

COST-EFFECTIVENESS OF TREATMENT FOR MODERATE-TO-SEVERE PSORIASIS

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OVERVIEW

- Definition and Prevalence
- Treatment
- Cost-Effectiveness Study
 - Background
 - Objective
 - Methods
 - Findings
 - Conclusion
- Discussion

DEFINITION

- Chronic polygenic disorder that results from predisposing & triggering factors (e.g., trauma, infection)
- Epidermal proliferation and differentiation
- Sharply demarcated, scaly erythematous plaques with silvery white scales
- During exacerbations, lesions often itch



PREVALENCE of MODERATE-TO-SEVERE PSORIASIS

- Affects up to 30% of patients
- Generally involves $> 2\%$ body surface area
- Disabling
 - Location (face, hands, fingernails, feet, genitals)
 - Symptoms (pain, tightness, bleeding, severe itching)



TREATMENT

– Oral Systemics

- acitretin (Soriatane® - Connetics)
- cyclosporine (Neoral® - Novartis)
- methotrexate (Trexall® - Barr)

– Biologics

- alefacept (Amevive® -Biogen)
- efalizumab (Raptiva® - Genentech/Xoma)
- etanercept (Enbrel® - Amgen)

– Phototherapy

- Ultraviolet B (UVB)
- Psoralen with Ultraviolet A (PUVA)
- Combined Phototherapy with acitretin

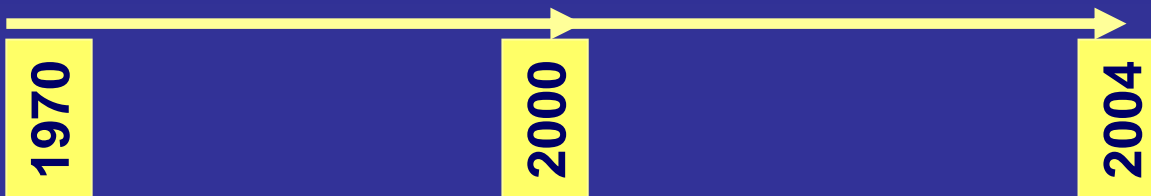
Systemic Treatment Options are Burgeoning

- methotrexate
- cyclosporine
- acitretin



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- methotrexate
- cyclosporine
- acitretin
- alefacept
- efalizumab
- etanercept



Systemic Treatment Options are Burgeoning

- methotrexate
- cyclosporine
- acitretin

- alefacept
- efalizumab
- etanercept

- rosiglitazone maleate
- bimosiamose
- pimecrolimus
- humira
- ISA247
- AE-941
- onercept
- alitretinoin
- psoraxine
- infliximab
- MEDI-507
- IR50 rosiglitazone maleate

1970

2000

2004

Systemic Treatment Options are Burgeoning

But, Head-to-Head Efficacy Comparisons are Lacking

- methotrexate
- cyclosporine
- acitretin

- alefacept
- efalizumab
- etanercept

- rosiglitazone maleate
- bimosiamose
- pimecrolimus
- humira
- ISA247
- AE-941
- onercept
- alitretinoin
- psoraxine
- infliximab
- MEDI-507
- IR50 rosiglitazone maleate

1970

2000

2004

OBJECTIVE

From the perspective of U.S. managed healthcare decision makers, to compare efficacy and costs across the range of treatments for moderate-to-severe psoriasis.

