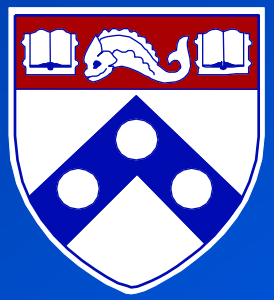
The Dermatology Clinical Effectiveness Research Network (DCERN): Early Findings for Psoriasis



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Disclosure statement

- I have been an investigator and/or consultant for Amgen, Abbott, Centocor, Pfizer, Novartis, and Celgene
- None of these consultancies exceed the threshold of a significant financial COI as defined by AAMC
- This presentation is the sole work of Dr. Gelfand

What is CER: AHRQ definition

"**Comparative effectiveness** research is the conduct and synthesis of research comparing the benefits and harms of various interventions and strategies for preventing, diagnosing, treating, and monitoring health conditions in real-world settings."

Conway PH and Clancy C NEJM 2009;361:328-330

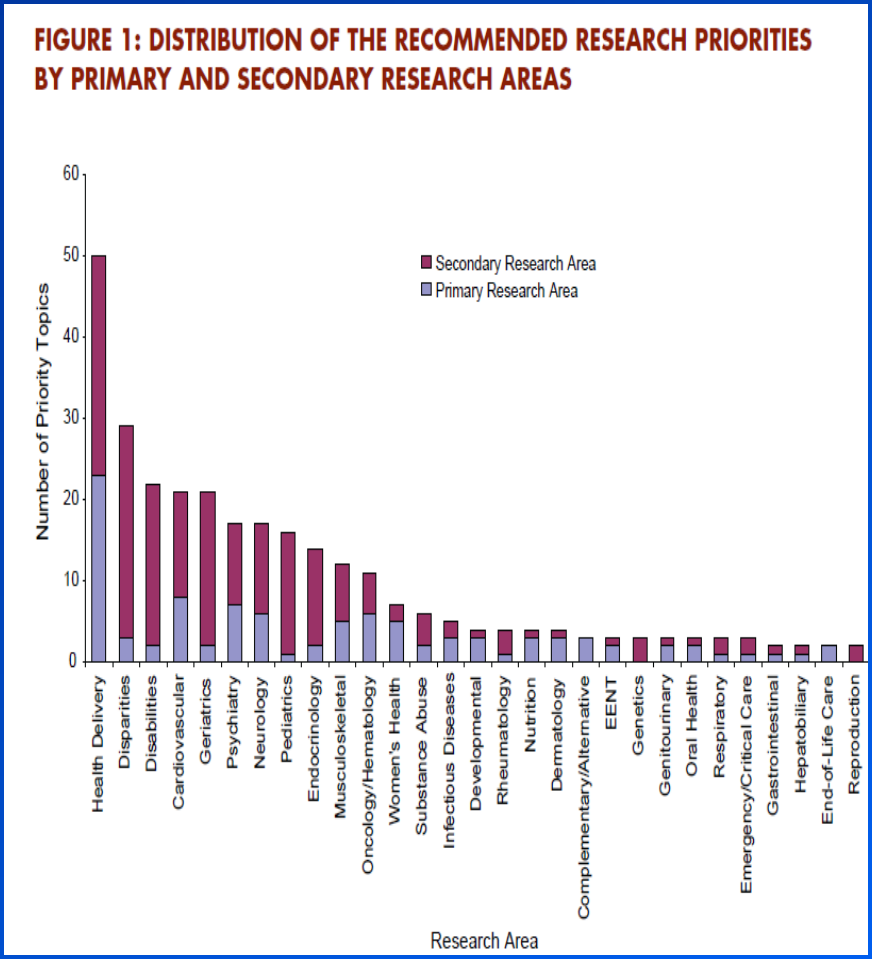
CER Funding

- Health services research
  - 1.5% of biomedical research expenditures
  - 0.1% of US expenditures on health care
- American Recovery and Reinvestment Act (ARRA) – targets CER
  - DHHS $400 million
  - NIH $400 million
  - AHRQ $300 million

Initial National Priorities for CER

- IOM received nominations > 2600 topics
- Priorities determined by:
  - Condition criteria (burden, cost, variability)
  - Priority criteria (appropriateness for CER, knowledge gaps, likelihood that results would improve health)
- Need for a robust CER enterprise
  - Public-private partnerships
  - Infrastructure for large trials, observational studies, and data network
  - Expand workforce: biostatisticians, epidemiologists, trialists, etc

IOM CER Priorities



- 2nd Quartile

  Compare the effectiveness of psoriasis treatment (topicals, UV, orals, biologics)

- 3rd Quartile

  Topical treatments for chronic lower extremity wounds

- 4th Quartile

  Compare long term treatments for acne

What is “Known” about CER for moderate to severe psoriasis

- EDEN Psoriasis Survey
  - 1977-2006 46% of RCT’s had active control groups (N=389)
  - Only 4 studies were comparing systemic treatments
  - Median duration 12 weeks (range 1-154)[1]

