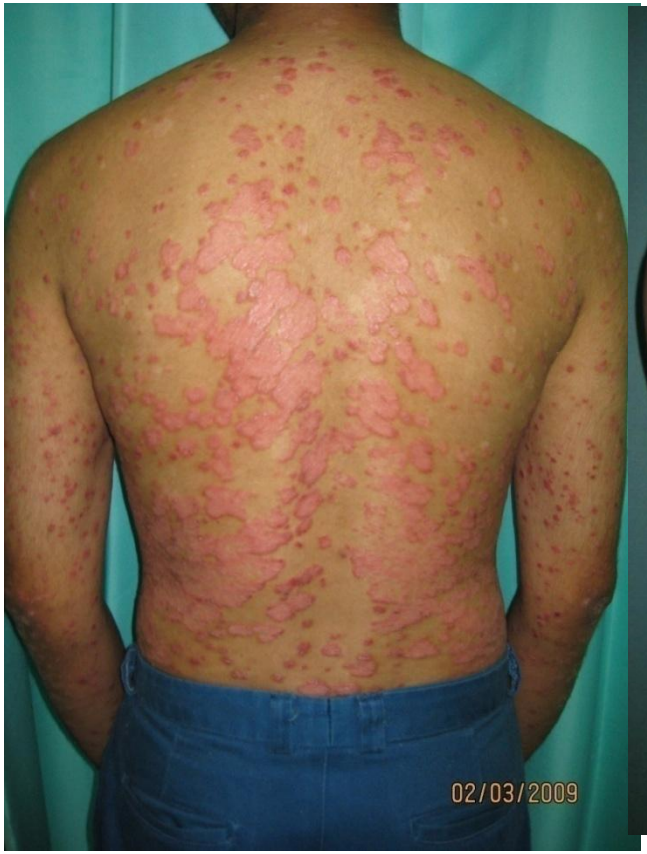
Kruger G et al. Arch dermatol 2001;137:280-4

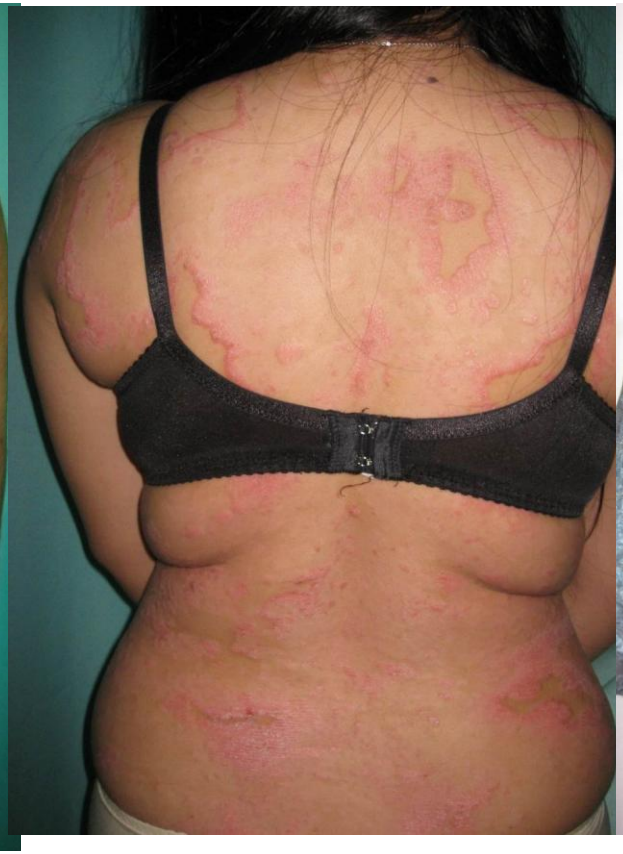
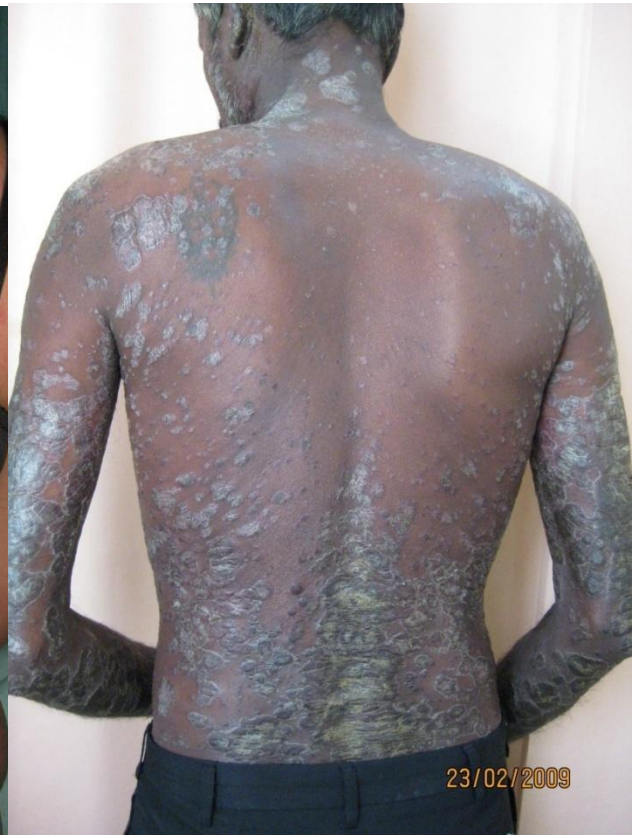
Emotional impact of Psoriasis

17 425 respondents



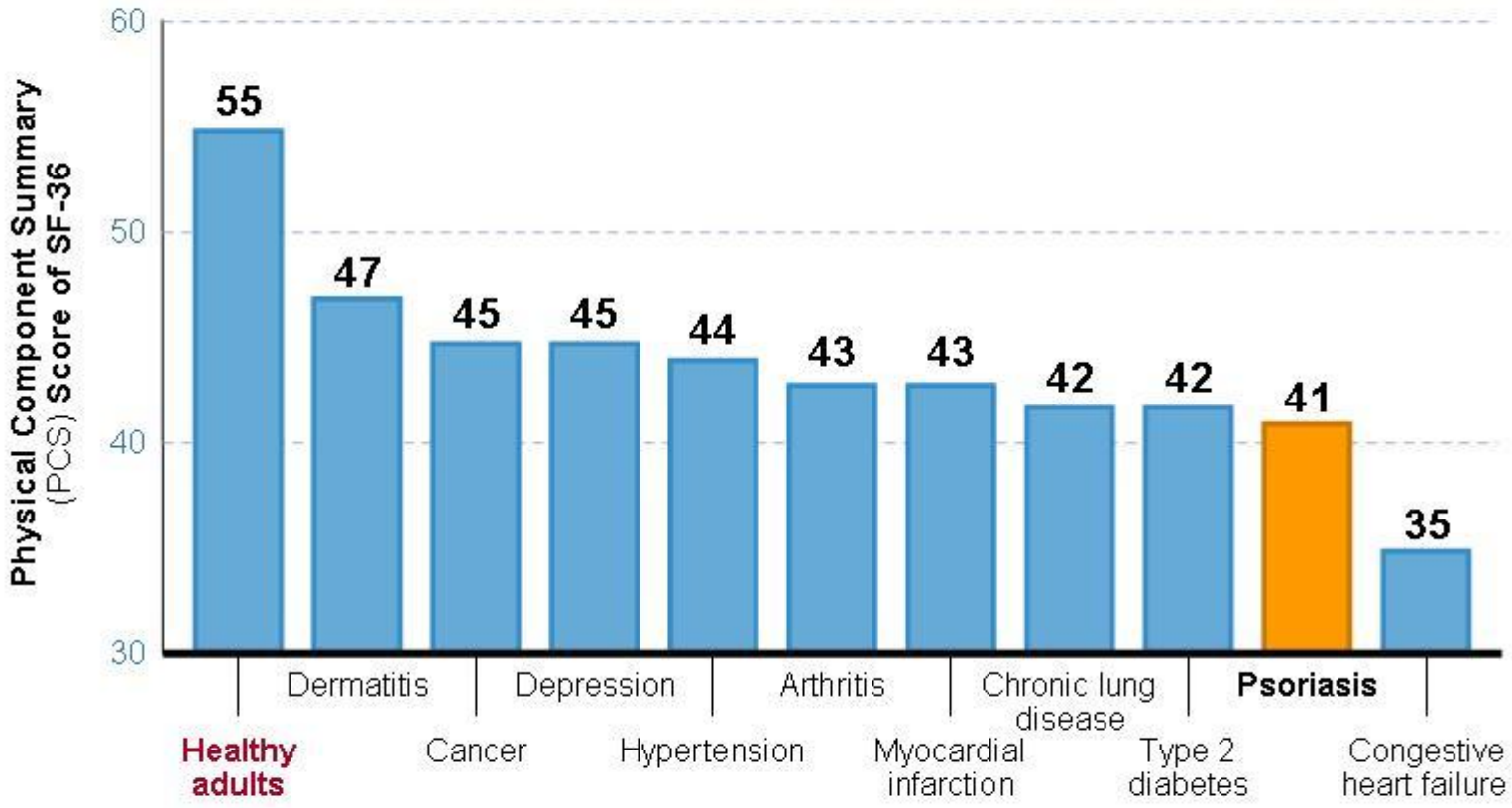
Kruger G et al. Arch dermatol 2001;137:280-4



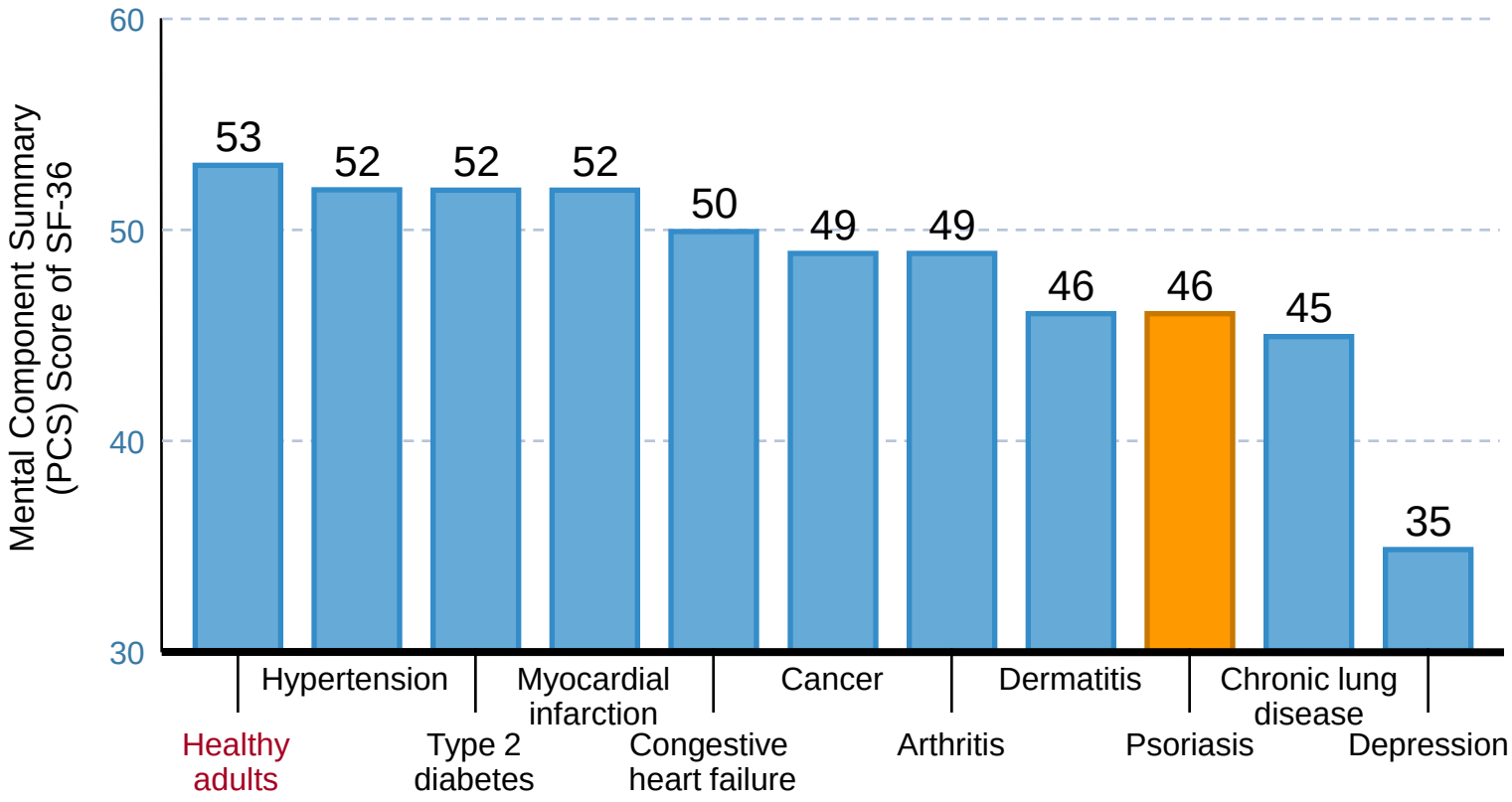
- Psoriasis causes as much disability as other major medical diseases such as cancer, heart disease, diabetes, hypertension, arthritis and depression. Weiss Sc, et al. 2002, level III; Rapp SR, et al. 1999, level III