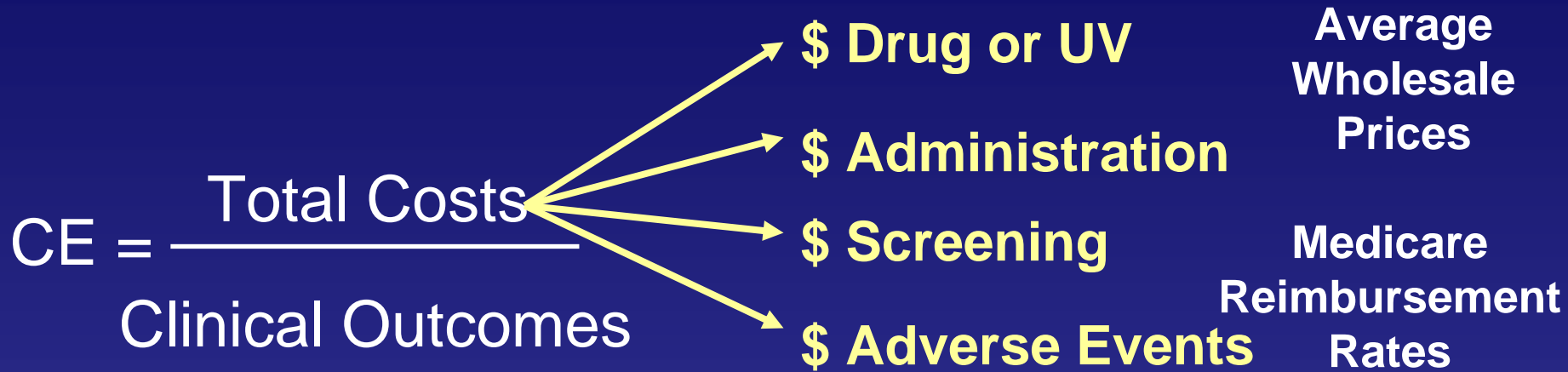
METHODS

$$CE = \frac{\text{Total Costs}}{\text{Clinical Outcomes}}$$

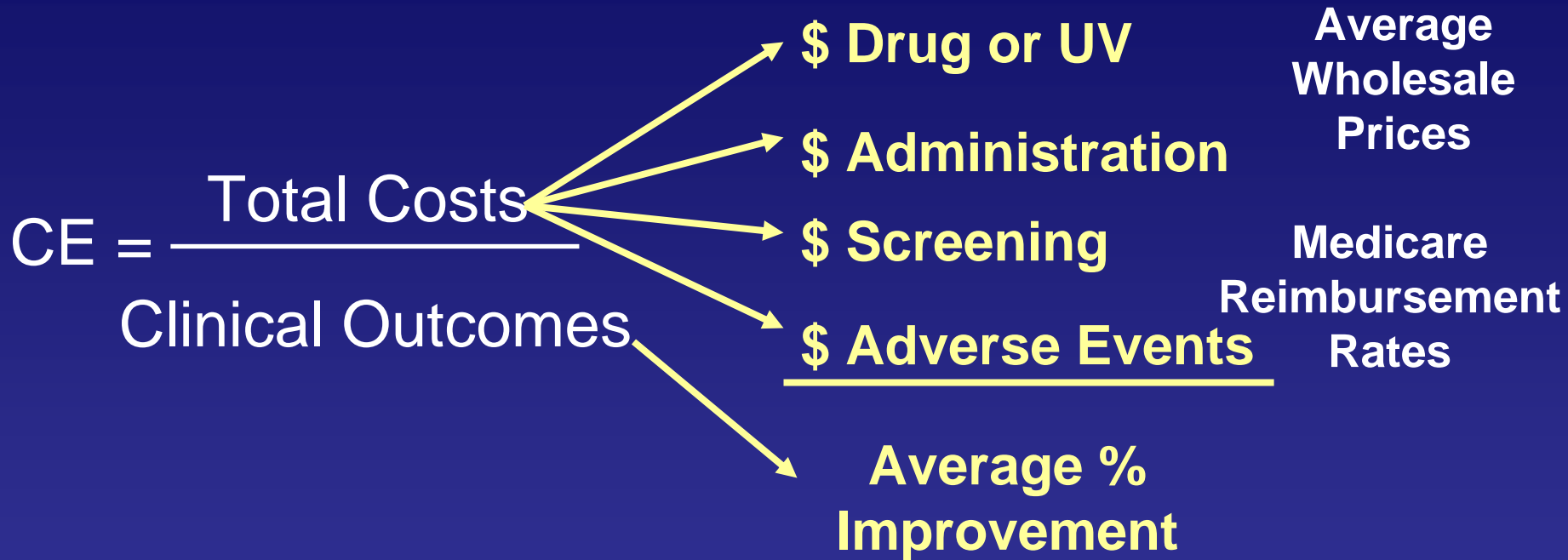
METHODS



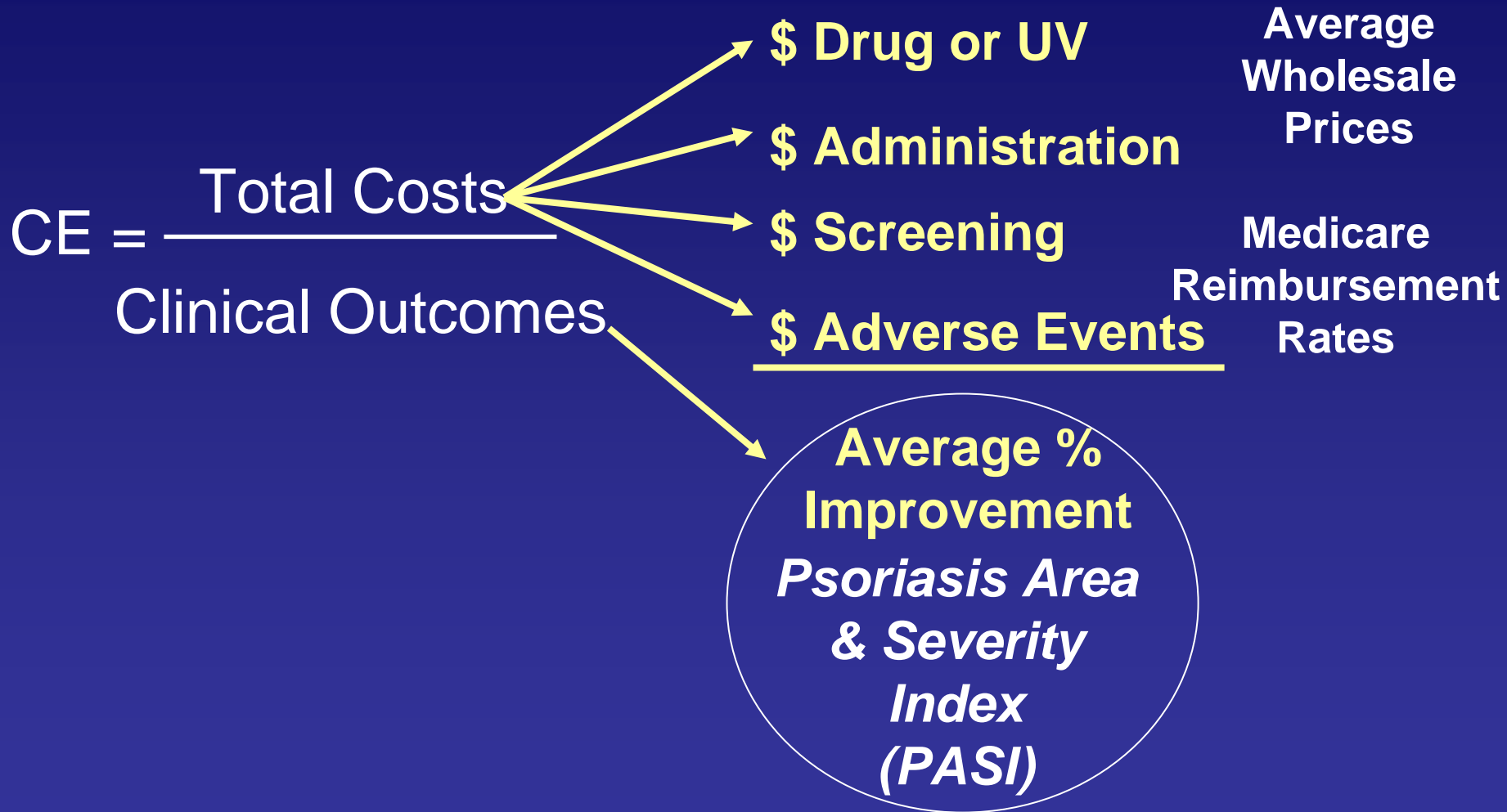
METHODS



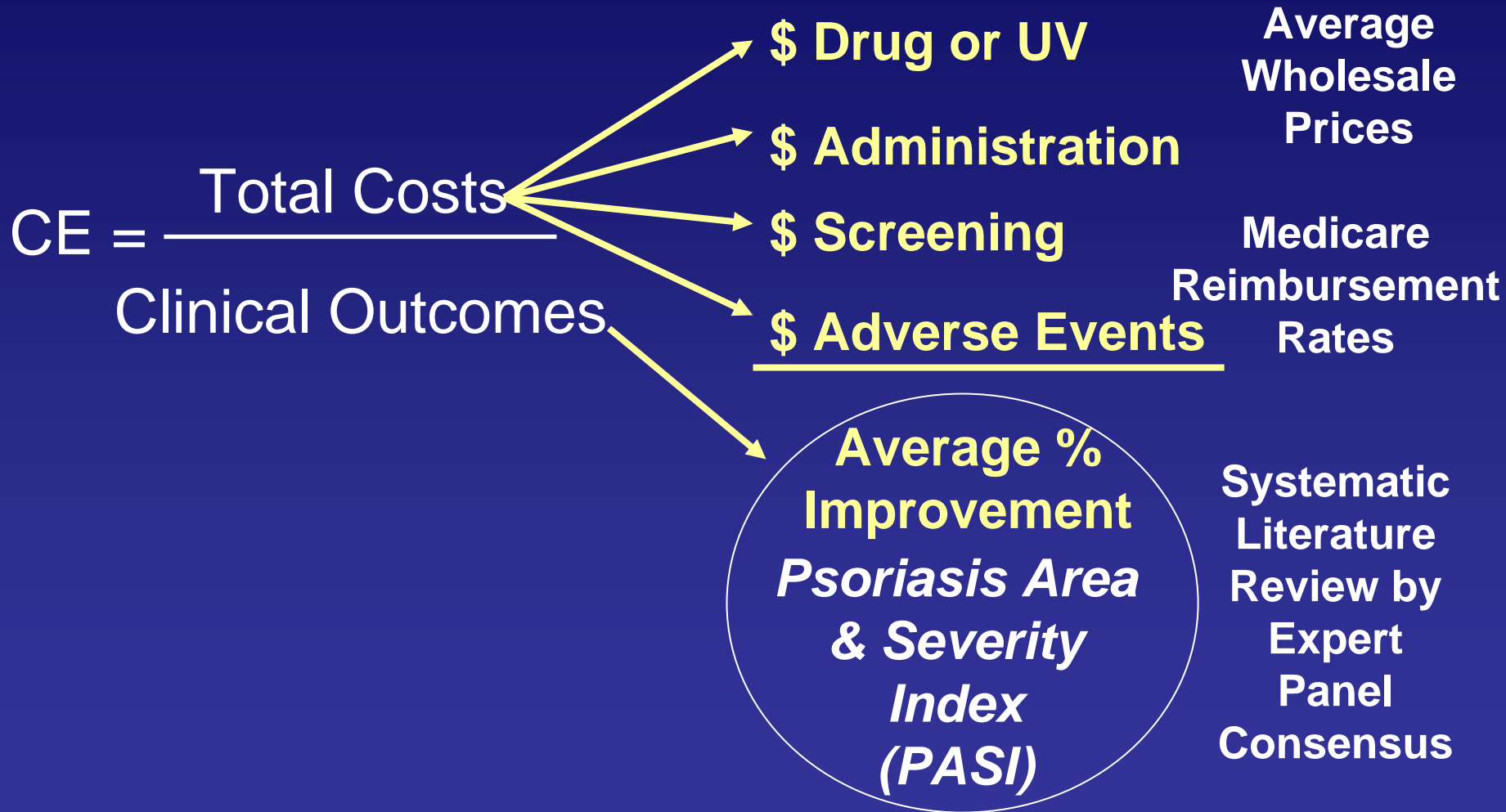
METHODS



METHODS



METHODS



METHODS



WHAT IS THE COST OF 1% PASI IMPROVEMENT ?

WHAT IS THE COST OF CLINICALLY MEANINGFUL IMPROVEMENT? (50%, 75%)

Average % Improvement Psoriasis Area & Severity Index (PASI)

Systematic Literature Review by Expert Panel Consensus

Cost-effectiveness Model Perspective

Viewpoint: *Health Systems*

Country of Analysis: *United States*

Target Population: *Adults with moderate-to-severe psoriasis*

Setting of Care: *Outpatient*

Time Frame: *1 year*

RESULTS OF SYSTEMATIC LITERATURE REVIEW OF PASI EFFICACY

- MEDLINE 1966-August 2004
- Psoriasis AND [Treatment]
- Published, Peer-Reviewed
- English Language

Total Articles Identified	3,886
Less Excluded Due To:	
Efficacy Characteristics	1,351
Sample Selection	225
Treatment Characteristics	398
Study Design	1,896
Total Excluded	3,870
Total Efficacy Studies Included	16

Treatment	Dose	PASI%
Broadband UVB	3 exp/wk	47%, 80.1%, 83.7%
Narrowband UVB	3 exp/wk	73.0%
PUVA	3 exp/wk	92.9%
	3 exp/wk	61.1%
acitretin	48.2 mg/day	60.4%
cyclosporine	1.5 mg/kg/day	33.4%
	3 mg/kg/day	52.0%
methotrexate	7.5 mg/wk	58.4%
	15 mg/wk	71.6%
alefacept	15 mg/wk 2-12wk courses	45.0%
efalizumab	1 mg/kg/wk	51%, 52.0%
etanercept	50 mg 2xs weekly	64.2%
infliximab	5 mg/kg wks 0, 2, 6	82.8%
UVB + acitretin	5- 7 exp/wk + 25 mg/d	80.7 %
PUVA + acitretin	3 exp/wk + 20mg	97.3%