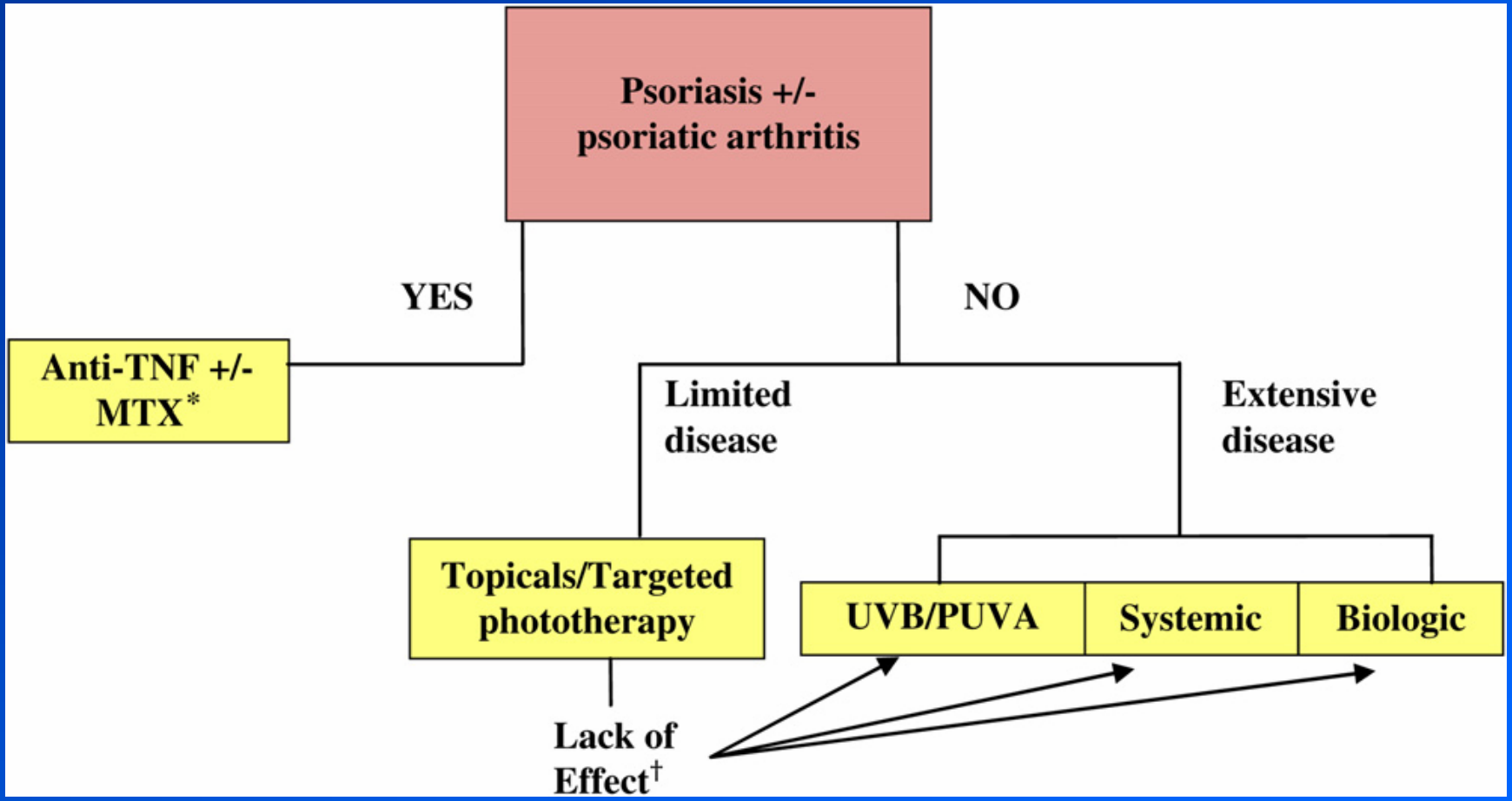
Naldi, L et al JID 2003;120:738-741
Naldi L, et al. BJD 2010;162: 384-389
[1]Data from 2001-2006

Published Comparative Studies of Systemic Treatments

Drugs	Duration (weeks)	N
adalimumab, methotrexate, placebo [1]	16	271
ustekinumab v. etanercept [2]	12	903
methotrexate v. cyclosporine [3, 4]	12, 16	68, 88
etretinate v. cyclosporine [5, 6]	12, 10	76, 210

[1]Saurat JH, Br J Dermatol. 2008;158(3):558-66 [2]Griffiths CE N Engl J Med. 2010;362(2):118-28.
[3]Flytström I, et al Br J Dermatol. 2008;158(1):116-21. [4]Heydendael VM, et al N Engl J Med. 2003 14;349(7):658 65. [5]Mahrle G, et al J Am Acad Dermatol. 1995;32(1):78-88. [6]Dermatology. 1993;187 Suppl 1:8-18

1st Line Treatment of Extensive Psoriasis: A-U



Menter, A et al. JAAD 2008;58:826-50

DCERN: Specific Aims

1. To develop an infrastructure and network that can conduct comparative effectiveness research in skin diseases (DCERN)

2. To determine the key elements of comparative effectiveness research of treatments for moderate to severe psoriasis necessary to inform patient care