Impact of psoriasis on physical health (SF36)



1. Rapp SR et al. J Am Acad Dermatol. 1999; 41:401.

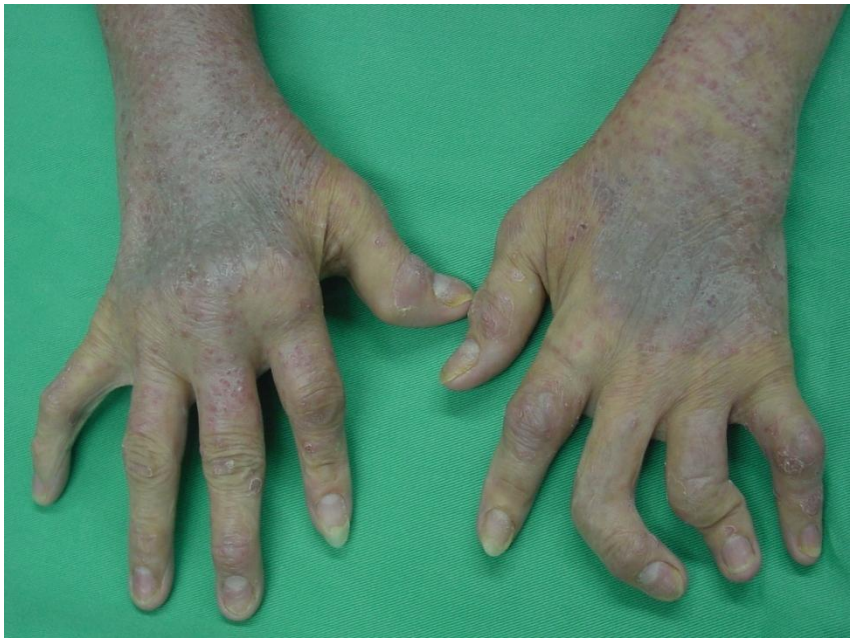
Impact of psoriasis on mental health

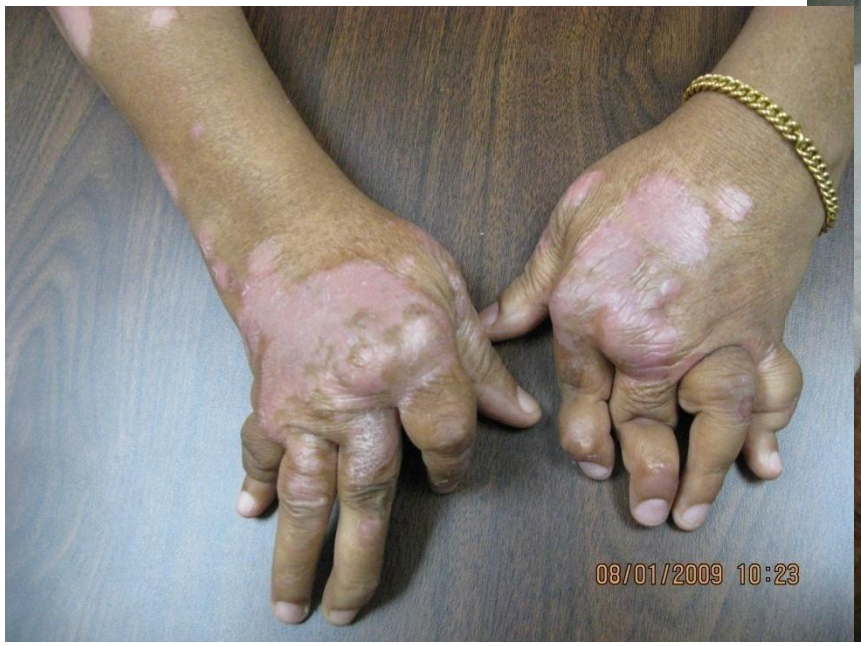


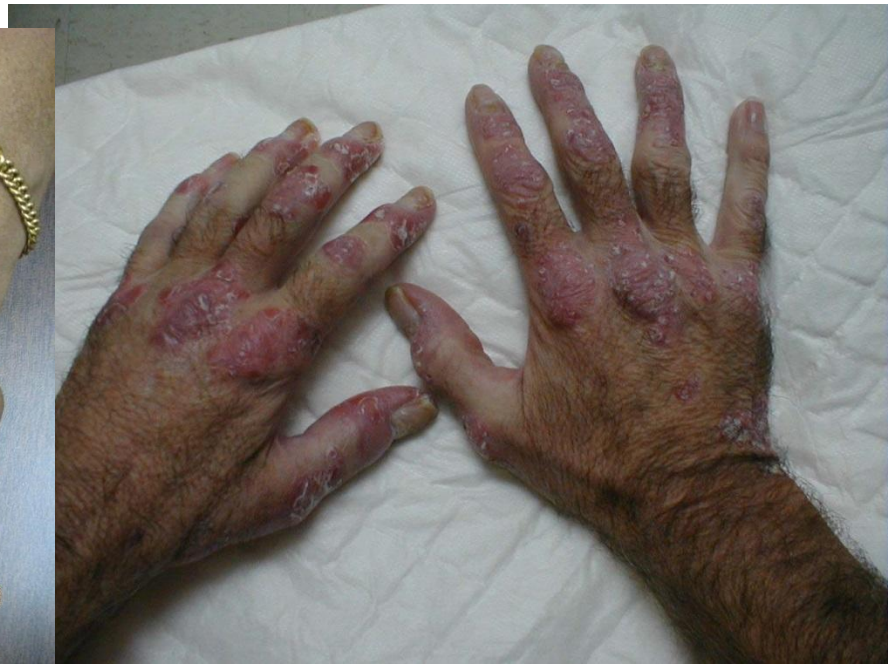
1. Rapp SR et al. J Am Acad Dermatol. 1999; 41:401.

Psoriatic Arthritis

- Affects 6% - 42%
- Skin disease precedes arthritis by about 10 years in up to 85%
- 50% deformed within 2 years
- Early recognition and prompt treatment of arthritis prevent deformity

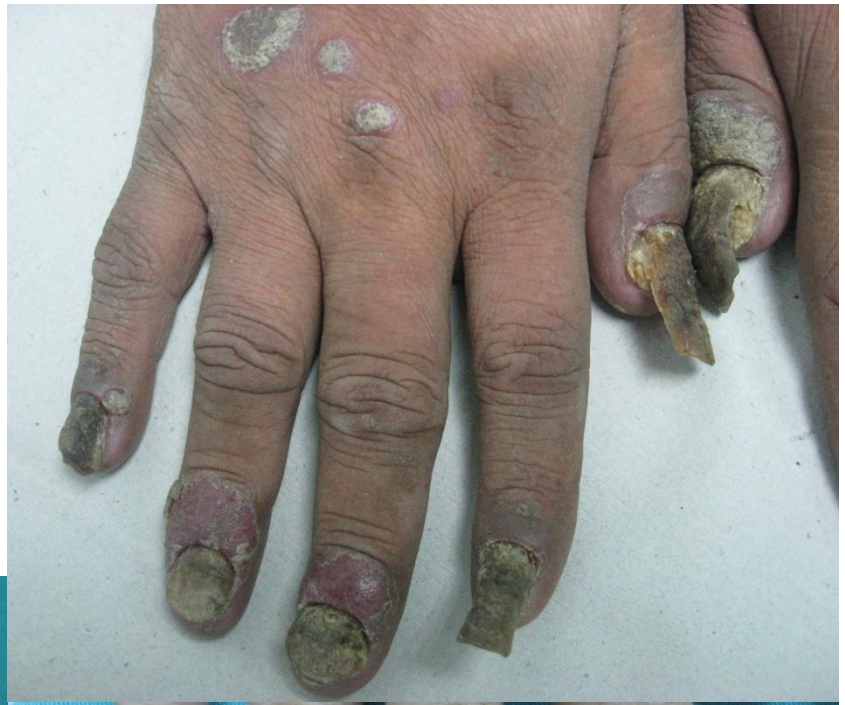


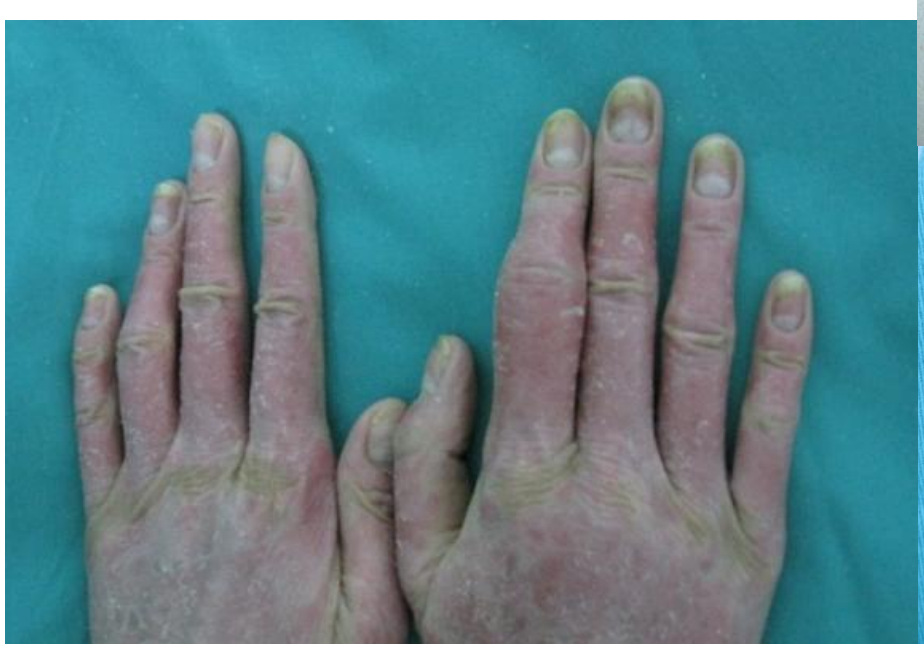


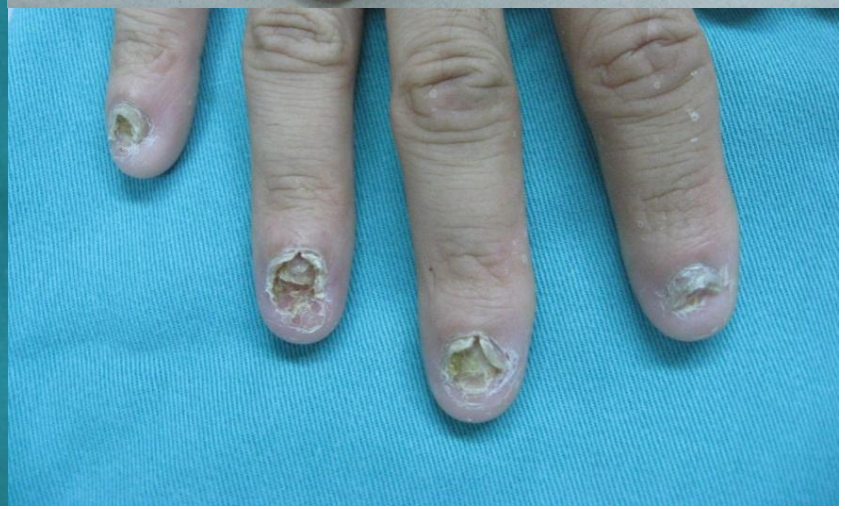


Nail Changes in Psoriasis

- 25% to 50%
- Pitting
- Onycholysis
- Subungual hyperkeratosis
- Discolouration
- Total dystrophy