ANNUALIZED COSTS (USD)

Treatment	Tx \$		
methotrexate 7.5 mg	\$595		
methotrexate 15 mg	\$1,190		
cyclosporine 1.5mg/kg	\$2,789		
PUVA 3xs/wk	\$3,737		
PUVA 3xs/wk	\$3,737		
BBUVB+acitretin 25mg	\$3,792		
BB UVB 3xs/wk	\$4,807		
cyclosporine 3 mg/kg	\$5,019		
PUVA+acitretin 20mg	\$6,773		
acitretin 50 mg	\$12,359		
efalizumab 1 mg/kg	\$17,836		
etanercept 50 mg	\$21,052		
alefacept 15 mg IM	\$23,880		
infliximab 5 mg/kg	\$24,898		

**January 2004
Average Wholesale
Price (AWP)**

**2004 Medicare
Reimbursement
Rates**

	ANNUALIZED COSTS (USD)			
Treatment	Tx \$	Admin \$		
methotrexate 7.5 mg	\$595	-		
methotrexate 15 mg	\$1,190	-		
cyclosporine 1.5mg/kg	\$2,789	-		
PUVA 3xs/wk	\$3,737	-		
PUVA 3xs/wk	\$3,737	-		
BBUVB+acitretin 25mg	\$3,792	-		
BB UVB 3xs/wk	\$4,807	-		
cyclosporine 3 mg/kg	\$5,019	-		
PUVA+acitretin 20mg	\$6,773	-		
acitretin 50 mg	\$12,359	-		
efalizumab 1 mg/kg	\$17,836	\$0		
etanercept 50 mg	\$21,052	\$0		
alefacept 15 mg IM	\$23,880	\$806		
infliximab 5 mg/kg	\$24,898	\$1,422		

Self-Administered

IV Injection (@ 2004 Medicare Rate)

IV Infusion (@ 2004 Medicare Rate)

	ANNUALIZED COSTS (USD)				
Treatment	Tx \$	Admin \$	Screen \$	Product Label @ 2004 Medicare Rate	
methotrexate 7.5 mg	\$595	-	\$1,188	Consensus Statements @ 2004 Medicare Rate	
methotrexate 15 mg	\$1,190	-	\$1,188		
cyclosporine 1.5mg/kg	\$2,789	-	\$1,794		
PUVA 3xs/wk	\$3,737	-	\$106		
PUVA 3xs/wk	\$3,737	-	\$106		
BBUVB+acitretin 25mg	\$3,792	-	\$618		
BB UVB 3xs/wk	\$4,807	-	\$106		
cyclosporine 3 mg/kg	\$5,019	-	\$1,794		
PUVA+acitretin 20mg	\$6,773	-	\$618		
acitretin 50 mg	\$12,359	-	\$618		
efalizumab 1 mg/kg	\$17,836	\$0	\$163		
etanercept 50 mg	\$21,052	\$0	\$106		
alefacept 15 mg IM	\$23,880	\$806	\$2,412		
infliximab 5 mg/kg	\$24,898	\$1,422	\$116		

	ANNUALIZED COSTS (USD)					
Treatment	Tx \$	Admin \$	Screen \$	AE \$		
methotrexate 7.5 mg	\$595	-	\$1,188	-		
methotrexate 15 mg	\$1,190	-	\$1,188	-		
cyclosporine 1.5mg/kg	\$2,789	-	\$1,794	\$138		
PUVA 3xs/wk	\$3,737	-	\$106	\$11		
PUVA 3xs/wk	\$3,737	-	\$106	\$11		
BBUVB+acitretin 25mg	\$3,792	-	\$618	\$54		
BB UVB 3xs/wk	\$4,807	-	\$106	\$18		
cyclosporine 3 mg/kg	\$5,019	-	\$1,794	\$138		
PUVA+acitretin 20mg	\$6,773	-	\$618	\$49		
acitretin 50 mg	\$12,359	-	\$618	\$83		
efalizumab 1 mg/kg	\$17,836	\$0	\$163	-		
etanercept 50 mg	\$21,052	\$0	\$106	-		
alefacept 15 mg IM	\$23,880	\$806	\$2,412	-		
infliximab 5 mg/kg	\$24,898	\$1,422	\$116	-		

Risk-adjusted Costs

	ANNUALIZED COSTS (USD)						
Treatment	Tx \$	Admin \$	Screen \$	AE \$	TOTAL COSTS		
methotrexate 7.5 mg	\$595	-	\$1,188	-	\$1,783		
methotrexate 15 mg	\$1,190	-	\$1,188	-	\$2,378		
cyclosporine 1.5mg/kg	\$2,789	-	\$1,794	\$138	\$4,721		
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854		
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854		
BBUVB+acitretin 25mg	\$3,792	-	\$618	\$54	\$4,464		
BB UVB 3xs/wk	\$4,807	-	\$106	\$18	\$4,931		
cyclosporine 3 mg/kg	\$5,019	-	\$1,794	\$138	\$6,951		
PUVA+acitretin 20mg	\$6,773	-	\$618	\$49	\$7,440		
acitretin 50 mg	\$12,359	-	\$618	\$83	\$13,060		
efalizumab 1 mg/kg	\$17,836	\$0	\$163	-	\$17,999		
etanercept 50 mg	\$21,052	\$0	\$106	-	\$21,158		
alefacept 15 mg IM	\$23,880	\$806	\$2,412	-	\$27,098		
infliximab 5 mg/kg	\$24,898	\$1,422	\$116	-	\$26,436		

	ANNUALIZED COSTS (USD)						
Treatment	Tx \$	Admin \$	Screen \$	AE \$	TOTAL COSTS	PASI	
methotrexate 7.5 mg	\$595	-	\$1,188	-	\$1,783	58.4	
methotrexate 15 mg	\$1,190	-	\$1,188	-	\$2,378	71.6	
cyclosporine 1.5mg/kg	\$2,789	-	\$1,794	\$138	\$4,721	33.4	
PUVA 3xs/wk				\$11	\$3,854	92.9	
PUVA 3xs/wk				\$11	\$3,854	61.1	
BBUVB+acitretin 25mg	\$3,792	-	\$618	\$54	\$4,464	80.7	
BB UVB 3xs/wk	\$4,807	-	\$106	\$18	\$4,931	80.1	
cyclosporine 3 mg/kg	\$5,019	-	\$1,794	\$138	\$6,951	52.0	
PUVA+acitretin 20mg	\$6,773	-	\$618	\$49	\$7,440	97.3	
acitretin 50 mg	\$12,359	-	\$618	\$83	\$13,060	60.4	
efalizumab 1 mg/kg	\$17,836	\$0	\$163	-	\$17,999	52	
etanercept 50 mg	\$21,052	\$0	\$106	-	\$21,158	64.2	
alefacept 15 mg IM	\$23,880	\$806	\$2,412	-	\$27,098	45	
infliximab 5 mg/kg	\$24,898	\$1,422	\$116	-	\$26,436	82.8	

Expert Panel Systematic Literature Review

Total Costs / PASI

ESTIMATED COSTS (USD)

ANNUAL COSTS TO ACHIEVE

Treatment	Tx	Admin	Screen	AE	TOTAL	PASI	PASI 1%
	\$	\$	\$	\$	COSTS		
methotrexate 7.5 mg	\$595	-	\$1,188	-	\$1,783	58.4	\$31
methotrexate 15 mg	\$1,190	-	\$1,188	-	\$2,378	71.6	\$33
cyclosporine 1.5mg/kg	\$2,789	-	\$1,794	\$138	\$4,721	33.4	\$141
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854	92.9	\$41
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854	61.1	\$63
BBUVB+acitretin 25mg	\$3,792	-	\$618	\$54	\$4,464	80.7	\$55
BB UVB 3xs/wk	\$4,807	-	\$106	\$18	\$4,931	80.1	\$62
cyclosporine 3 mg/kg	\$5,019	-	\$1,794	\$138	\$6,951	52.0	\$134
PUVA+acitretin 20mg	\$6,773	-	\$618	\$49	\$7,440	97.3	\$76
acitretin 50 mg	\$12,359	-	\$618	\$83	\$13,060	60.4	\$216
efalizumab 1 mg/kg	\$17,836	\$0	\$163	-	\$17,999	52	\$346
etanercept 50 mg	\$21,052	\$0	\$106	-	\$21,158	64.2	\$330
alefacept 15 mg IM	\$23,880	\$806	\$2,412	-	\$27,098	45	\$602
infliximab 5 mg/kg	\$24,898	\$1,422	\$116	-	\$26,436	82.8	\$319