3. To determine and compare the current effectiveness of therapies for moderate to severe psoriasis that patients are receiving at the time of their routine dermatologic evaluation

Aim 1: Develop an Infrastructure

- Goals
  - Geographically representative
  - “Real World”
  - Embedded in busy clinical practice
  - High quality data

DCERN: An Infrastructure for CER

Investigators	Site
Joel Gelfand MD MSCE Abby Van Voorhees MD	Univ. of Penn, Philadelphia and Radnor PA
Kristina Callis Duffin MD Gerald Krueger MD	University of Utah, Salt Lake City UT
Robert Kalb MD	Private practice, Buffalo, NY
Jamie Weisman, MD	Private Practice, Atlanta GA
Bruce Brod MD Abby Jacobson, PA	Private Practice, Lancaster, PA
Stephen Schleicher, MD	Private Practice, Hazelton, PA
Michael B Stierstorfer, MD	Private Practice, North Wales, PA
Brian Sperber, MD PhD	Private Practice, Colorado Springs, CO

Governance

- **Executive Committee**
  Joel Gelfand, Kristina Callis, Bruce Bebo, Jamie Weisman, Andy Blauvelt
- **Steering Committee**
  Kevin Cooper, Meg Chren, Bruce Strober, Andy Blauvelt, Alexa Kimball, Abrar Qureshi
- **Scientific Committee**
  Brian Strom, David Margolis, Sean Hennessy, Andrea Troxel

DCERN Infrastructure Development: Challenges and Opportunities

- Wide variation in training, knowledge, and infrastructure for conducting research in a busy clinical practice setting
- Financial Conflicts of Interest
  - What venue assesses and manages?
  - How do you apply academic institutional policies on COI to those in private practice?

Aim 2: Determine Key Elements of CER for Moderate to Severe psoriasis

- Which treatments to compare?
- What are the key elements that define effectiveness?
  - Short vs. long term efficacy?
  - Safety?
  - Cost?
- Measure uncertainty, variation in practice, knowledge, etc

Aim 2 approach

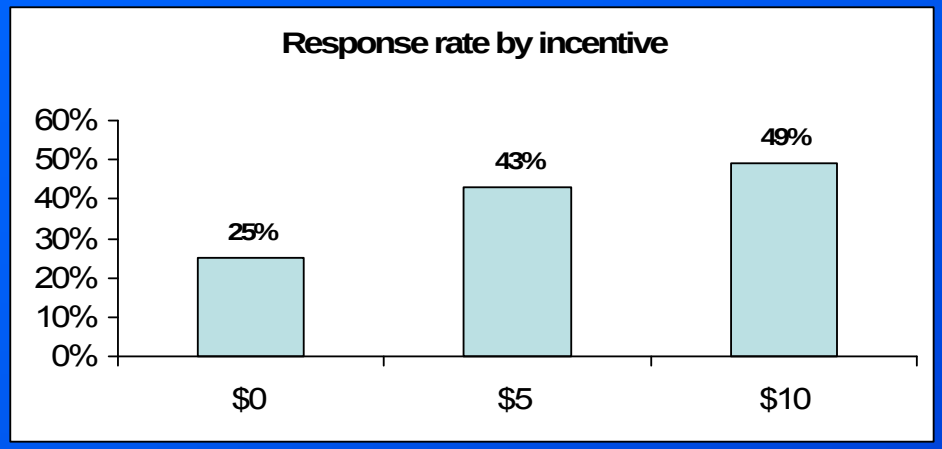
- Expert opinion
  - DCERN investigators
  - DCERN steering committee
  - DCERN scientific committee
- Survey data

Methods

- 1000 dermatologists (500 NPF, 500 AAD)
  - Sub study: randomized equally to $0, $5, or $10 incentive enclosed with survey
- Outcomes of interest:
  - Physician priorities for CER in psoriasis
  - Preferences for first line treatment
  - Impact of incentives on response rate

