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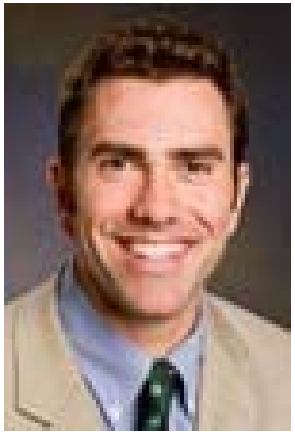
Disclosures (not relevant to this talk)

- Consultant:Janssen, Pfizer, Eli Lilly, Amgen, AbbVie, Novartis, Bristol-Myers Squibb, Astra Zeneca, Celgene

- Grant/salary support as investigator: Janssen, Eli Lilly, Amgen, AbbVie, Novartis, Bristol-Myers Squibb, Stiefel, Celgene

- No speaker bureaus





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IDEOM: Mission

- “To establish patient-centered measurements to enhance research and treatment for those with dermatologic disease”
- Perspectives of patients, health economists, payers, physicians and regulatory agencies are included from the onset
- IDEOM’s goal is to establish validated and standardized outcome measures that satisfy the needs of all stakeholders and can be applied to clinical research and clinical practice

Outcome Measures of Psoriasis

Many measures in use

PASI
SPASI
SPI
PLASI
SAPASI
PSSI
PPPASI
PGA 5pt
PGA 6pt
IGA
IGA mod2011
NPF-PS
LS-PGA

CoPSI
NAPSI
mNAPSI
SPI
DLQI
SF-36
SF-12
EQ-5D
DIDS
PSSI
BIPSIOLS
PASS
PSI
PSD
PSSD

Psoriasis probably has the greatest number of instruments in use owing to

- **industry/researcher need**
- **how the disease lends itself to measurement**

Many lack validity/reliability, "legacy" measures

Many domains constructs, concepts" NOT measured

OMERACT

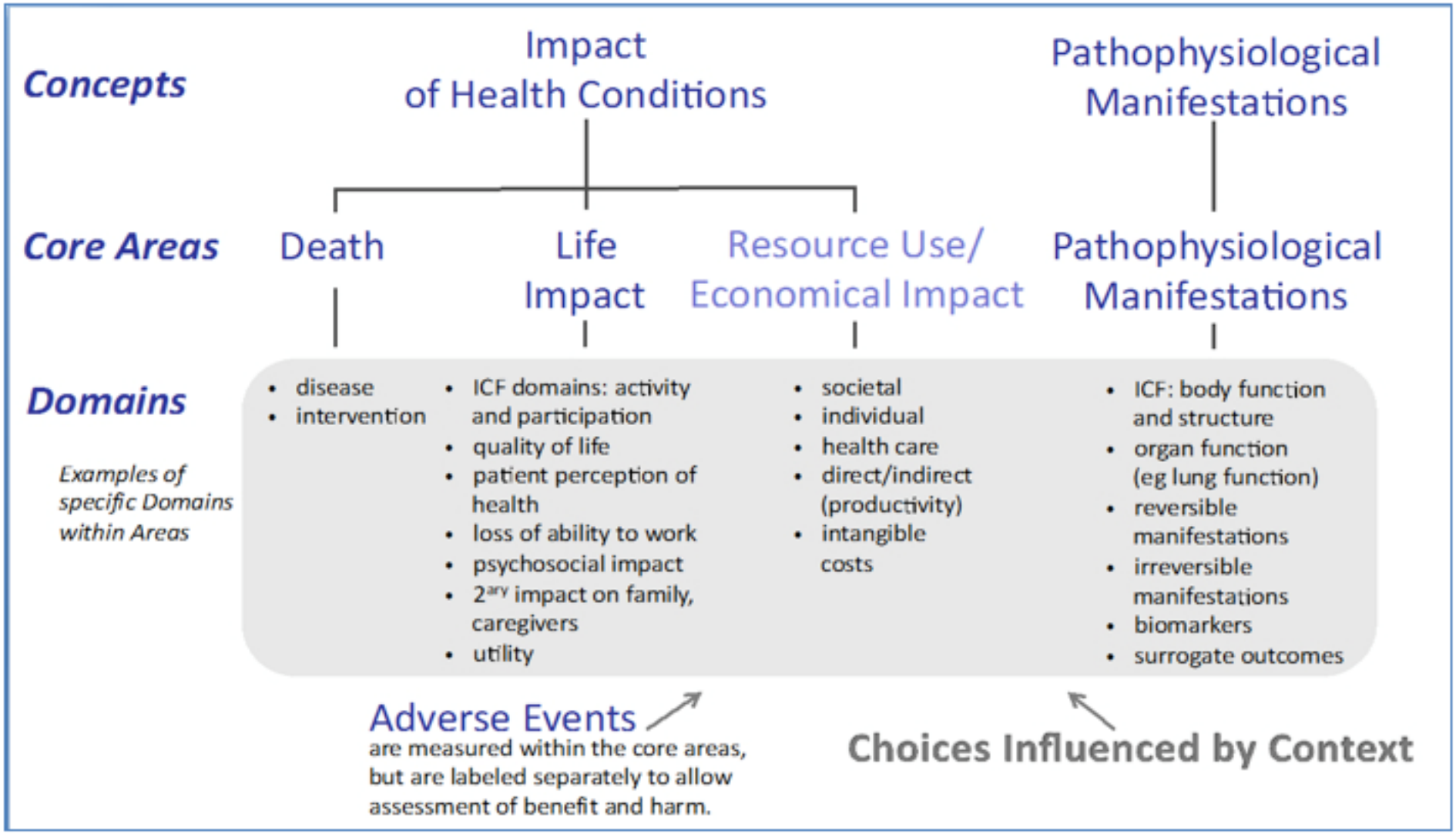
Outcome Measures in Rheumatoid Arthritis Clinical Trials
now
Outcome Measures in Rheumatology