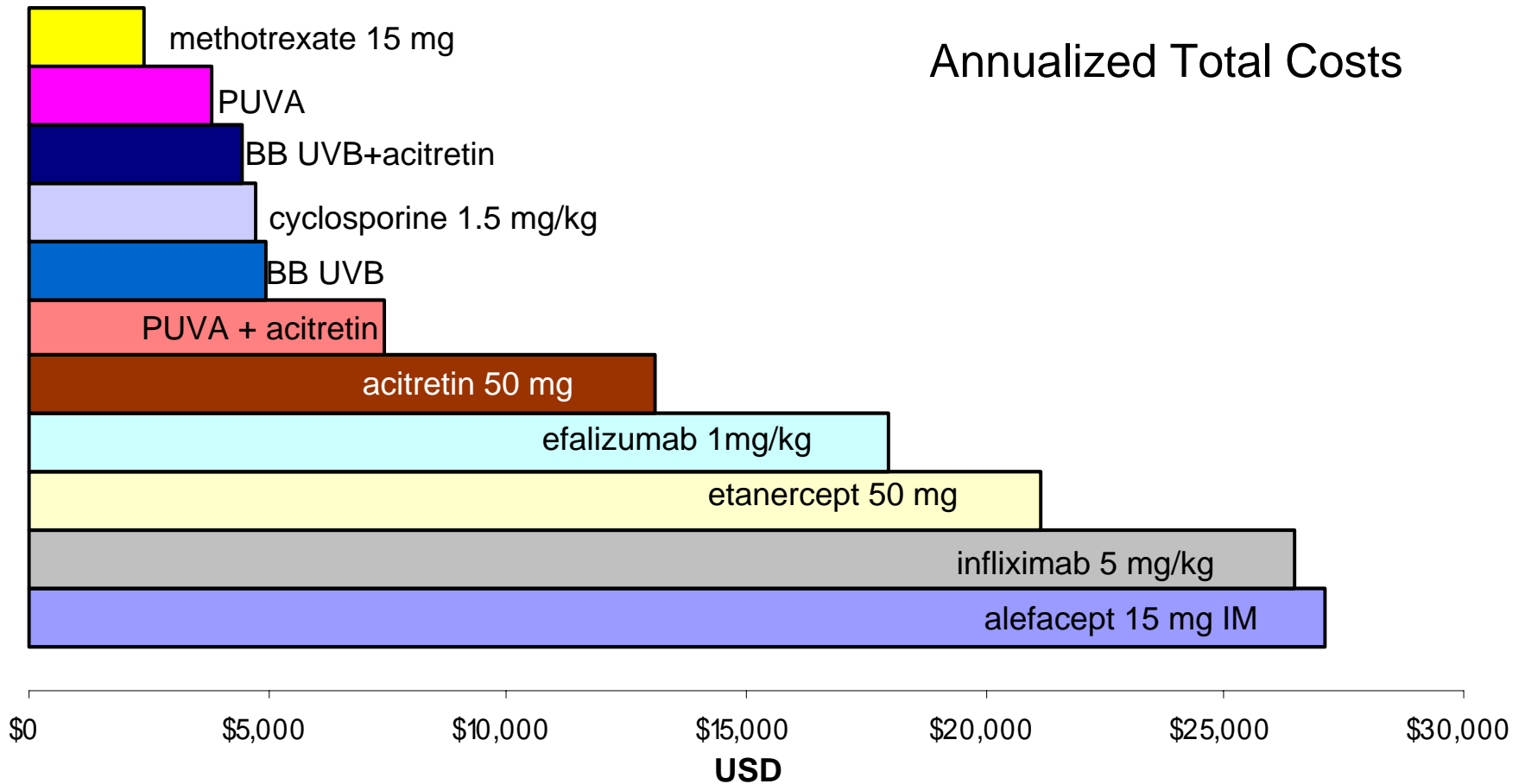
PASI 1% * 75

Treatment	TOTAL COSTS (USD)					PASI	ANNUAL COSTS TO ACHIEVE	
	Tx \$	Admin \$	Screen \$	AE \$	TOTAL COSTS		PASI 1%	PASI 75%
methotrexate 7.5 mg	\$595	-	\$1,188	-	\$1,783	58.4	\$31	\$2,290
methotrexate 15 mg	\$1,190	-	\$1,188	-	\$2,378	71.6	\$33	\$2,491
cyclosporine 1.5mg/kg	\$2,789	-	\$1,794	\$138	\$4,721	33.4	\$141	\$10,600
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854	92.9	\$41	\$3,111
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854	61.1	\$63	\$4,731
BBUVB+acitretin 25mg	\$3,792	-	\$618	\$54	\$4,464	80.7	\$55	\$4,149
BB UVB 3xs/wk	\$4,807	-	\$106	\$18	\$4,931	80.1	\$62	\$4,617
cyclosporine 3 mg/kg	\$5,019	-	\$1,794	\$138	\$6,951	52.0	\$134	\$10,025
PUVA+acitretin 20mg	\$6,773	-	\$618	\$49	\$7,440	97.3	\$76	\$5,735
acitretin 50 mg	\$12,359	-	\$618	\$83	\$13,060	60.4	\$216	\$16,217
efalizumab 1 mg/kg	\$17,836	\$0	\$163	-	\$17,999	52	\$346	\$25,960
etanercept 50 mg	\$21,052	\$0	\$106	-	\$21,158	64.2	\$330	\$24,717
alefacept 15 mg IM	\$23,880	\$806	\$2,412	-	\$27,098	45	\$602	\$45,163
infliximab 5 mg/kg	\$24,898	\$1,422	\$116	-	\$26,436	82.8	\$319	\$23,946

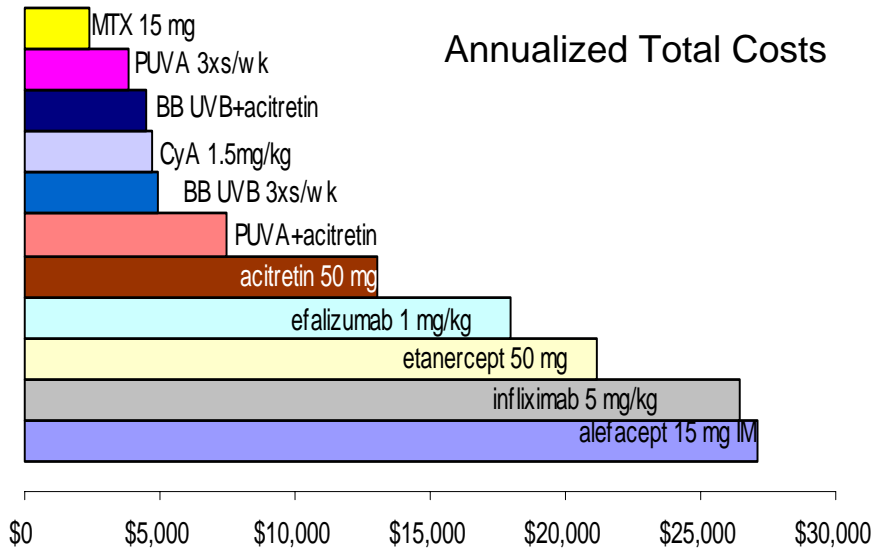
	ANNUALIZED COSTS (USD)						ANNUAL COSTS TO ACHIEVE	
Treatment	Tx \$	Admin \$	Screen \$	AE \$	TOTAL COSTS	PASI	PASI 1%	PASI 75%
methotrexate 7.5 mg	\$595	-	\$1,188	-	\$1,783	58.4	\$31	\$2,290
methotrexate 15 mg	\$1,190	-	\$1,188	-	\$2,378	71.6	\$33	\$2,491
cyclosporine 1.5mg/kg	\$2,789	-	\$1,794	\$138	\$4,721	33.4	\$141	\$10,600
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854	92.9	\$41	\$3,111
PUVA 3xs/wk	\$3,737	-	\$106	\$11	\$3,854	61.1	\$63	\$4,731
BBUVB+acitretin 25mg	\$3,792	-	\$618	\$54	\$4,464	80.7	\$55	\$4,149
BB UVB 3xs/wk	\$4,807	-	\$106	\$18	\$4,931	80.1	\$62	\$4,617
cyclosporine 3 mg/kg	\$5,019	-	\$1,794	\$138	\$6,951	52.0	\$134	\$10,025
PUVA+acitretin 20mg	\$6,773	-	\$618	\$49	\$7,440	97.3	\$76	\$5,735
acitretin 50 mg	\$12,359	-	\$618	\$83	\$13,060	60.4	\$216	\$16,217
efalizumab 1 mg/kg	\$17,836	\$0	\$163	-	\$17,999	52	\$346	\$25,960
etanercept 50 mg	\$21,052	\$0	\$106	-	\$21,158	64.2	\$330	\$24,717
alefacept 15 mg IM	\$23,880	\$806	\$2,412	-	\$27,098	45	\$602	\$45,163
infliximab 5 mg/kg	\$24,898	\$1,422	\$116	-	\$26,436	82.8	\$319	\$23,946

Annualized Total Costs (USD)