Results: Response Rate

- Overall response rate: 39%



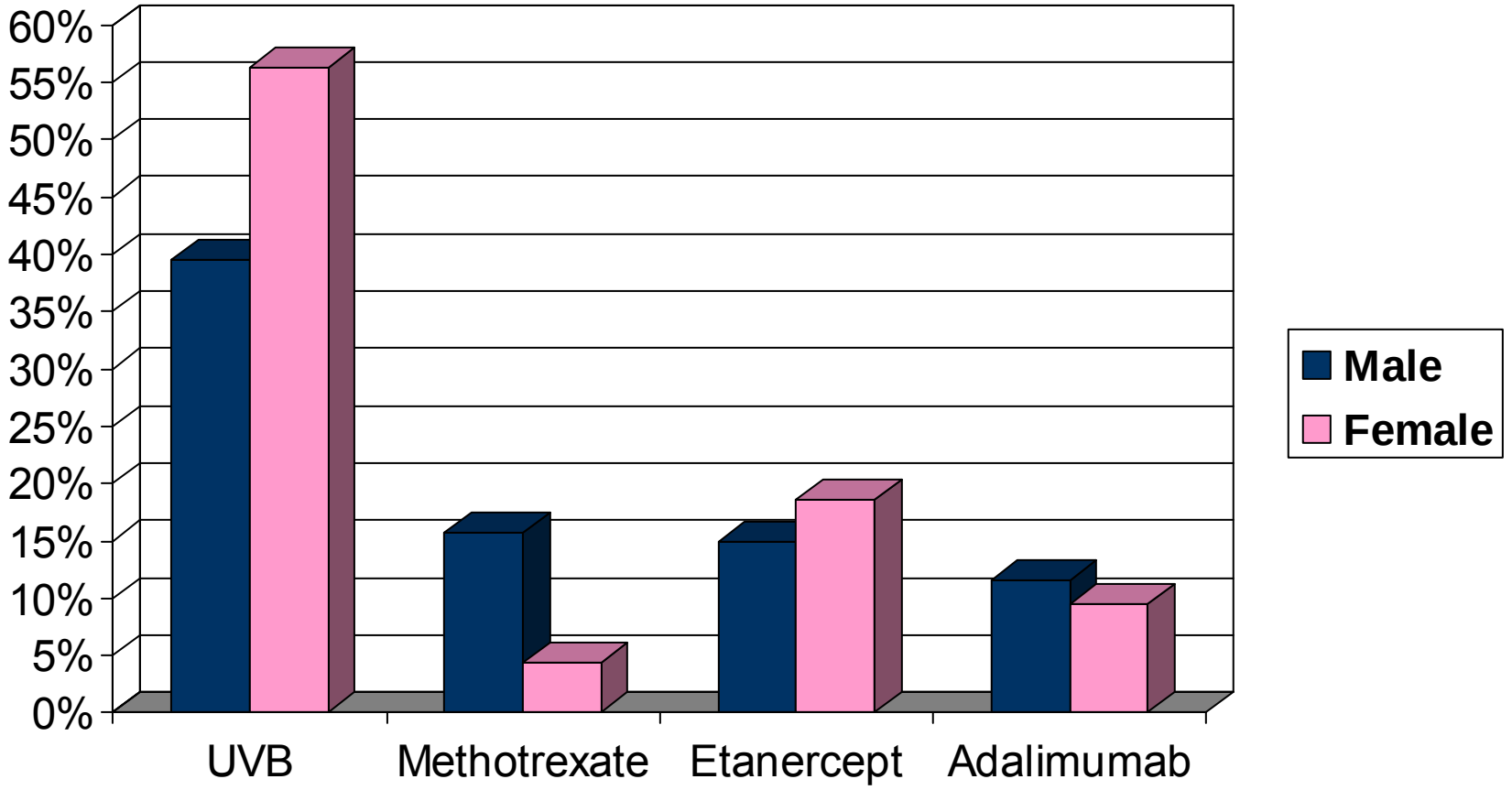
*p<0.001

  - OR (incentive vs. none): 2.51 (1.87-3.39)
- Cost per response in $0 group exceeded that of $5 group when variable costs surpassed $1.88 per questionnaire