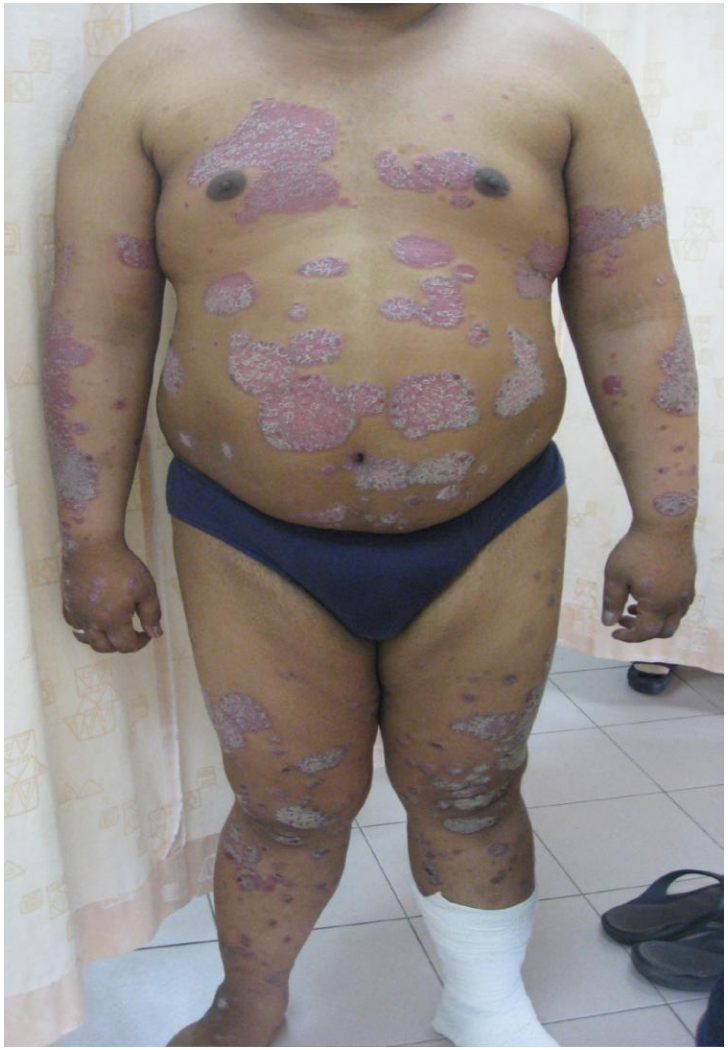






Psoriasis : chronic systemic inflammatory disease

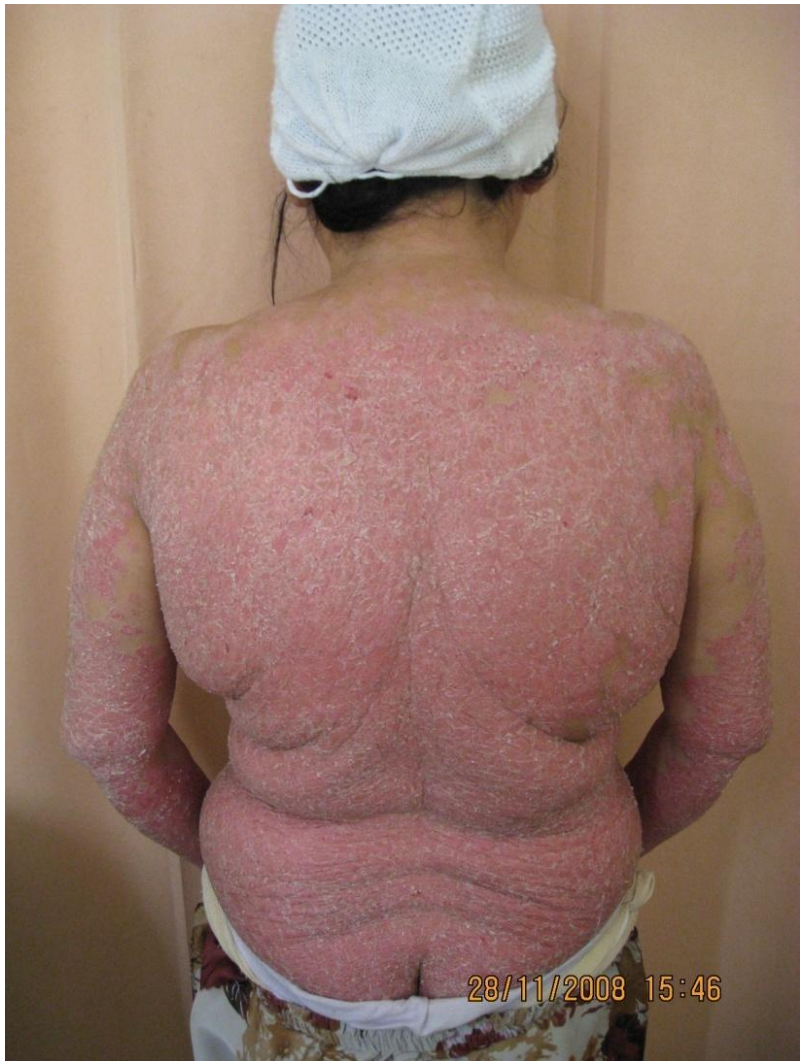
- Increased risk of cardiovascular morbidity and mortality
- Metabolic syndrome
  - Obesity, diabetes, dyslipidemia, hypertension
- Cardiovascular diseases
  - Myocardial infarct
  - Stroke
- Lymphoma
  - Hodgkin's lymphoma and CTCL
- Non-melanoma skin cancer
- Psychiatric/psychologic disorders
- Increased all-cause mortality



1. Herron MD, et al. Arch Dermatol. 2005; 141:1527-34. 2. Henseler T, et al. J Am Acad Dermatol. 1995;32:982-6. 3. Gelfand JM, et al. JAMA. 2006; 296:1735-41. 4. Mallbris L, et al. Eur J Epidemiol. 2004;19:225-30. 5. Gupta MA, Gupta AK. Br J Dermatol. 1998;139:846-50. 6. Gelfand JM, et al. Arch Dermatol. 2007; 143:1493-9.

Psoriasis and Life Expectancy

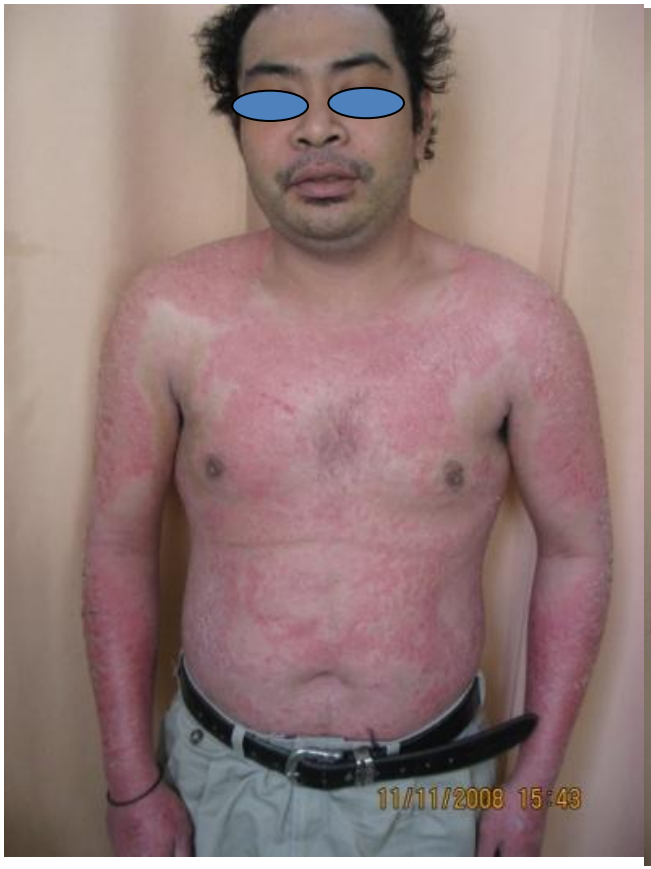
- Patients with **severe** psoriasis
  - 3 fold increased risk of developing MI
  - 3-4 year decrease in life expectancy, similar to severe hypertension
    - **Men 3.5 yrs**
    - **Women 4.4 yrs**

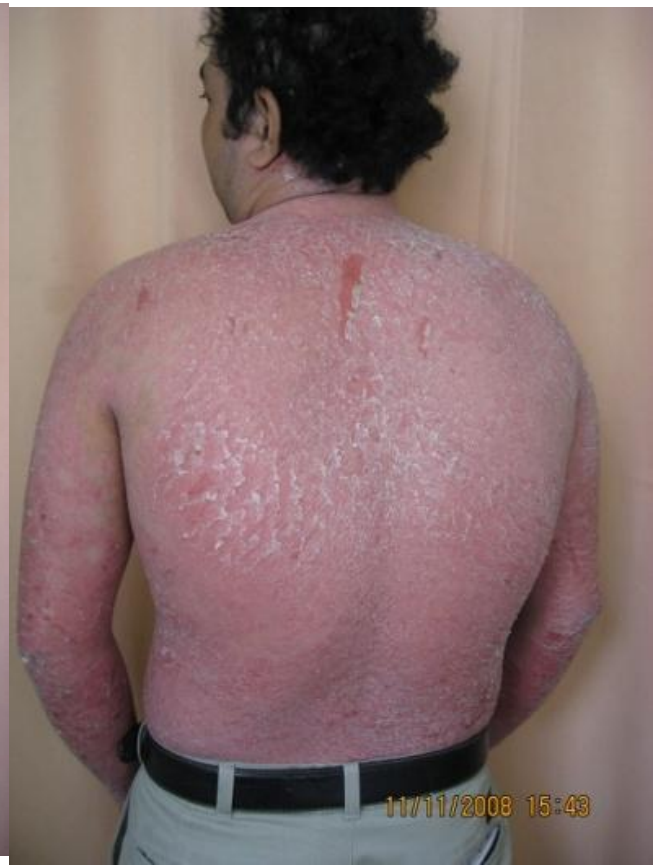


Mehta NN, et al. 2011, level II-2; Mehta NN, et al. 2010; level II 2; Gelfand JM, et al. 2006, level II-2

Shorter lifespan in severe psoriasis

- Risk of myocardial infarct and associated mortality highest in young patients with severe psoriasis





Controlling chronic inflammation of psoriasis with systemic agents or biologics **reduces** cardiovascular co-morbidities & mortality

1. Ahlehoff O et al.Cardiovascular disease rates in patient with severe psoriasis treated with systemic antinflammatory drug: a Danish real world cohort study. J int Med 2013;273:197-204
2. Wu JJ et al. Association Between Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients With Psoriasis *Arch Dermatol.* 2012;148(11):1244-1250
3. Prodanovich S et al. Association of Psoriasis With Coronary Artery, Cerebrovascular, and Peripheral Vascular Diseases and Mortality. Arch Dermatol, 2009. 145(6):700-703.
4. Prodanovich S et al. Methotrexate reduces incidence of vascular diseases in veterans with psoriasis or rheumatoid arthritis. J Am Acad Dermatol 2005.52:262-267.
5. Wu Y, Mills D, Bala M. Psoriasis: cardiovascular risk factors and other disease comorbidities. J Drugs Dermatol, 2008 7(4):373-377

ONLINE FIRST

Association Between Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients With Psoriasis

Jashin J. Wu, MD; Kwun-Yee T. Poon, MS; Jennifer C. Channual, MD; Albert Yuh-Jer Shen, MS, MD

Retrospective cohort study

- 8845 patients with psoriasis
  - 1667 on TNF inhibitor therapy
  - 2097 on oral agent/phototherapy
  - 5075 topical therapy
- Both the TNF-inhibitor and oral agent/phototherapy cohorts had a significantly reduced risk for myocardial infarction
- The incidence of MI
  - TNF inhibitor : 3.05 per 1000 patient-years
  - Oral agent/phototherapy : 3.85 per 1000 patient-years
  - Topical therapy : 6.73 per 1000 patient-years

Wu JJ et al. *Arch Dermatol.* 2012;148(11):1244-1250

ONLINE FIRST

Association Between Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients With Psoriasis

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Table 3. Pairwise Comparison of MI Rate Ratios

Pair	MI Rate Ratio (95% CI)	*P* Value
TNF inhibitors vs topical agents	0.45 (0.30-0.68)	<.001
Oral agents/phototherapy vs topical agents	0.57 (0.41-0.81)	<.001
TNF inhibitors vs oral agents/phototherapy	0.79 (0.49-1.28)	.34

Abbreviations: MI, myocardial infarction; TNF, tumor necrosis factor.