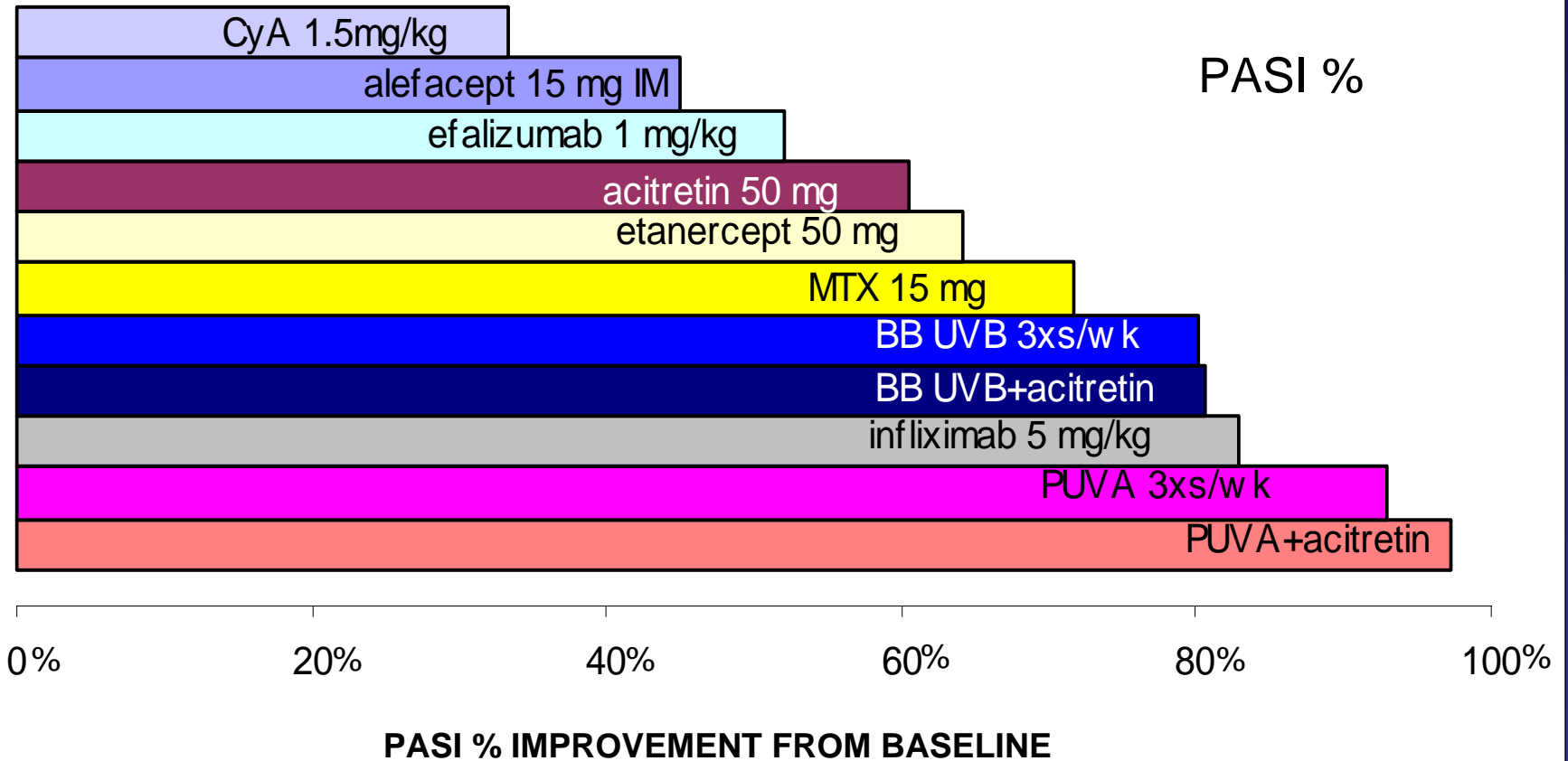
(\$ Rx/Tx + \$ Admin + \$ Screen + \$ AE)

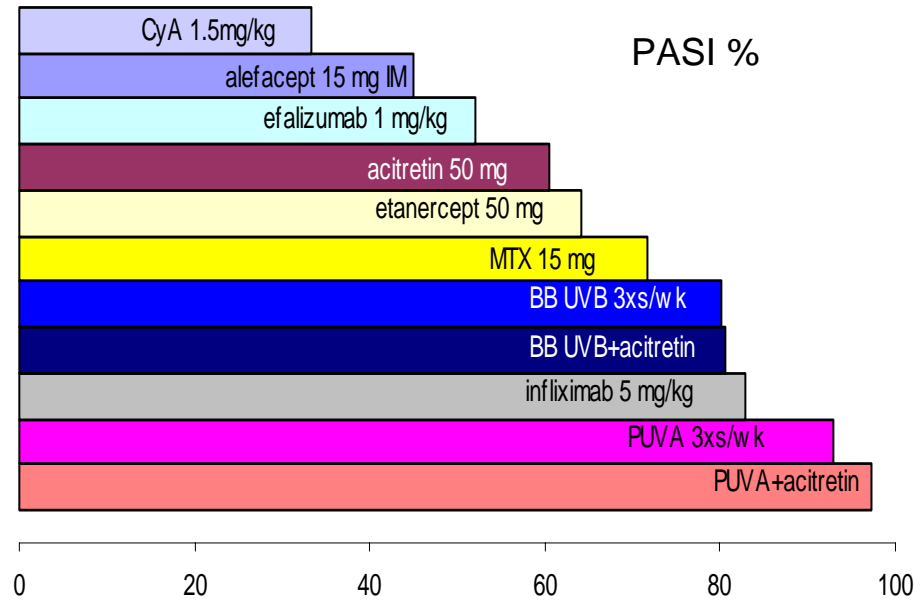
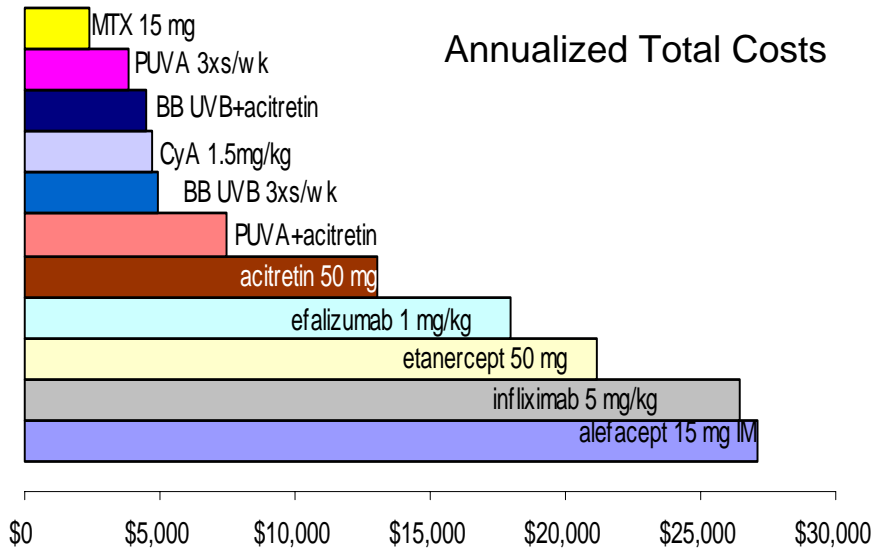