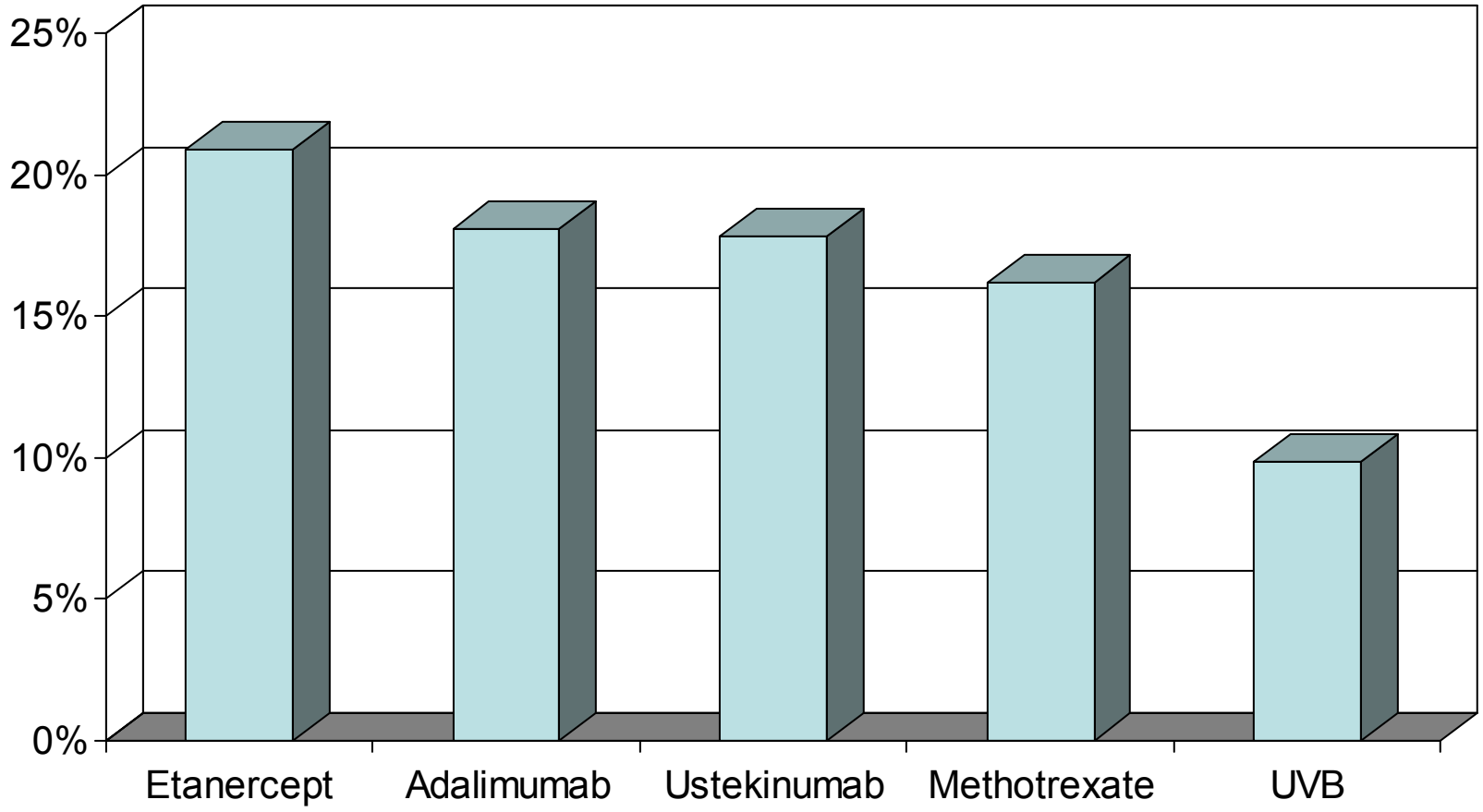
Results: Respondent Characteristics

- Sex: 72% male
- Duration in practice: 23 years (SD 10.6)
- Practice type
  - Private 70%
  - Academic 10%
  - Multi-specialty 10%
- Practice characteristics:
  - 66% administered phototherapy
  - 21% affiliated with infusion center
  - 39% employed physician extenders (NP, PA, etc.)
    - 71% of physician extenders managed psoriasis pts on oral or biologic rx
- # moderate-to-severe psoriasis pts in last 3 months: median 30 (IQR 15-60)
- % of pts on concurrent topicals and systemic rx: median 90 (70-100)

Results: Dermatologist Preferences for First-Line Treatment in a Healthy Adult with Moderate-Severe Psoriasis



Results: Dermatologist Preferences For Treatments in a 3 Arm RCT

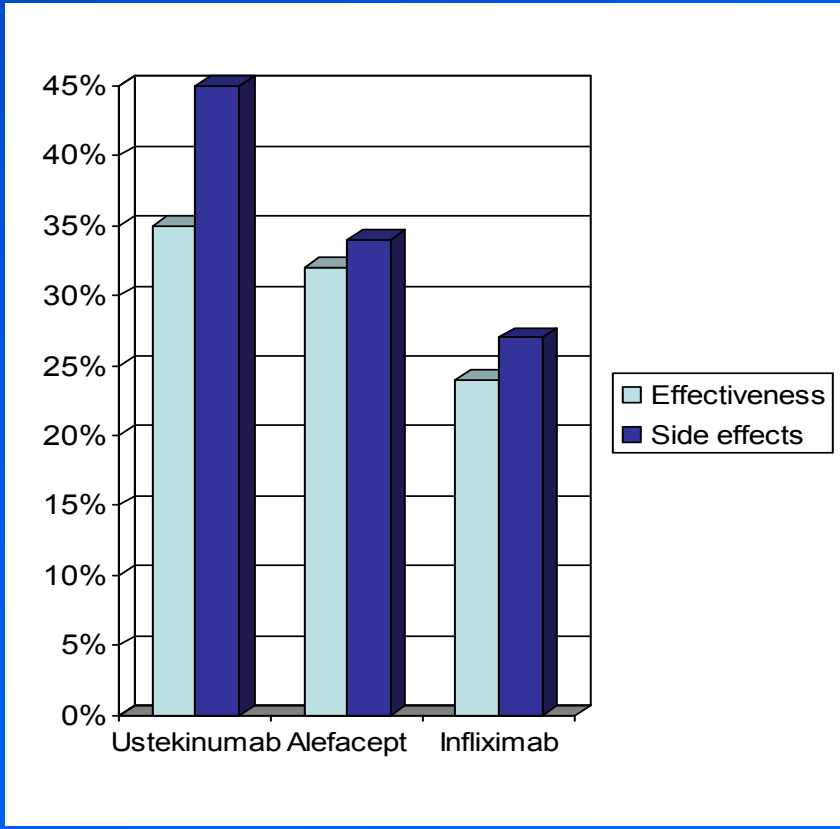


Results: Effectiveness and Safety

Most effective therapies
1. Infliximab
2. Ustekinumab
3. Cyclosporine

Least likely to be stopped due to side effects
1. Etanercept
2. Adalimumab
3. UVB

Many respondents did not know the effectiveness or rate of side effects for:



Aim 3: Compare current effectiveness of therapies for moderate to severe psoriasis