Wu JJ et al. *Arch Dermatol.* 2012;148(11):1244-1250

Cardiovascular disease event rates in patients with severe psoriasis treated with systemic anti-inflammatory drugs: a Danish real-world cohort study

O. Ahlehoff[1,2], L. Skov[3], G. Gislason[1], J. Lindhardsen[1], S. L. Kristensen[1], L. Iversen[4], S. Lasthein[5], R. Gniadecki[6], T. N. Dam[7], C. Torp-Pedersen[1] & P. R. Hansen[1]

From the [1]Department of Cardiology, Copenhagen University Hospital Gentofte, Hellerup; [2]Department of Cardiology, Copenhagen University Hospital Roskilde, Roskilde; [3]Department of Dermatology, Copenhagen University Hospital Gentofte, Hellerup; [4]Department of Dermatology, Aarhus University Hospital, Aarhus; [5]Department of Dermatology, Odense University Hospital, Odense; [6]Department of Dermatology, Copenhagen University Hospital Bispebjerg, Bispebjerg; and [7]Department of Dermatology, Copenhagen University Hospital Roskilde, Roskilde, Denmark

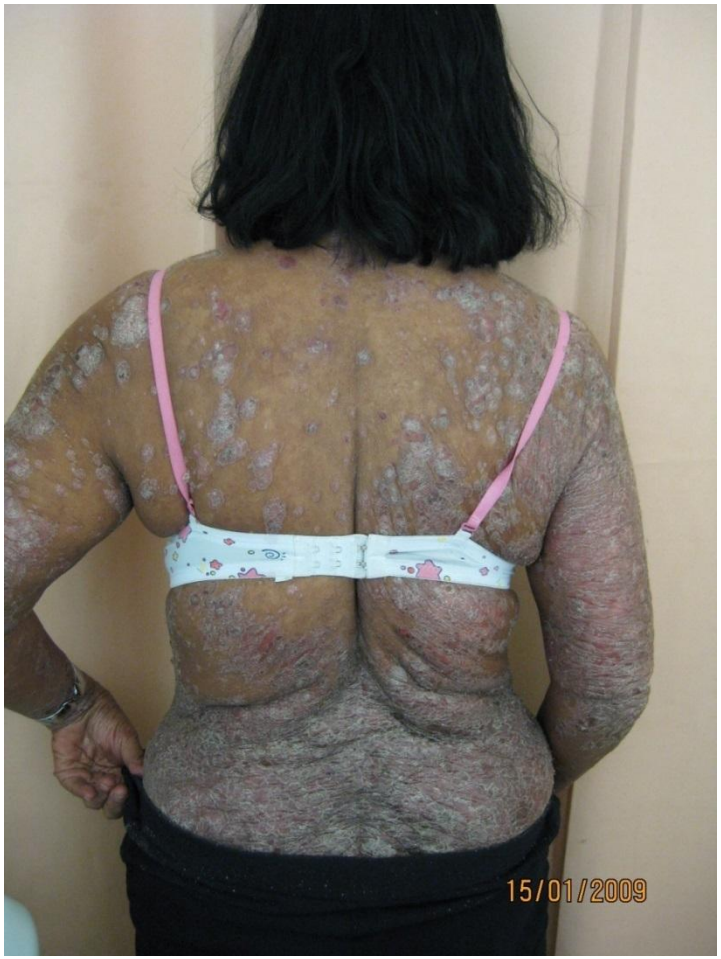
- Danish nationwide retrospective cohort study
- 893 patients on biologics, 799 patients on methotrexate with other antipsoriatic therapy
- Inicidence rate per 1000 patient-years for the composite end-point of death, myocardial infarction and stroke
  - 6.0 (95% CI 2.7–13.4) for biologics
  - 17.3 (95% CI 12.3–24.3) for Methotrexate
  - 44.5 (95% CI 34.6–57.0) other therapies
- Hazard Ratio adjusted for age and sex
  - 0.28 (95% CI 0.12–0.64) for biologics vs other therapy
  - 0.65 (95% CI 0.42–1.00) for Methotrexate vs other therapy

J Int Med 2013;273:197-204

Treatment of psoriasis in Malaysia

Malaysian Psoriasis Registry

- Does not capture symptoms
- Capture psoriasis severity
  - Extent of disease (% BSA)
  - Lesional severity (Skin score)
    - Erythema, induration, scaling
  - DLQI
  - PASI score from 2012
- 4445 patients till 2009
  - 20 % had BSA >10%
  - 40% had DLQI > 10
  - Only 21% received systemic treatment



Source: Annual report ,Malaysian psoriasis registry 2007-2009

Dermatology Life Quality Index (DLQI)

- 10-item dermatology-specific questionnaire
- Measures impact of skin disease and its treatment on patient's life
  - Symptoms & feelings
  - Daily activities
  - Leisure
  - Work & school
  - Personal relationships
  - Difficulties with psoriasis treatment (Treatment-related distress)
- Each question is given a score of 0-3
- DLQI is calculated by summing up score of every question
- Score range 0-30

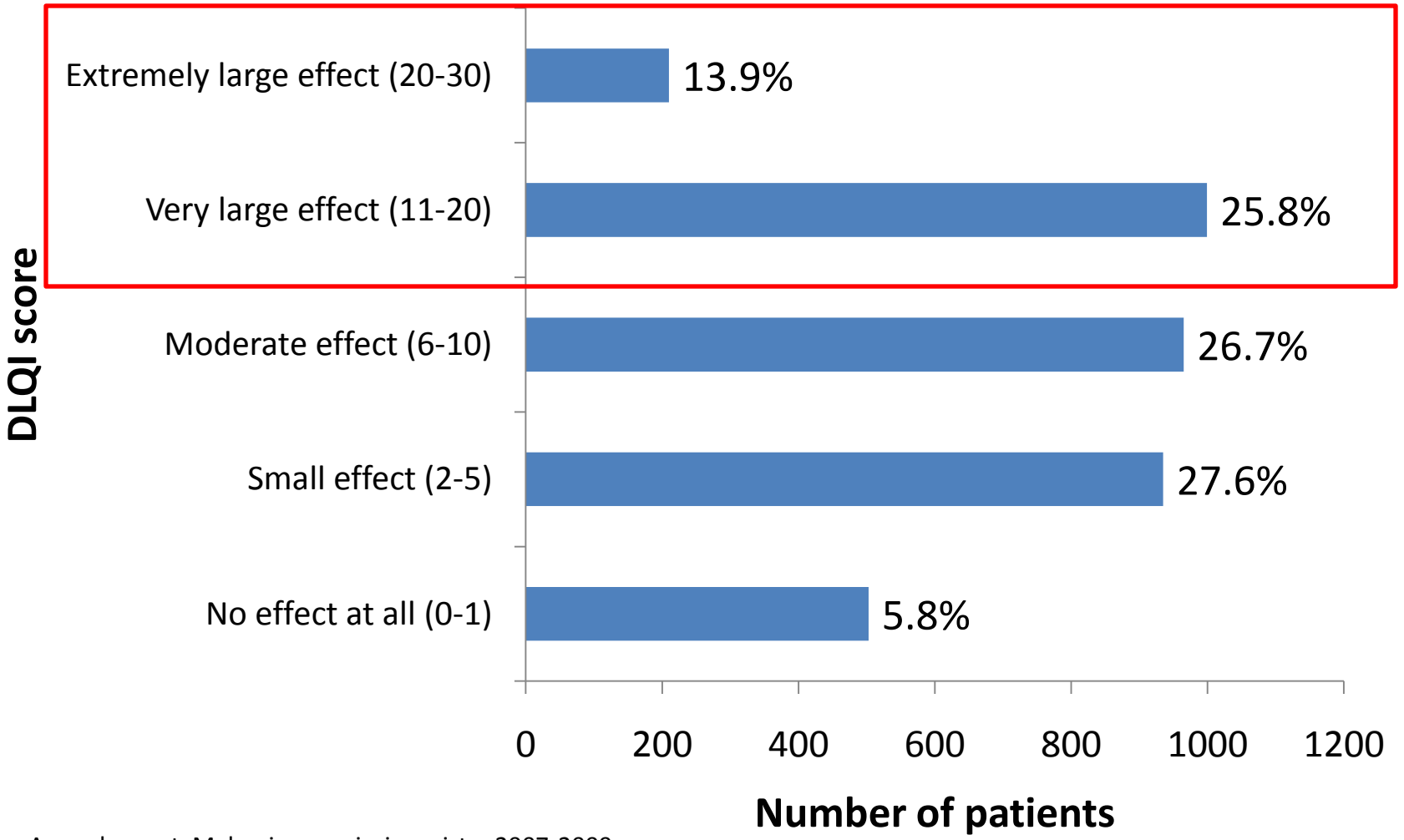
Dermatology Life Quality Index (DLQI)

DLQI score	Effect on Quality of life
0-1	No effect
2-5	Small effect
6-10	Moderate effect
11-20	Very large effect
21-30	Extremely large effect

- A DLQI reduction of > 5 points is considered as a clinically meaningful improvement in QoL
  - Used in clinical trials to measure improvement in QoL after treatment

Dermatology Life Quality Index (DLQI)