Annualized Total Costs

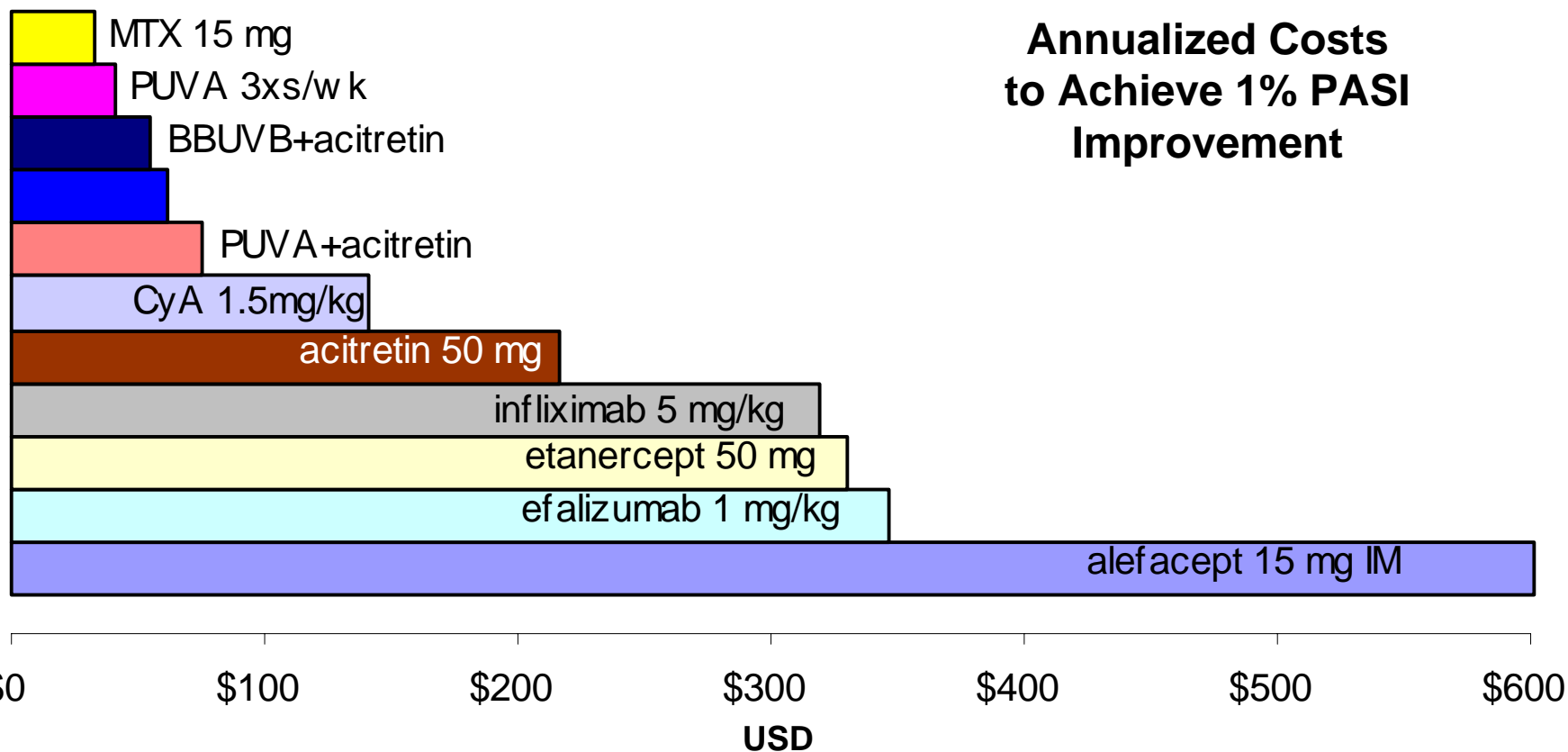


Reported Average PASI % Improvement from Baseline (% Efficacy)

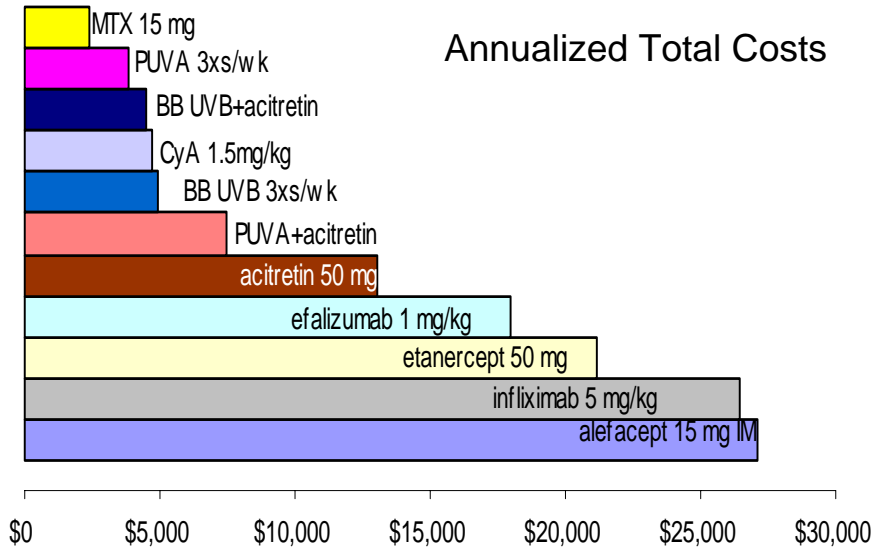




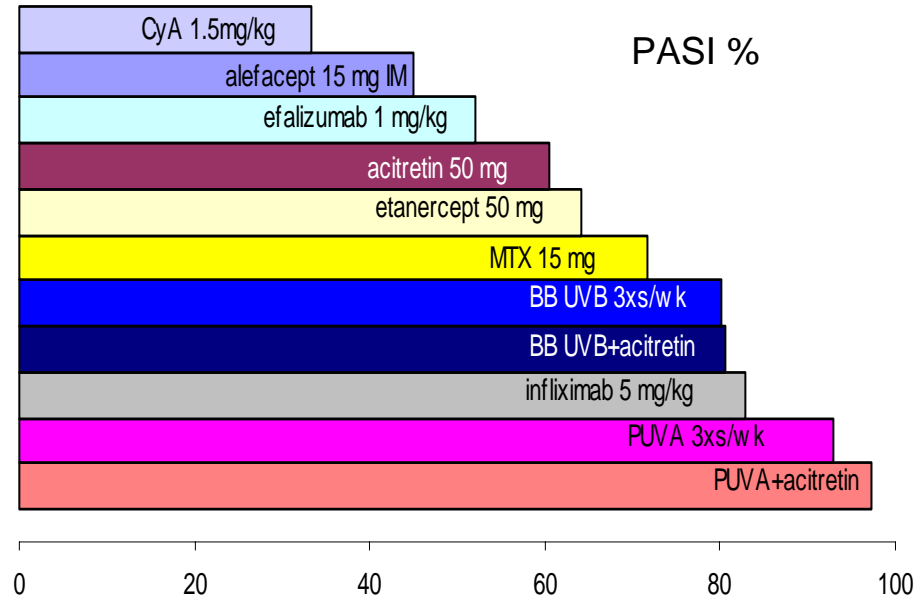
Annualized Costs to Achieve 1% PASI Improvement (USD)