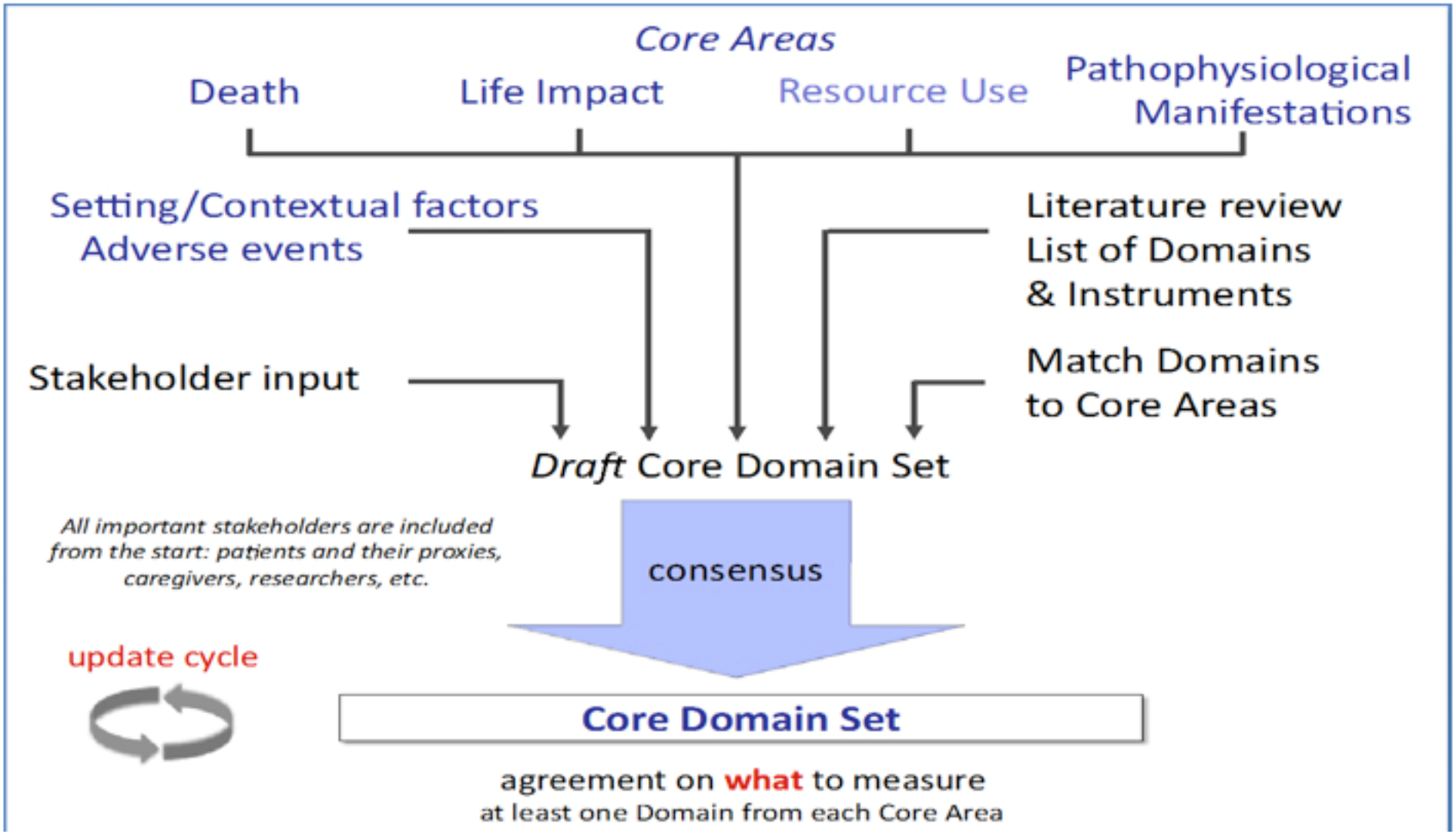
- 1992: formed to develop international consensus on RA outcome measures