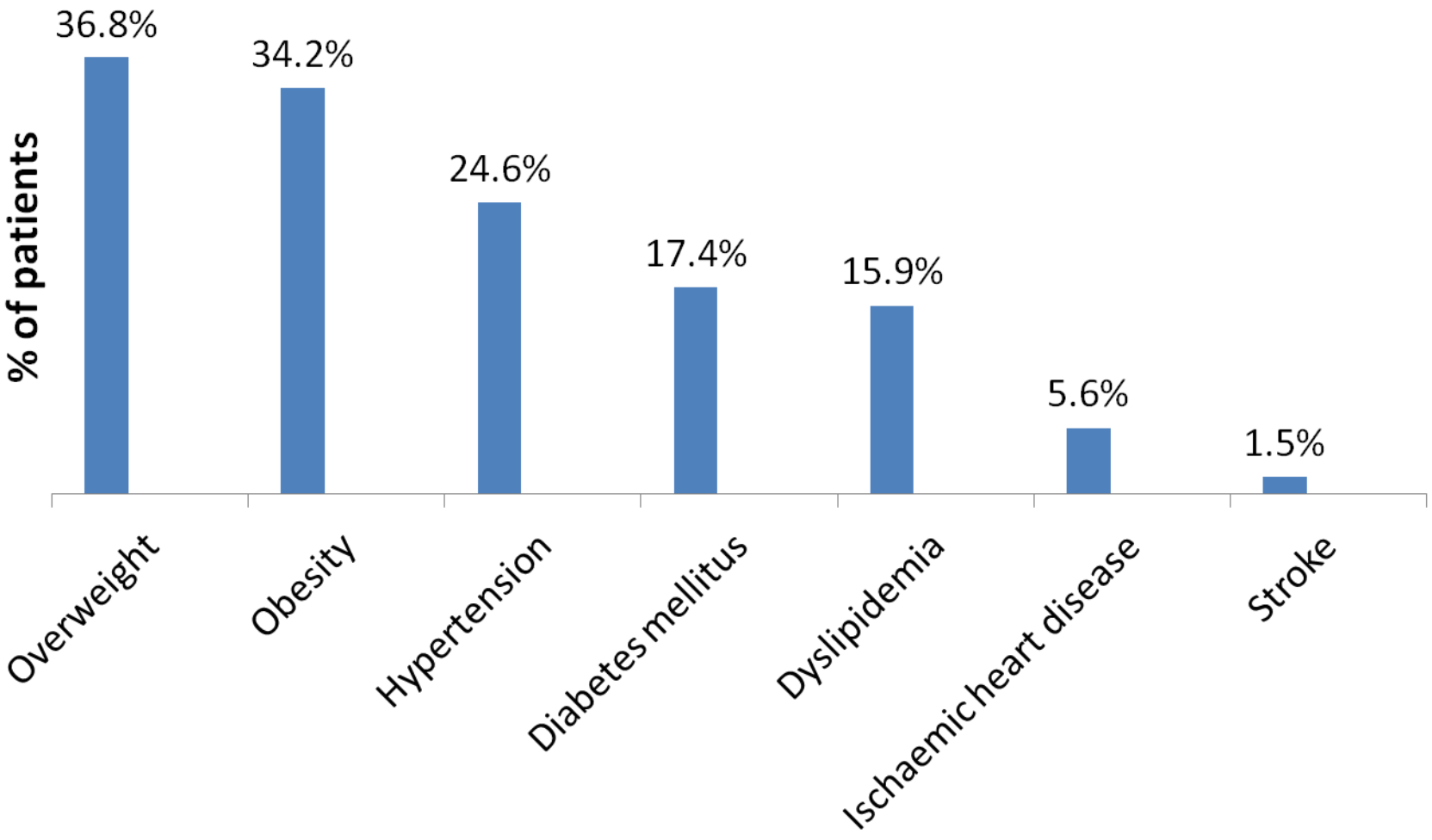
n= 3612 adult Malaysians with psoriasis



Source: Annual report ,Malaysian psoriasis registry 2007-2009

Co-morbidities of psoriasis in Malaysia

Adults age 18 and above

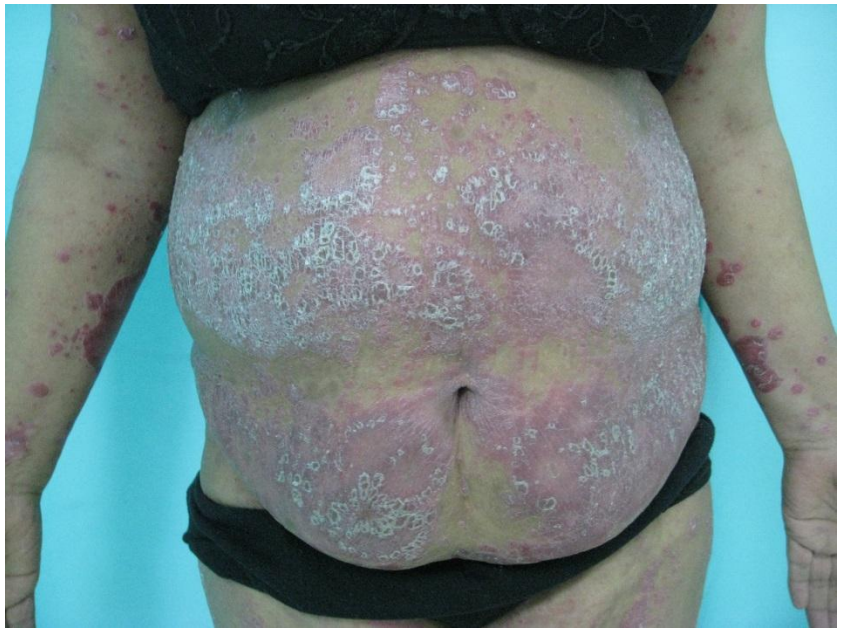


Source: Annual report ,Malaysian psoriasis registry 2007-2009

Treatment of psoriasis in Malaysia

Mean 12 (SD ±5.7) month follow-up of 989 patients

- Mean skin score (erythema, induration, scales)
  - **Improved 75% in 0.2%**
  - **Improved 50-75% in 2.9%**
  - Improved 25-50% in 15.2%
  - Improved < 25% in 30%
  - **No change in 24.8%**
  - **Worsened in 26.7 %**
- % BSA
  - **no change in 58.6%**
  - **16.4 % worsened**
- Only 20% have DLQI improvement of >5 points
- Our patients are inadequately treated!

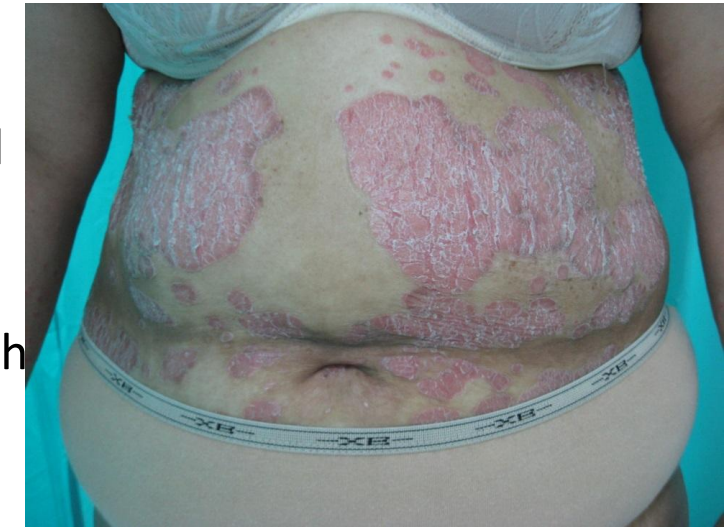


Source: Annual report ,Malaysian psoriasis registry 2007-2009

Malaysian CPG on management of Psoriasis vulgaris
Rationale for CPG

We need to improve care of patients with psoriasis

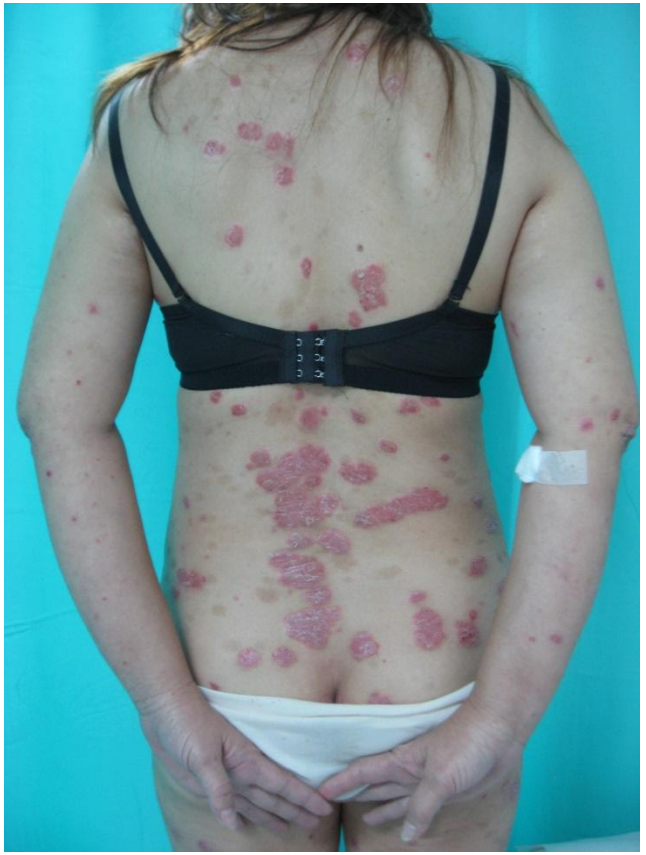
- Psoriasis causes severe physical and emotional morbidities
- Chronic systemic inflammatory disease
  - Significant cardiovascular morbidity and mortality
  - Risk of developing cardiovascular co-morbidities and mortality correlates with the **severity of skin lesions**
  - Control of severe psoriasis is cardio-protective
  - Although no cure, skin can be clear with appropriate treatment
- We need to manage patients better
  - reduce skin-related morbidity
  - reduce risk of developing comorbidities



Malaysian CPG on management of Psoriasis vulgaris
Rationale for CPG

We need to improve care of patients with psoriasis

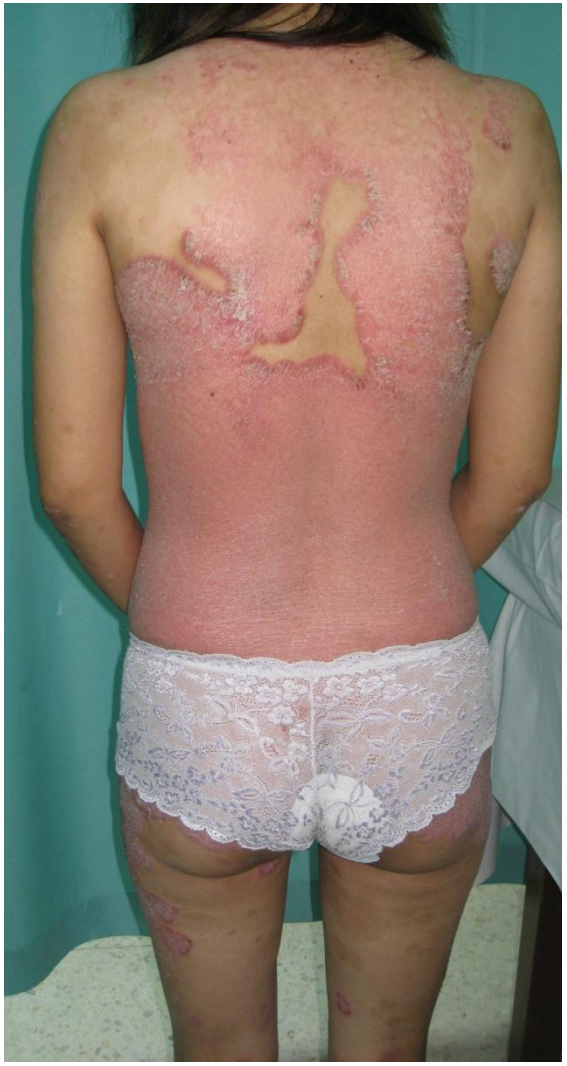
- Only 85 dermatologists in Malaysia, the majority of patients managed by primary healthcare providers
  - Wide variations in clinical practice for the treatment of psoriasis
- No culture to measure severity using validated tools
- No treatment standard
- No treatment goal



Malaysian CPG on management of Psoriasis vulgaris

Objective

- Assist clinicians and other healthcare providers in making evidence-based decisions on the management of psoriasis
- Implement treatment goals to improve outcome of patients living with psoriasis



Treatment goals

- Treatment goals
  - measure efficacy of therapy
  - prevent complications due to uncontrolled disease activity

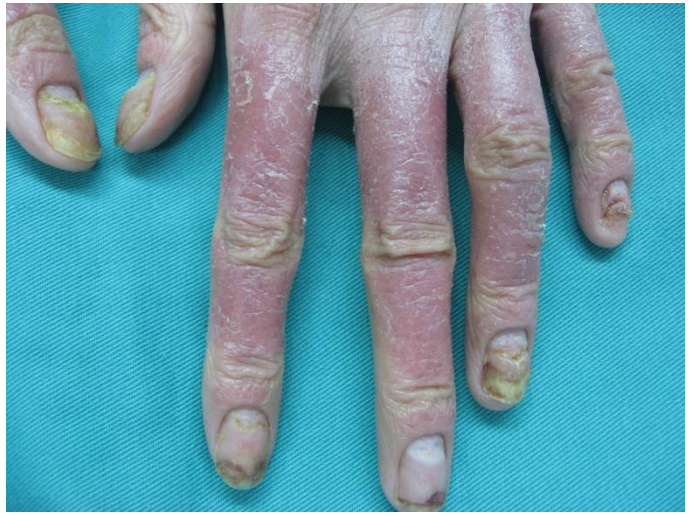
Condition	Treatment goals
Diabetes mellitus	HbA1c < 7 %
Hypertension	BP ≤ 140/90

- Need to implement and regularly monitor treatment goals for psoriasis
  - based on disease severity
  - ensure **appropriate** and **adequate long-term effective** treatment
  - prevent complications due to uncontrolled disease activity