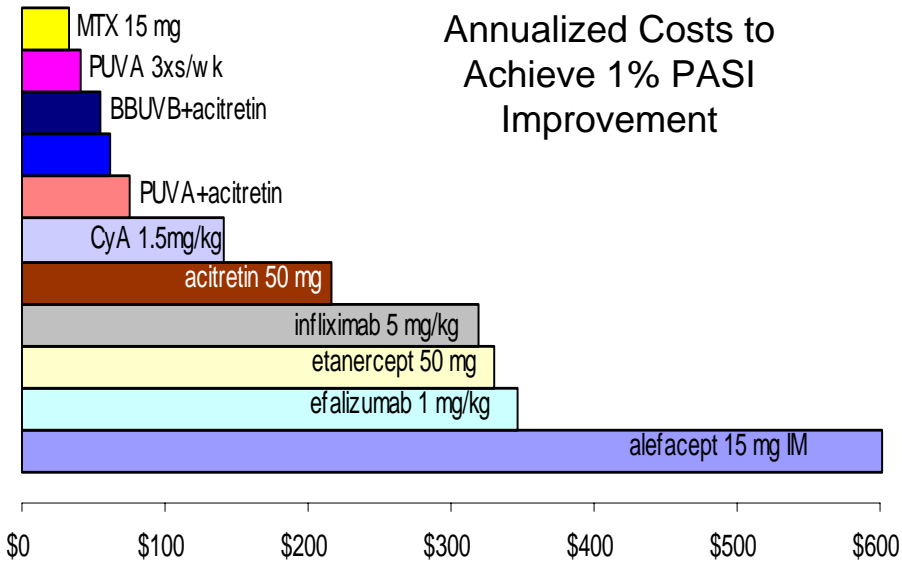
Annualized Total Costs



PASI %

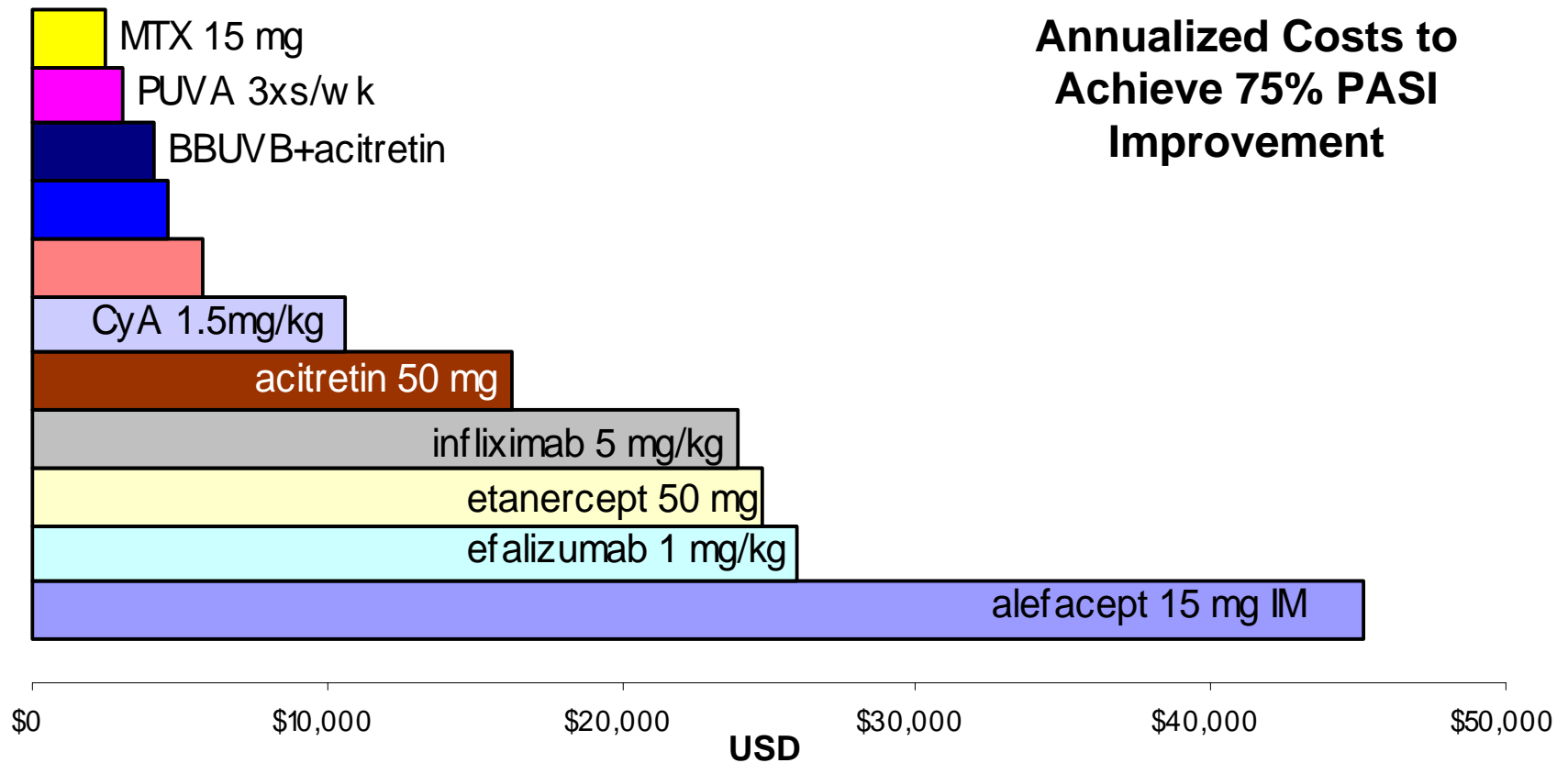


Annualized Costs to Achieve 1% PASI Improvement

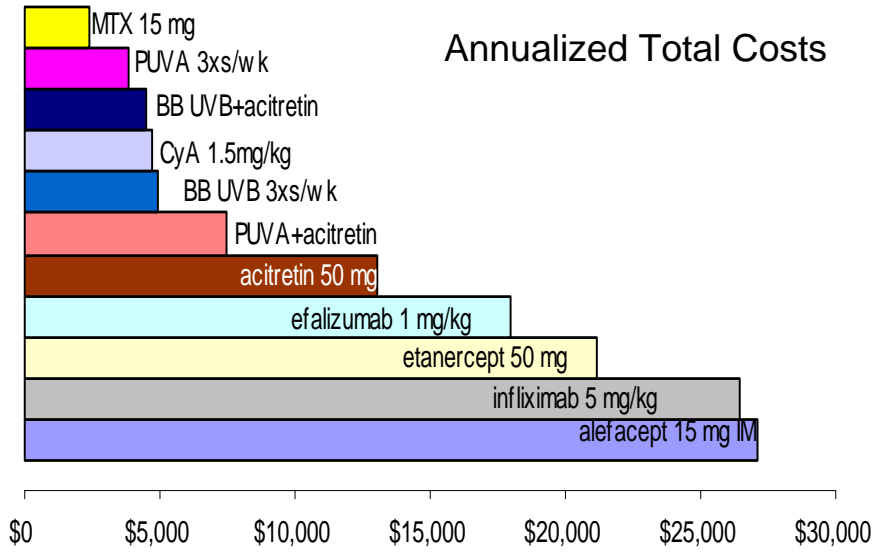


Annualized Costs to Achieve 75% PASI Improvement (USD)

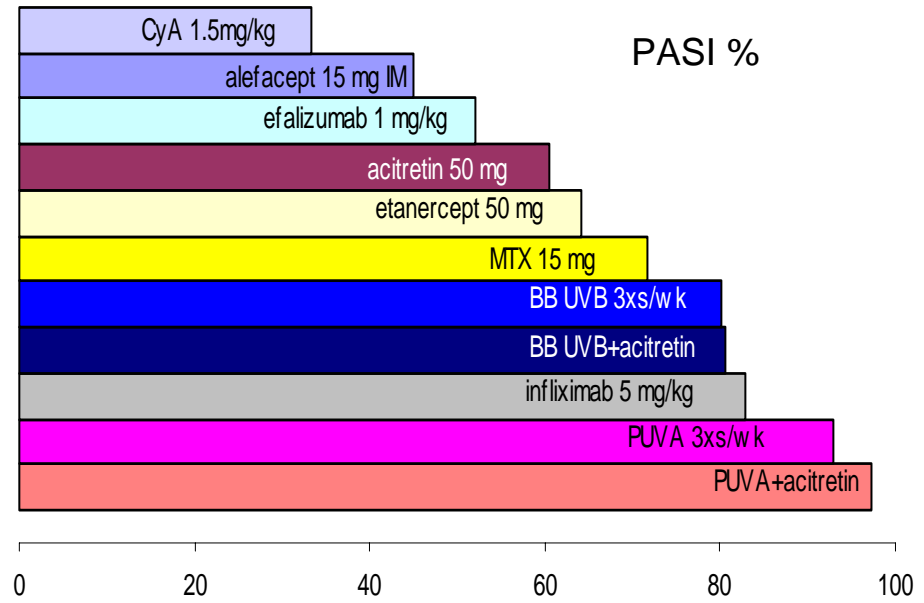
Annualized Costs to Achieve 75% PASI Improvement



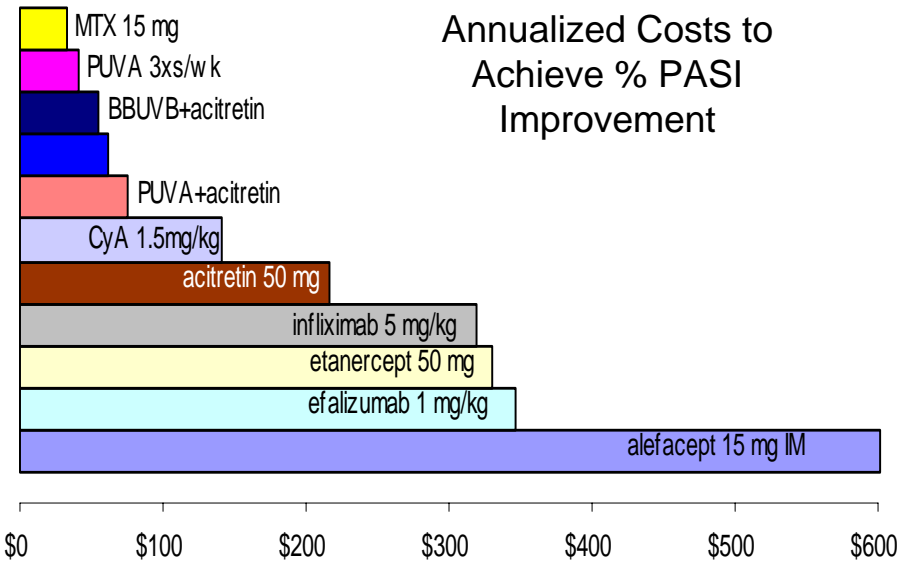
Annualized Total Costs



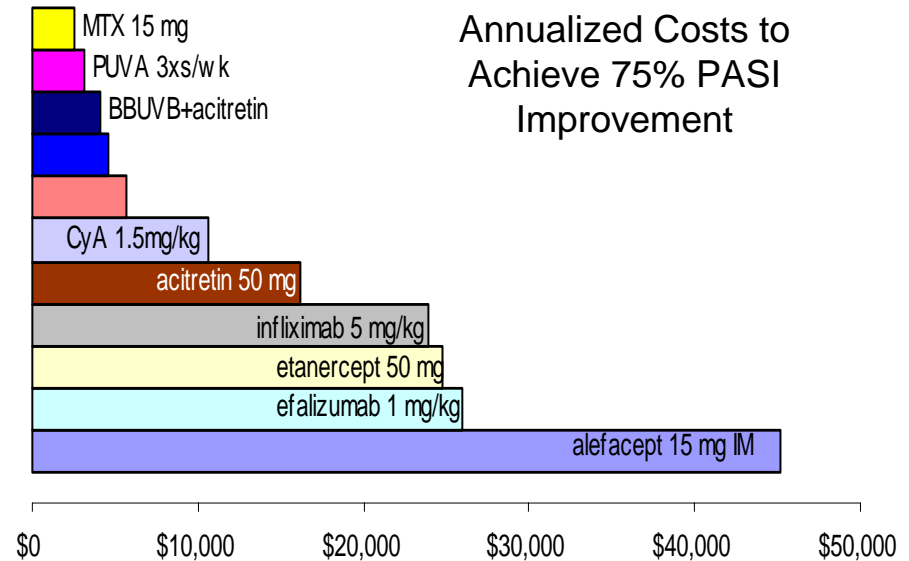
PASI %



Annualized Costs to Achieve % PASI Improvement



Annualized Costs to Achieve 75% PASI Improvement



Conclusions

- The most costly treatments are not necessarily the most efficacious.
- Biologics do not appear to be as cost-effective as oral systemics, phototherapies, or combined phototherapy with acitretin.
- Our results do not justify positioning biologics as first-line therapy for moderate-to-severe psoriasis.