- Study Design
  - Consecutive patients
  - Inclusion: Current or previous treatment for mod/severe psoriasis or history of BSA ≥ 5%
  - Occurs during regularly scheduled clinic visit
  - Enrollment goal: 2000
- Outcomes
  - Patient reported (confirmed by medical record)
    - Medical and Psoriasis history
    - DLQI, EQ-5D, TSQM
    - Detailed data on current and prior psoriasis treatment history
    - SES
  - Physician reported
    - PGA
    - PASI
    - BSA

Aim 3: Initial Data: Demographics

N	840
Age Mean (SD) Median (IQR)	 48.9 (16.0) 50 (37, 61)
Sex Male (%) Female (%)	 419 (49.9%) 420 (50.1%)

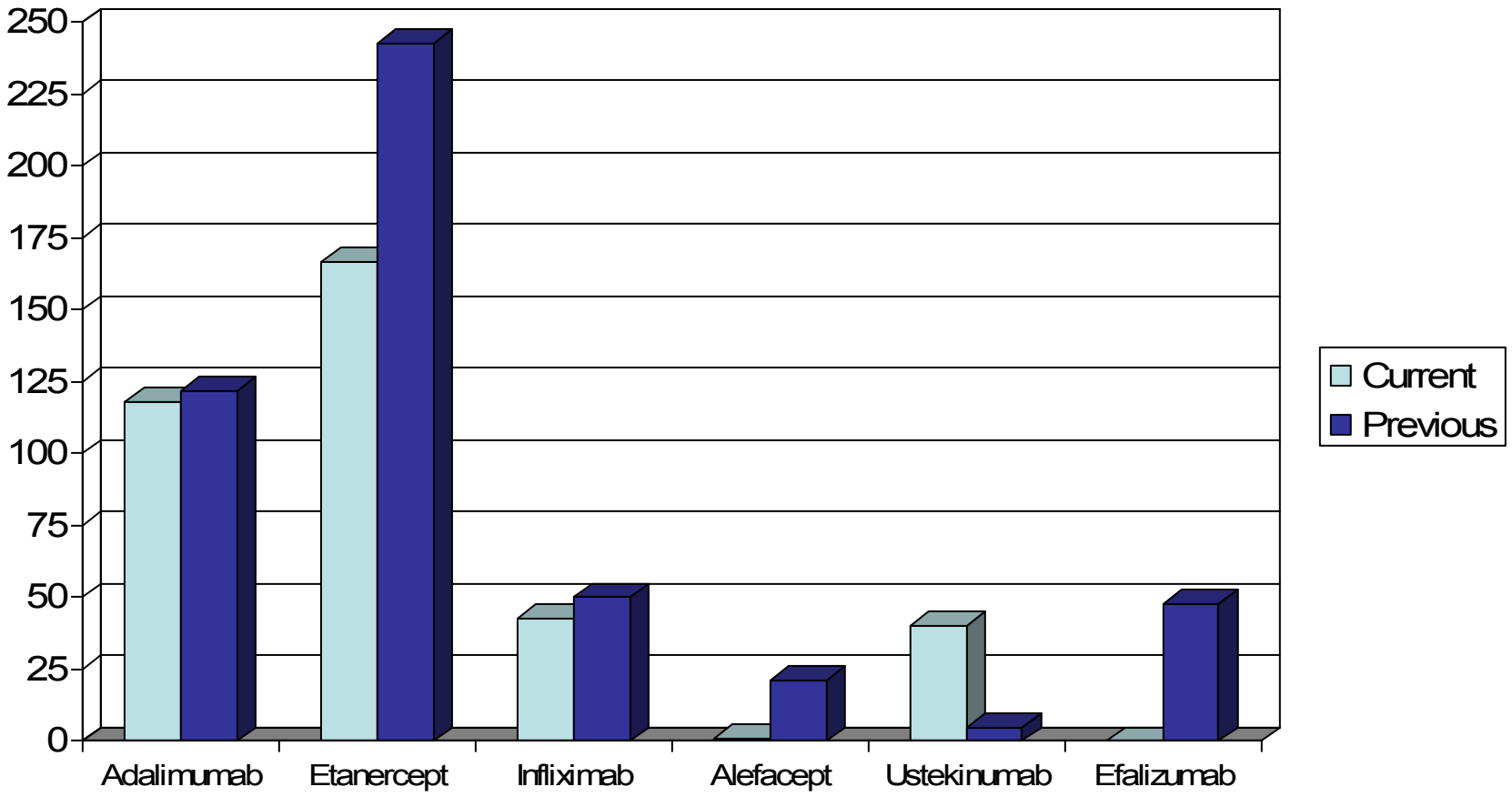
Aim 3: Initial Data: Demographics

Race	
White/Caucasian	725 (86.4%)
Black/African American	31 (3.7%)
Asian	30 (3.6%)
Other/Multiracial	44 (5.2%)
Prefer not to answer	9 (1.1%)
Income	
< $25K	96 (11.5%)
$25K - $49K	126 (15.1%)
$50K - $74K	127 (15.1%)
$75K - $99K	111 (13.3%)
> $100K	217 (26%)
DK/Prefer not to answer	158 (18.9%)
Marital Status	
Single	202 (24.1%)
Married	526 (62.8%)
Divorced	84 (10%)
Widowed	25 (3%)