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

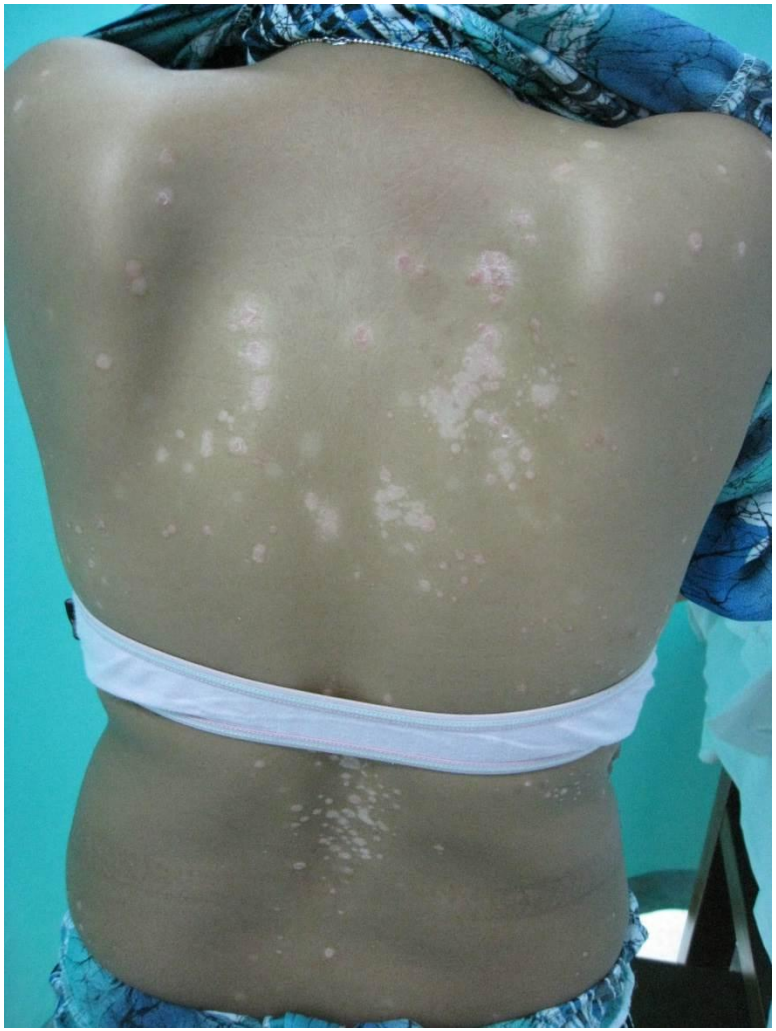
U. Mrowietz · K. Kragballe · K. Reich · P. Spuls · C. E. M. Griffiths · A. Nast · J. Franke · C. Antoniou · P. Arenberger · F. Balieva · M. Bylaite · O. Correia · E. Daudén · P. Gisondi · L. Iversen · L. Kemény · M. Lahfa · T. Nijsten · T. Rantanen · A. Reich · T. Rosenbach · S. Segaert · C. Smith ·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

- Mild psoriasis
  - BSA ≤ 10% and PASI ≤ 10 and DLQI ≤ 10
- Moderate to severe psoriasis
  - (BSA > 10% or PASI >10) and DLQI >10
- Face, hands, genital & nails involvement
  - moderate to severe psoriasis
- Topical therapy for mild psoriasis
- Systemic therapy for moderate-severe psoriasis
- Treatment goals defined are for moderate-severe psoriasis
  - **PASI ≥75**
  - **PASI 50- <75 DLQI ≤ 5**



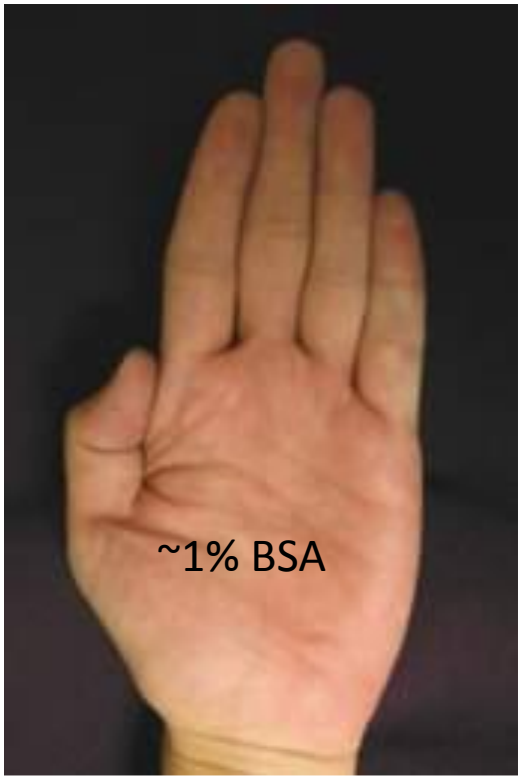
Tools to measure physical severity of psoriasis

- BSA (% of body surface involvement)
  - widely used in daily clinical practice
  - not validated
- PASI (Psoriasis Area and Severity Index)
  - best validated tool
  - good internal consistency
  - good intra-observer consistency
  - acceptable inter-observer variation
- PGA (Physician Global Assessment)
  - validated
  - good intra-observer consistency
  - acceptable inter-observer variation



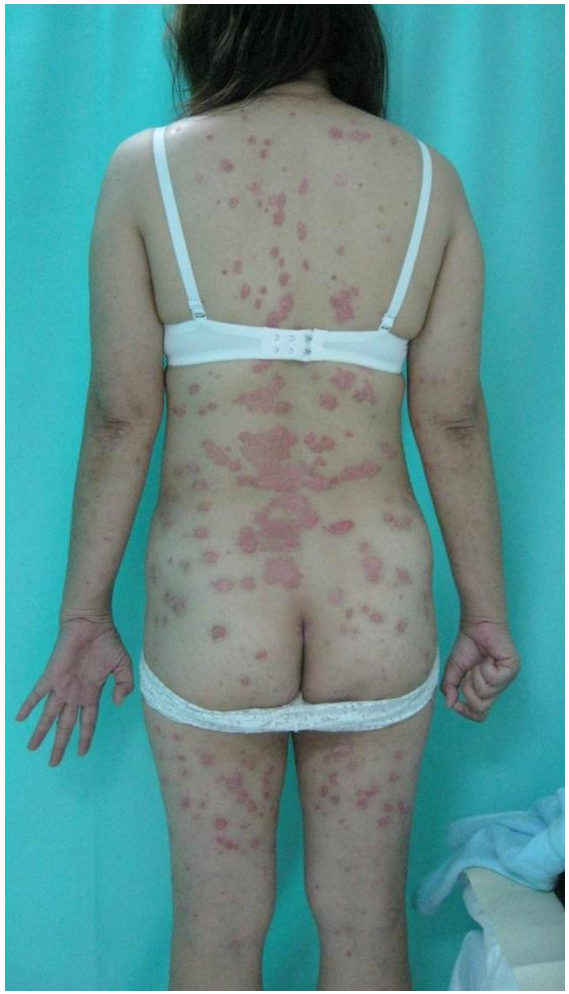
% Body surface area involvement (BSA)

- Measures extent of skin lesions
  - % body surface involvement
    - "rule of 9" or
    - taking patient's one palm size (flat hand with thumb and fingers) as 1%
- Familiar to dermatologists
- Easily taught, easily learnt
- Simple to use



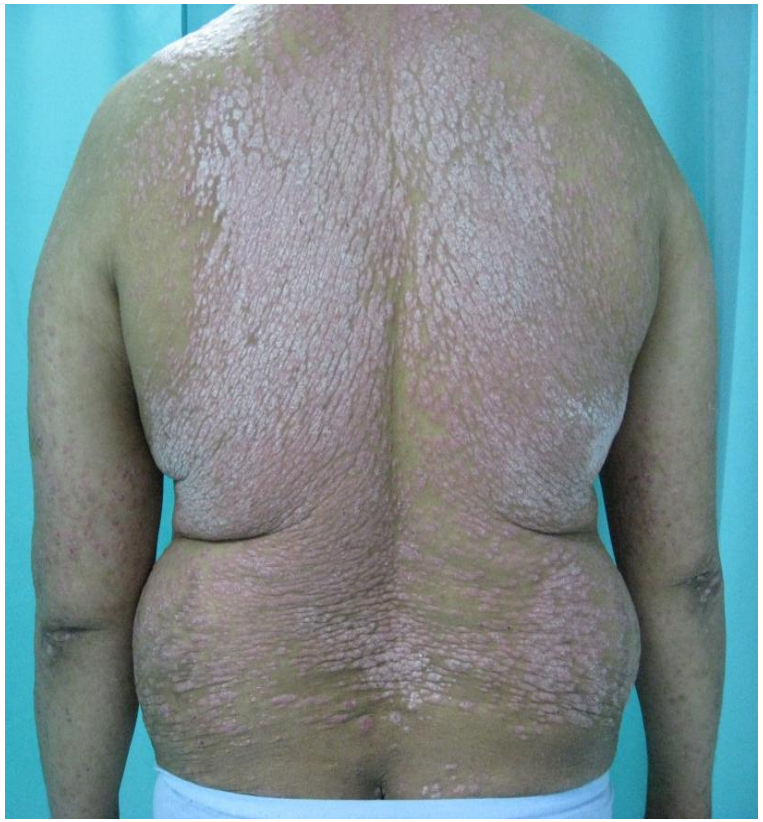
Psoriasis Area and Severity Index (PASI)

- First published in 1978 for quantifying skin disease in psoriasis
- Four regions
  - head and neck (10%)
  - upper limbs (20%)
  - trunk (include axillae and groins) (30%)
  - lower limbs (include buttocks) (40%)
- Severity of skin lesions (erythema, scaling and induration) and extent of involvement within each region
- Score range from 0 - 72
- PASI 75 = 75% reduction in PASI score
  - Used to measure efficacy in clinical trials



Tools to measure impact of psoriasis on Quality of life

- Short Form 36 (SF36)
- Psoriasis Disability Index (PDI)
- Dermatology Life Quality Index (DLQI)
  - validated
  - simple to use in clinical practice
  - DLQI in English, BM, Chinese, Tamil
  - Required for psoriasis registry
  - Need literate patients
  - Not practical for clinical practices with heavy patient load



Malaysian CPG on the management of Psoriasis vulgaris

Assessment of psoriasis severity

Recommendation

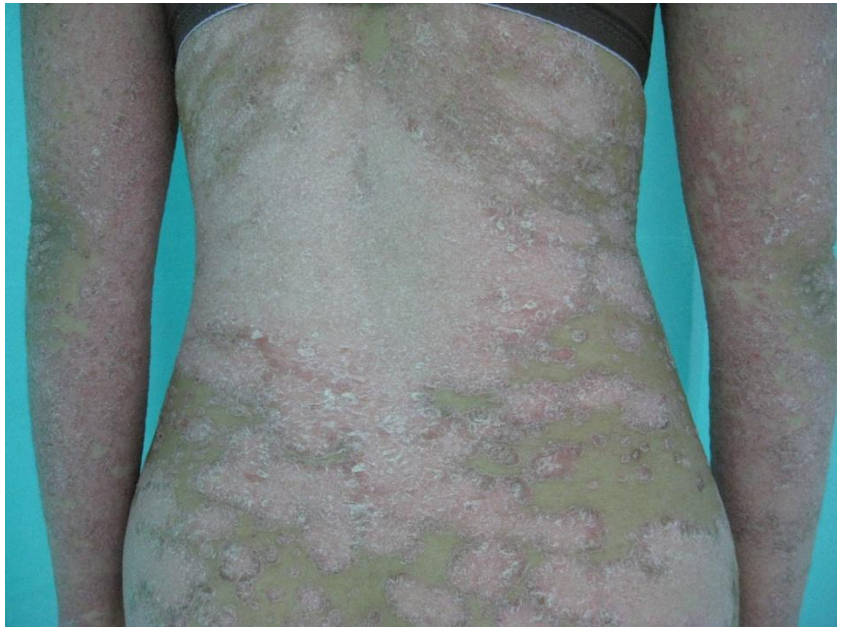
- **BSA or PASI**
  - physical severity of psoriasis
- **DLQI**
  - impact of psoriasis on the quality of life

– Assessment of psoriasis severity
  - First consultation before treatment
  - Every 6 months

Malaysian CPG on the management of Psoriasis vulgaris

Definition of psoriasis severity

	Definition of severity
Mild psoriasis	BSA ≤ 10% or PASI ≤ 10 or DLQI ≤ 10
Moderate psoriasis	BSA >10% to 30% or PASI >10 to 20 or DLQI >10 to 20
Severe psoriasis	BSA > 30% or PASI > 20 or DLQI >20