Discussion

Cheryl S. Hankin, Ph.D.

President and Chief Scientific Officer

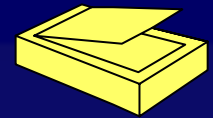
BioMedEcon Group

San Jose, California

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Backup

STUDY EXCLUSION CRITERIA



- PASI % improvement from baseline not reported or unavailable for calculation.
- Number of Ss receiving active treatment <10.
- Treatment duration <6 or > 14 wks.
- Diagnosis other than moderate to severe psoriasis or PASI < 8.
- Sample does not consist predominantly of plaque psoriasis (vs other variants).
- Mean dose unspecified.
- For monotherapies, concomitant systemic or phototherapy psoriasis medication/treatment was received in addition to targeted treatment.
- Maintenance following stabilization (rather than de novo) treatment.
- Dose exceeds current recommendation.
- Duration of study or time at endpoint evaluation unspecified.
- Study is duplication and previously reviewed by us.
- Poor Study Quality (did not apply Intent To Treat).
 - Disposition of dropouts unclear.
 - Dropouts excluded from analysis.
- Biased sample selection (e.g., Ss excluded from participation if poor response to treatment previously).
- Study Design
 - Retrospective review.
 - Case Study.
 - Randomized assignment to groups?

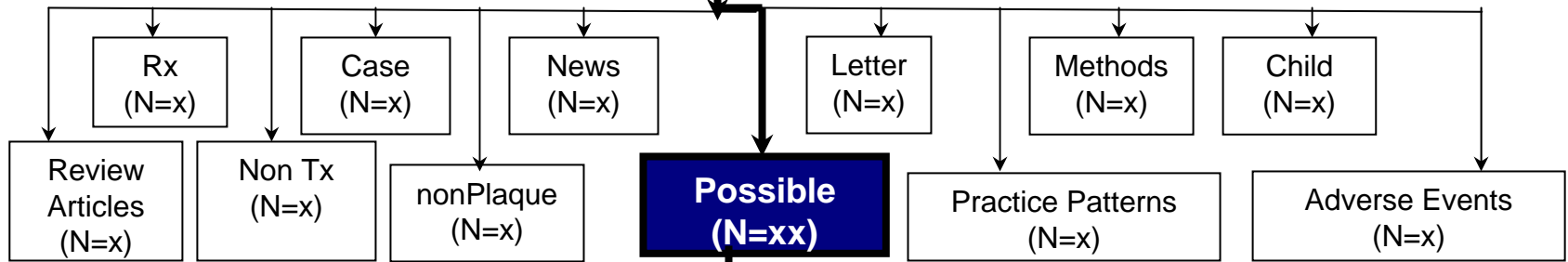
SEARCH PROCEDURE

CONDUCT SEARCH

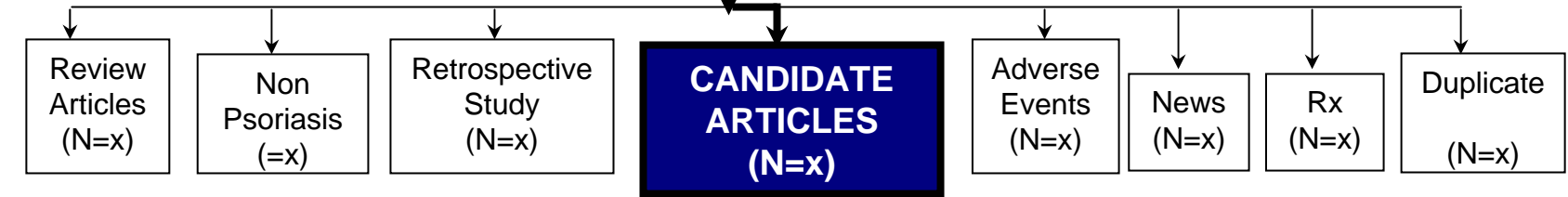
Medline: 1966-7/2004 for
(Psoriasis AND Tx) Limit English
N=xxx

Handsearch (Using References
Obtained from Medline Articles)
N=xxx

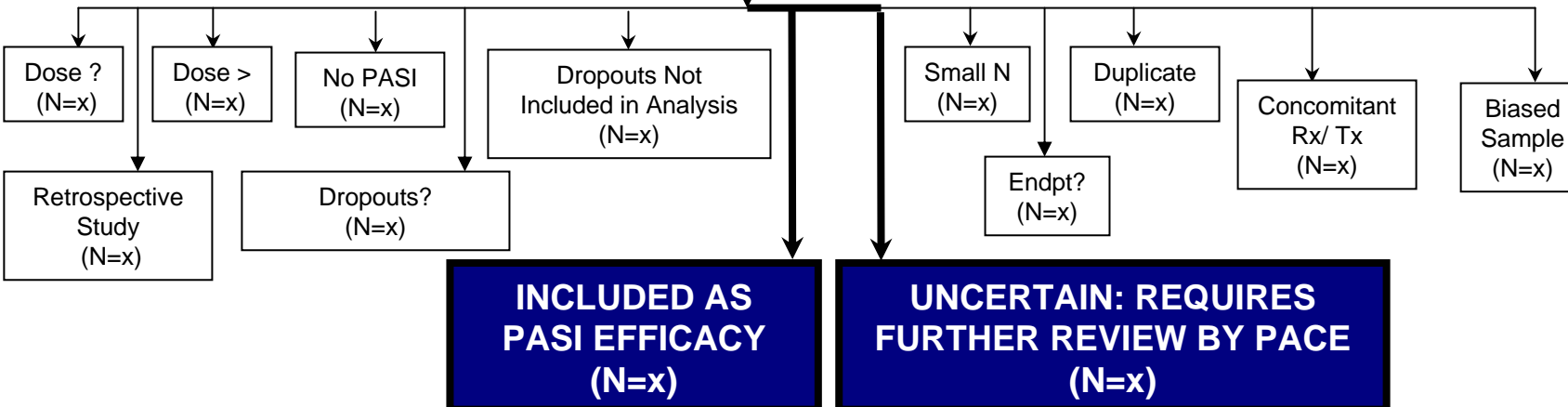
REVIEW TITLES & ABSTRACTS



EXAMINE ARTICLES



WRITTEN EVALUATION of ARTICLES



Systemic Psoriasis Drugs Under Development

Drug Name	Company	Description	Status
Avandia (rosiglitazone maleate)	GlaxoSmithKline	oral antidiabetic agent	phase III for psoriasis
Bimosiamose	Encysive	endothelin A receptor antagonist	phase II
Elidel (pimecrolimus)	Novartis	oral anti-inflammatory	phase II
Humira	Abbott	monoclonal antibody	phase II for psoriasis
ISA247	Isotechnika	systemic immunosuppressant	phase II complete
Neovastat (AE-941)	Aeterna	angiogenesis inhibitor	phase II complete
Onercept	Serono	anti-TNF protein	phase III
Panretin (alitretinoin)	Ligand	oral vitamin A derivative	phase II
Psoraxine	Astralis	injectable immuno-therapeutic agent	phase I/II
Remicade (infliximab)	Centocor	anti-TNF	phase III for psoriatic
Siplizumab (MEDI-507)	Medimmune	monoclonal antibody against T-cell receptor (CD2)	phase II
Zorcell (IR502)	Immune Response	causes immune system to shut down activated T cells	phase II

PASI Scoring (0 to 72)

Head

$$0.1 (\text{Erythema}_H + \text{Infiltration}_H + \text{Desquamation}_H) * \text{Area}_H$$

+

Torso

$$0.3 (\text{Erythema}_T + \text{Infiltration}_T + \text{Desquamation}_T) * \text{Area}_T$$

+

Upper Extremities

$$0.2 (\text{Erythema}_U + \text{Infiltration}_U + \text{Desquamation}_U) * \text{Area}_U$$

+

Lower Extremities

$$0.4 (\text{Erythema}_L + \text{Infiltration}_L + \text{Desquamation}_L) * \text{Area}_L$$

Note: Severity of Erythema, Infiltration, Desquamation assessed on a 5-pt scale (0=no involvement, 4=extreme involvement); Area assessed on a 7-pt scale (0=<10% involvement, 6= 90-100% involvement)