- Goal: To develop recommendations for:
  - Core Sets for rheumatologic diseases
    - ***What should we measure?***
    - minimum number of domains to be assessed in RCTs
    - Secondarily in Observational studies, Registries, Clinical practice
  - Core Outcome Measures to assess domains
    - ***What instruments (measures)* should we use?**
    - Responder indices – definition of state, response, minimal clinically important difference (MCID), remission, low disease activity (LDA), flare
    - Research agenda

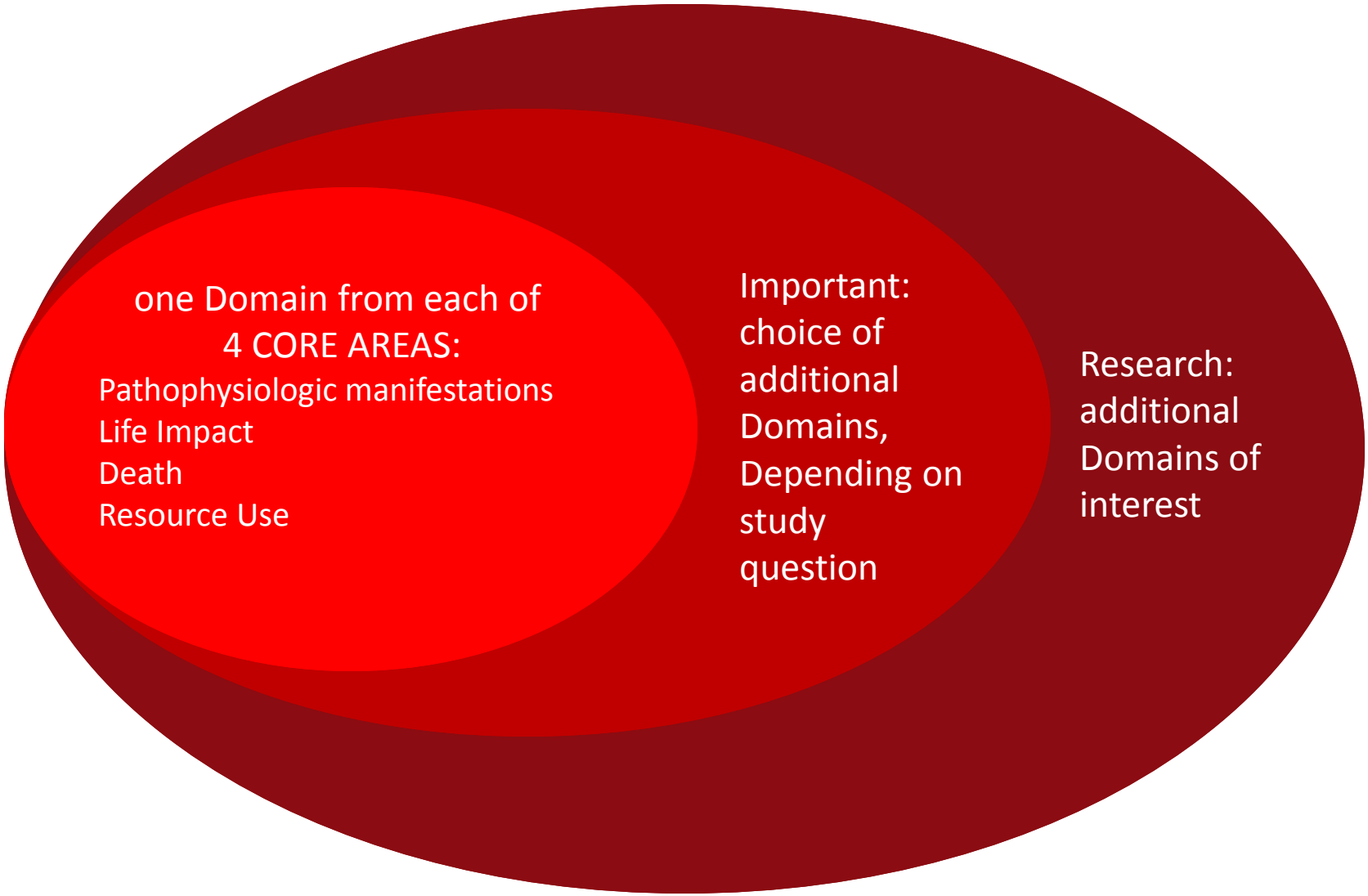
What should we measure?