Treatment phase

- Induction phase
  - Expected time for a therapy to work
  - Vary depending on individual therapy
    - Topical and phototherapy: 6weeks
    - Systemic therapy
      - Methotrexate, cyclosporin: 16 weeks
      - Acitretin: 24 weeks
    - Biologics
      - Infliximab: 10 weeks
      - Adalimumab and ustekinumab: 16 weeks
      - Etanercept 24 weeks
- Maintenance phase
  - Time after induction of remission

Treatment goals

Aim of treatment

- **Improve** and **maintain** patients' health-related QoL
  - control of symptoms and signs of psoriasis
- For all modalities of treatment
  - **DLQI ≤ 5**

DLQI score	Effect on Quality of life
0-1	No effect
2-5	Small effect
6-10	Moderate effect
11-20	Very large effect
21-30	Extremely large effect

Treatment goals

Ideal treatment goal is complete clearance of skin lesions

Minimal targets for improvement

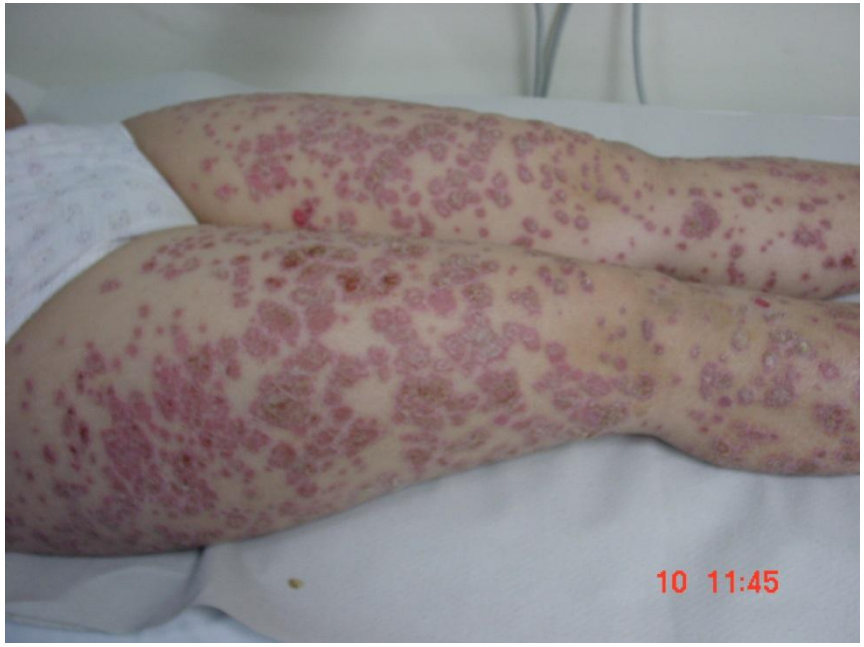
- Topical therapy
  - 50% or more reduction in BSA (↓ BSA ≥ 50) or
  - 50% or more reduction in PASI score (PASI ≥ 50) or
  - DLQI ≤ 5
- Systemic and phototherapy
  - 75% or more reduction in BSA (↓ BSA ≥ 75) or
  - 75% or more reduction in PASI score (PASI ≥ 75) or
  - DLQI ≤ 5
- Biologics
  - PASI ≥ 75 or
  - PASI 50 to <75 plus DLQI ≤ 5

Malaysian CPG on the management of Psoriasis vulgaris
Treatment Goals

Treatment	Minimal targets	Time for Evaluation (Induction phase) (weeks)	Subsequent Evaluation (Maintenance phase) (months)
Topical therapy	↓ BSA ≥ 50 or PASI ≥ 50 or DLQI ≤ 5	6	6 -12
Phototherapy	↓BSA ≥ 75 or PASI ≥ 75 or DLQI ≤ 5	6	6
Methotrexate		16	
Cyclosporin		16	
Acitretin		24	
Infliximab	PASI ≥ 75 or PASI 50 to <75 plus DLQI ≤ 5	10	6
Adalimumab		16	
Ustekinumab		16	
Etanercept		24	

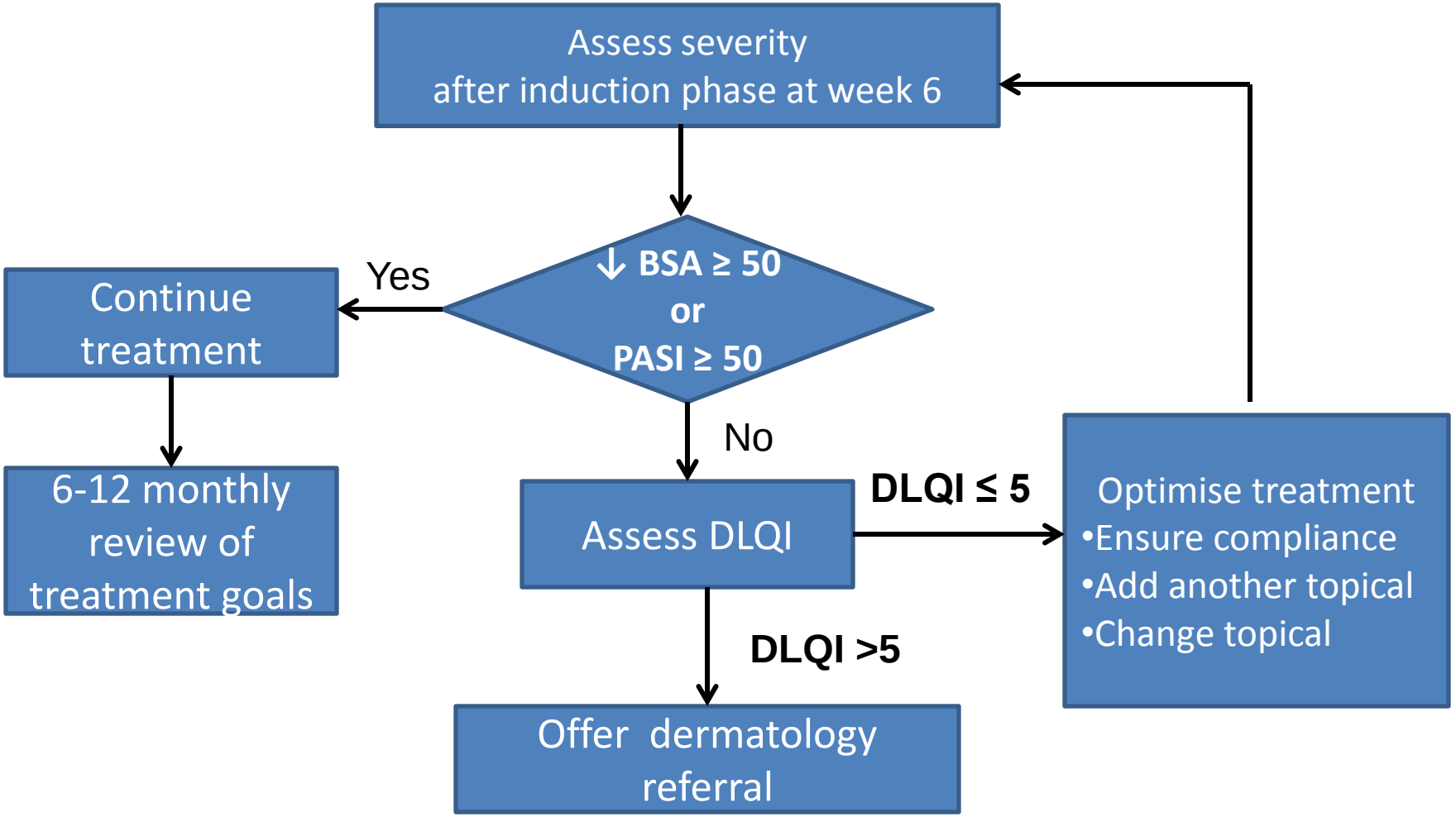
Malaysian CPG on management of Psoriasis vulgaris
Principles of care

- Treatment should be a shared decision between patients and their healthcare providers
- Therapeutic interventions should start with patient education
  - Patients should be given adequate information regarding their disease and current available treatment options
- Treatment goal and minimal target set should be based on **disease severity** and **patient's preference**
- Treatment goals achieved must be **monitored regularly to ensure long-term effective therapy**