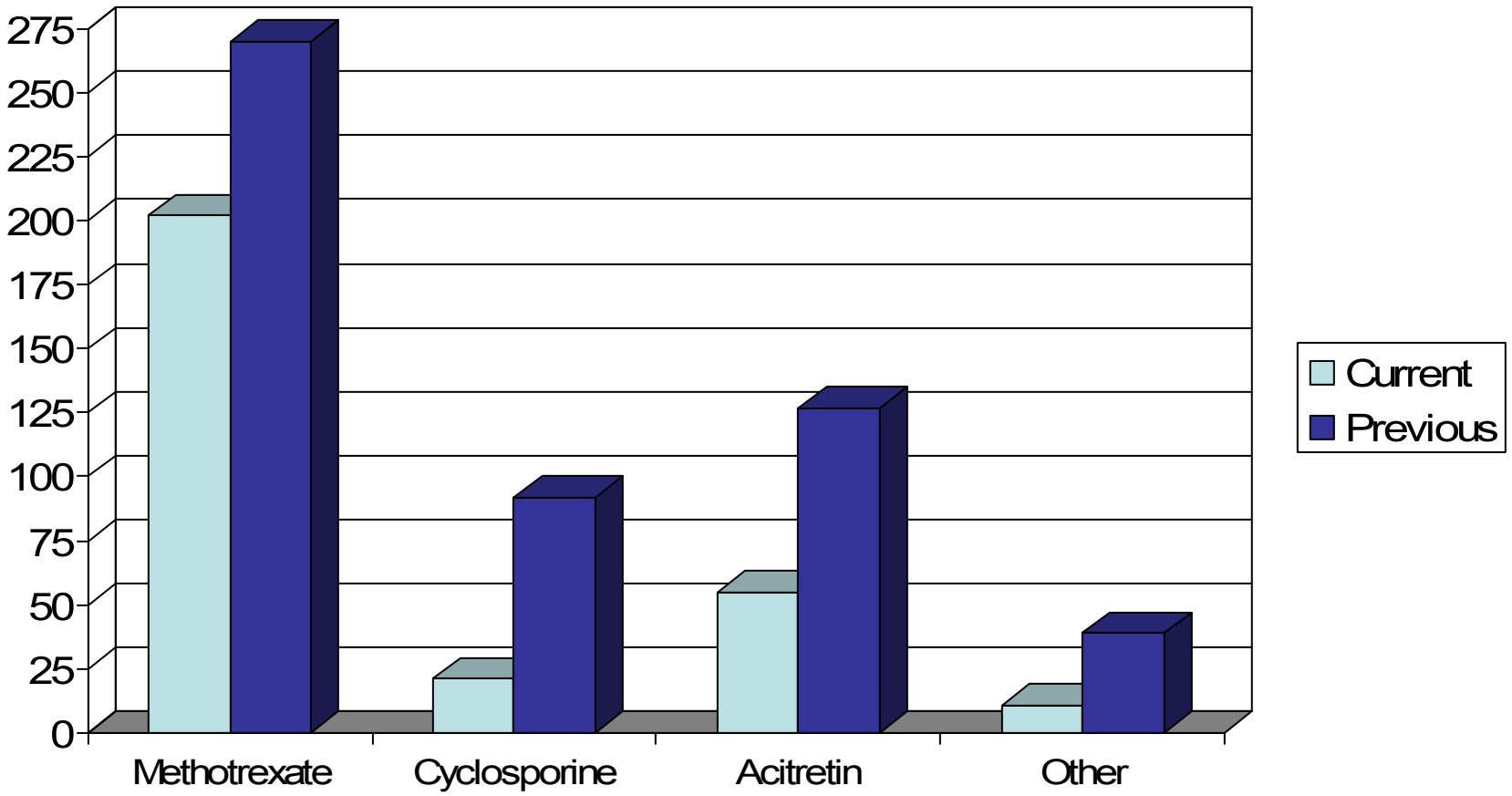
Aim 3: Initial Psoriasis Data

Duration of disease in years	Mean 20 (SD 15) Median 17 (IQR 8, 29)
Primary Indication for treatment	Plaque 89% Palmar Plantar 4% Psoriatic arthritis 2.4%
Body Surface Area	Mean 5.5% (SD 8.4) Median 3.2% (IQR 1.6, 5.6)
PASI	Mean 4.3 (SD 4.4) Median 3.2 (IQR 1.6, 5.6)
Physician's Global Assessment (1-5)	Mean 1.6 (SD 0.8) Median 1.7 (IQR 1,2)