What instruments (measures) **should we use?**


Concepts
Impact of Health Conditions
Pathophysiological Manifestations
Core Areas
Death
Life Impact
Resource Use/ Economical Impact
Pathophysiological Manifestations
Domains
Examples of specific Domains within Areas
disease
intervention
ICF domains: activity and participation
quality of life
patient perception of health
loss of ability to work
psychosocial impact
2ary impact on family, caregivers
utility
societal
individual
health care
direct/indirect (productivity)
intangible costs
ICF: body function and structure
organ function (eg lung function)
reversible manifestations
irreversible manifestations
biomarkers
surrogate outcomes
Adverse Events
are measured within the core areas, but are labeled separately to allow assessment of benefit and harm.
Choices Influenced by Context


Core Areas
Death
Life Impact
Resource Use
Pathophysiological Manifestations
Setting/Contextual factors
Adverse events
Literature review
List of Domains
& Instruments
Stakeholder input
Match Domains
to Core Areas
Draft Core Domain Set
All important stakeholders are included from the start: patients and their proxies, caregivers, researchers, etc.
consensus
update cycle
Core Domain Set
agreement on what to measure
at least one Domain from each Core Area

Core set


one Domain from each of
4 CORE AREAS:
Pathophysiologic manifestations
Life Impact
Death
Resource Use
Important:
choice of
additional
Domains,
Depending on
study
question
Research:
additional
Domains of
interest

2007 Psoriatic Arthritis Core set with domains

CORE:
Peripheral joint activity
Skin activity
Patient global
Pain
Physical Function
Health Related Quality of Life

Areas of interest:
Dactylitis
Enthesitis
Spinal
Fatigue
Radiology
Acute phase reactants

Research:
MRI
CT
Ultrasound
Tissue analysis
Participation

From *Gladman DD, Mease PJ, Strand V, et al. Consensus on a ore set of domains for psoriatic arthritis. J Rheumatol. 2007 May;34(5):1167-70*

LITERATURE REVIEW and GENERATION of CANDIDATE DOMAINS/SUBDOMAINS

1st IDEOM Meeting, Boston, MA
January 2013:

- Literature Review, generation of items

Post meeting:

- Preliminary Delphi to generate items

Through face-to-face meetings and a pre-Delphi survey, we generated a list of over 193 items