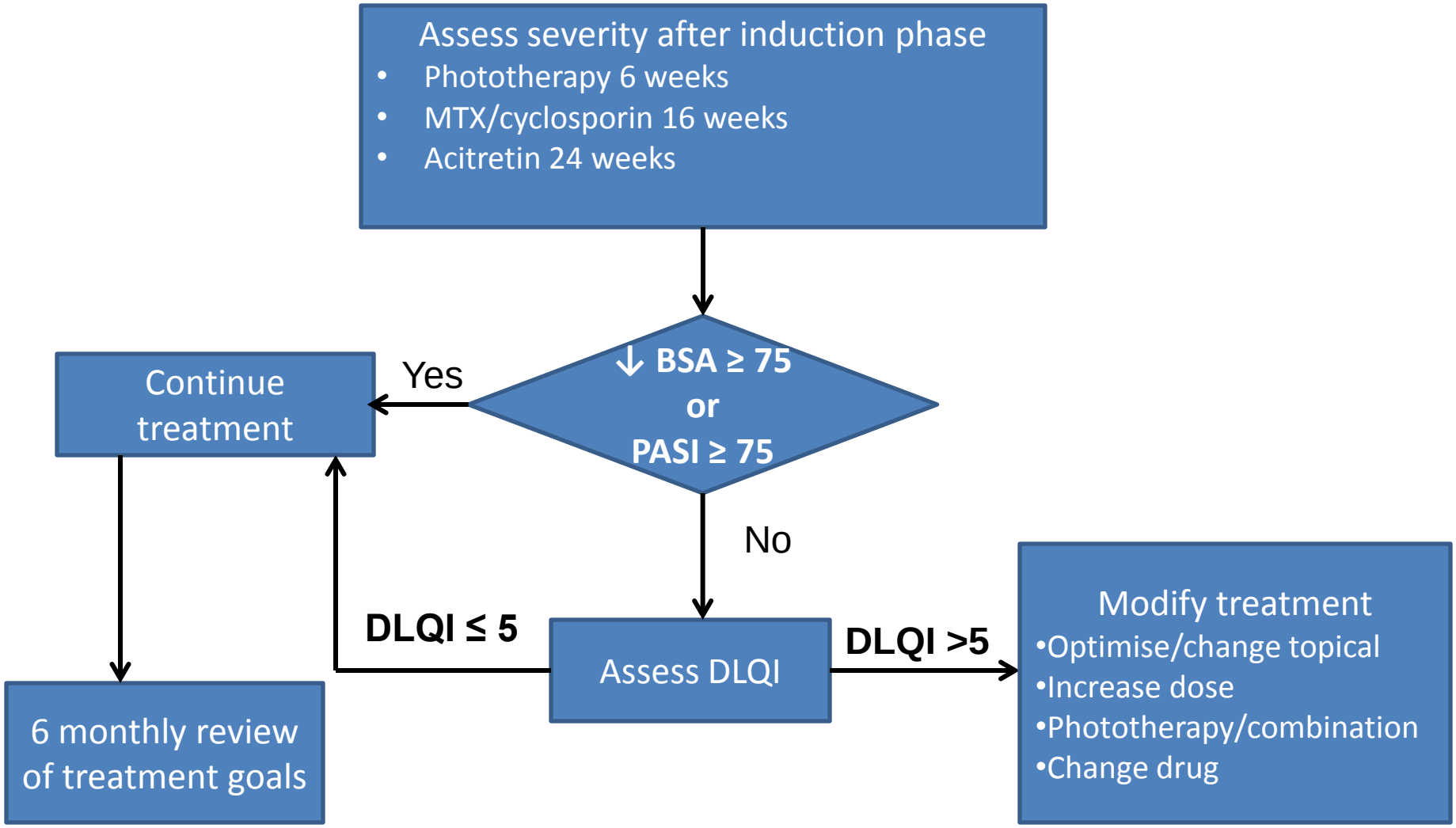
Monitoring efficacy of topical therapy

Treatment goal algorithm



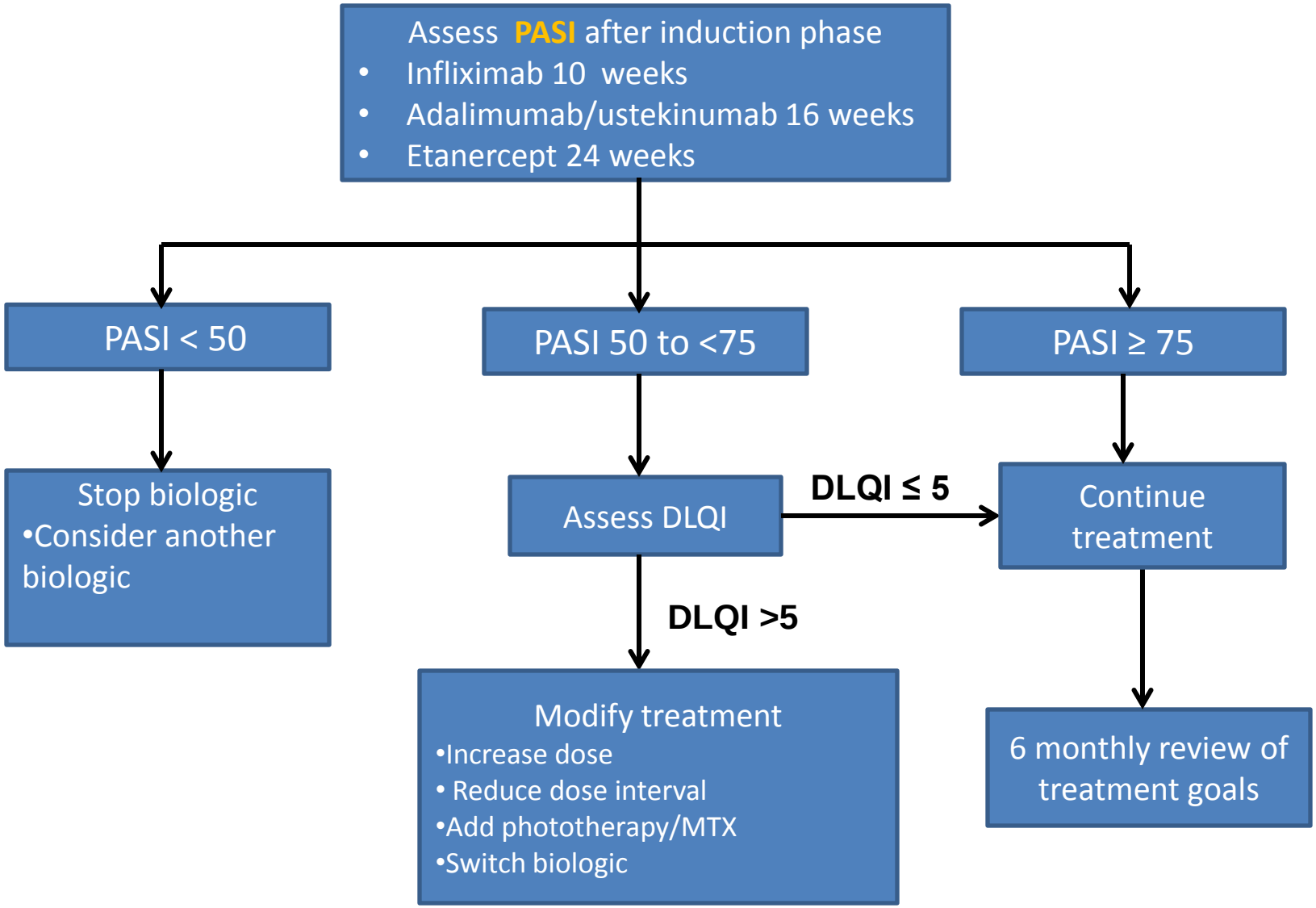
Monitoring efficacy of systemic/phototherapy

Treatment goal algorithm

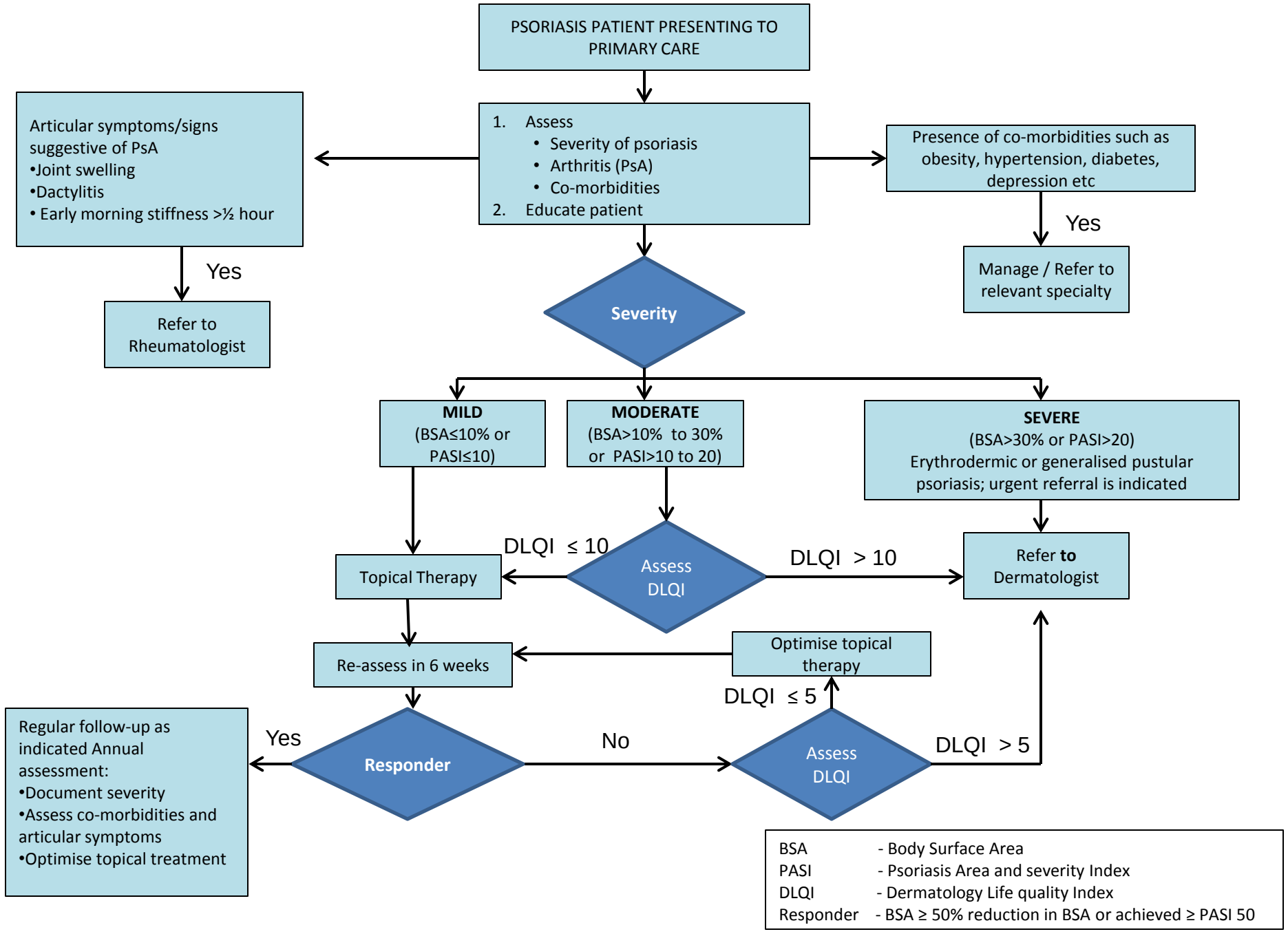


Monitoring efficacy of biologics therapy

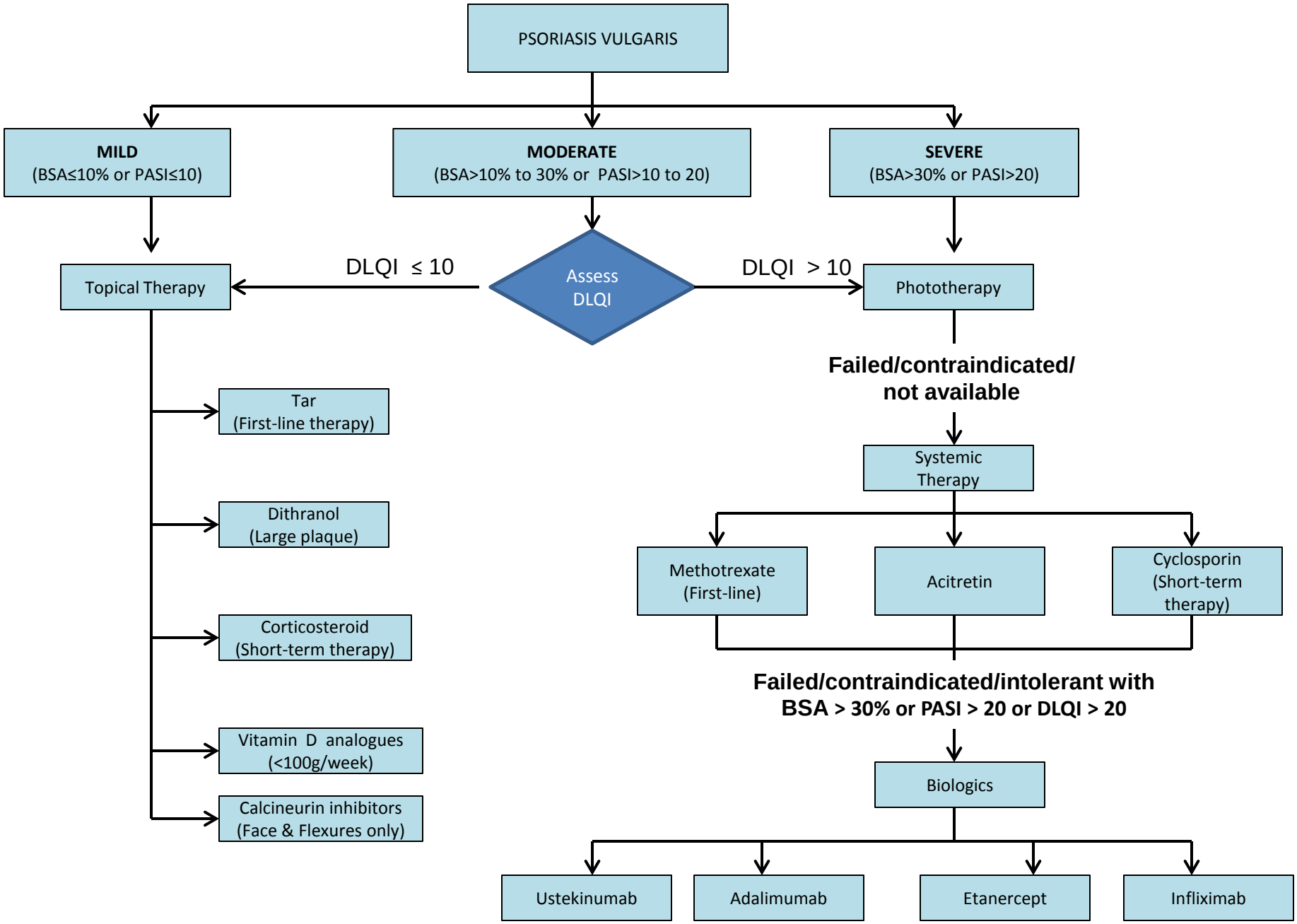
Treatment goal algorithm



ALGORITHM 1: MANAGEMENT OF PSORIASIS VULGARIS IN PRIMARY CARE



ALGORITHM 2: TREATMENT OF PSORIASIS VULGARIS



Malaysian CPG: Management of psoriasis vulgaris Improving care with treatment goals

Summary of talk

- Psoriasis is no longer just a skin disease
- It is a chronic inflammatory systemic disease
  - Significant cardiovascular morbidity and mortality
- Adequate control of psoriasis is cardio-protective
- Implementing and regular monitoring of treatment goals is necessary
  - to ensure adequate and effective long-term therapy
  - to prevent complications from uncontrolled disease activity

Thanks

Let’s implement treatment goals

to improve care of patients with psoriasis!