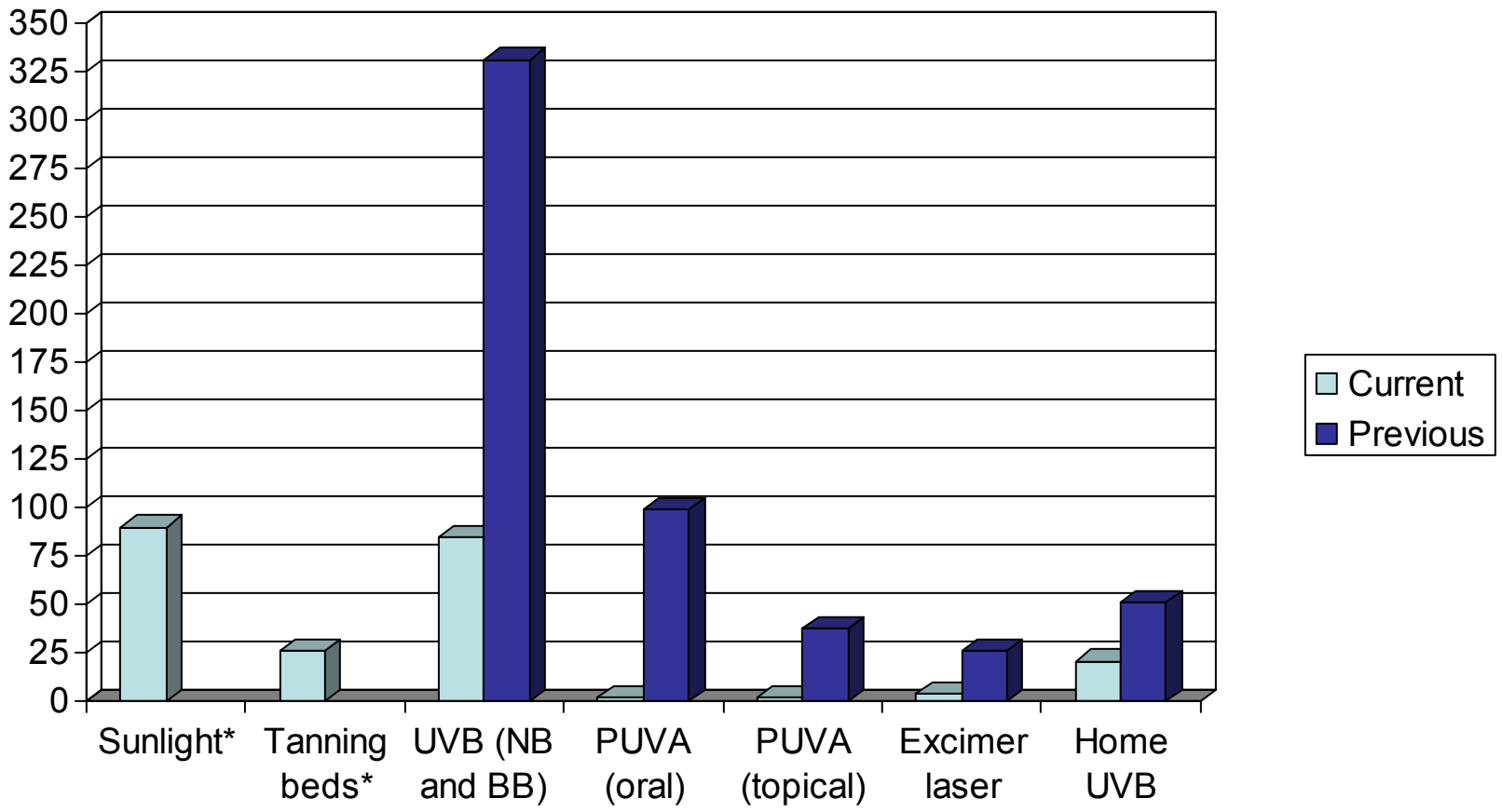
Aim 3 Treatment Data: Biologic Medication Use



Aim 3 Treatment Data: Traditional Oral Medication Use



Aim 3 Treatment Data: Light Therapy Use



*data on previous use non-applicable

Top Reasons for Discontinuing Rx

Etanercept (N=256)		Methotrexate (N=281)	
1. Lost efficacy	30.2%	1. Other*	26.8%
2. Did not work well enough	23.5%	2. Side effects (non-life threatening)	26.4%
3. Other†	17.3%	3. Did not work well enough	18.9%
4. Side effects (non-life threatening)	12.5%	4. Psoriasis improved	18.6%
5. Unrelated illness	9.4%	5. Lost efficacy	12.9%
Life-threatening side effects	*0.8%*	*Life-threatening side effects*	*0.4%*

* e.g. physician changed rx, switched to biologic, pregnancy, exceeded max dose, pt stopped on own, surgery, inability to drink alcohol

† e.g. physician changed rx, switched to another biologic, disliked self-injections, pregnancy

Aim 3: Initial Patient Reported Data

DLQI	
Mean (SD)	4.9 (5.7)
Median (IQR)	3 (1,7)
EQ5D VAS	
Mean (SD)	77 (19.4)
TSQM (Mean, SD)	
Effectiveness	69 (24)
Side Effects	95 (13)
Convenience	73 (19)
Global Satisfaction	74 (21)

Conclusions: Psoriasis CER

1. There is wide variation in treatment preferences
2. Large gaps in knowledge required to inform best practices
3. Detailed psoriasis data can be collected in a busy practice setting
4. DCERN data necessary to plan prospective studies
   - Large simple trials
   - Observational approaches

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