Erythema (redness)
Induration (thickness of lesions relative to normal skin)
Scale (white flaky scale on the top)
Pustules
Body surface area (extent of area covered by disease)
Location of lesions (for example: scalp, groin/genital, palms, soles; nail involvement)
Secondary changes
Desquamation (flaking, shedding)
Fissuring/cracking (cracked skin)\
Dyspigmentation (lightening or darkening of the skin's normal pigment / tone)
Maceration (slightly broken-down skin due to wetness or moisture)
Erosion (superficially open skin)
Bleeding
Odor
Pruritus (Itch)
Burning
Stinging
Skin pain
Nail pain
Inflexibility from thick plaques
Plaque type psoriasis (the most common type of psoriasis)
Pustular (development of small pus-filled skin lesions)
Pustular psoriasis (located on the trunk/extremities)
Palmo-plantar pustulosis (located on the palms and soles)
Inverse / intertriginous psoriasis (psoriasis that involves predominantly the body folds, armpits, groin)
Palmo-plantar (involvement of the palms and soles, predominantly)
Guttate psoriasis (small scattered lesions of psoriasis, often associated with strep infections / 'strep throat')
Erythrodermic Psoriasis (the entire body is red from psoriasis)
Nail psoriasis
Investigator Global Measure
Patient global measure (patient-reported)
Observer global measure
Sleep disturbance
Inflammatory arthritis
Joint pain
Joint pain
Joint tenderness
Joint swelling
Joint damage
Dactylitis (swelling of the entire finger or toe)
Enthesitis (tenderness or pain at sites of ligament or tendon insertions):
Pain
Stiffness
Decreased range of motion
Axial Disease / Spine disease
Cardiometabolic Comorbidities
Adverse cardiovascular events
Cerebrovascular events (stroke)
Congestive heart failure (heart failure)
Cardiovascular death (death from heart or blood vessel disease)
Metabolic Syndrome (medical diseases that increase the risk of heart disease)
Central Obesity (excess fat around the abdomen)
Insulin resistance
Hypertension (high blood pressure)
Dyslipidemia (abnormal blood fats) including hypertriglyceridemia (high bad blood fats) and low HDL (low good blood fats)
Diabetes
Ophthalmologic
Uveitis (inflammation of a part of the eye)
Impact on cognition (Mental impairment, cognitive dysfunction, inability to focus)
Renal (Kidney) Disease
Constitutional
Fatigue
Mood Disturbance
Depression
Suicidal ideation (thoughts of suicide) and other self-destructive behaviors
Anxiety
Frustration
Fear
fear of rejection, fear of relapse/flare
Anger
Emotions & Feelings of Concern
Shame/humiliation/embarrassment
Self consciousness
Worry
Withdrawal
Low Self Esteem
Sleep Disturbance
Impact on family relationships and well-being
Effect on reproduction
Family planning
Concern of passing on disease to the next generation
Pregnancy
Lactation
Social inhibition
Discrimination
Isolation (exclusion)
Avoiding physical contact Social dysfunction Stigmatization Bullying Decreased recreational activity Poor intimacy Sexual dysfunction
Impact on ability to work or perform well in school
Health related quality of life
Treatment satisfaction
Direct Cost Health sector costsOutpatient health servicesInpatient health servicesMedications
Non-medication therapies
Laboratory and radiographic tests
Patient and Caretaker
CostsOut-of-pocket payments (user fees) for hospitals and drugs
Transportation of the patient for healthcare visits
Costs for taking care of dependents as a result of the patient not able to care for them
Modifications in home as a result of illness
Indirect Cost
Patient's Inability to work as productively as a result of illness
Earnings lost while spending time receiving healthcare for illness
Earnings lost while traveling to healthcare providers' facility
Earnings lost while not able to work as productively on the job
Caregiver's earning loss as a result of spending time caring for the patient
Death
Tobacco smoking
Alcohol consumption
Substance abuse
Lack of exercise
Poor diet

Item generation:

listing of all signs and symptoms of psoriasis that could be measured (done by live meeting/ nominal group process, pre-Delphi survey, working group meetings)

Erythema/redness
Induration /thickness
Scale
Pustules
Body surface area
Location of lesions
Desquamation
Flaking
Shedding
Fissuring
Cracking
Skin pigment changes
Maceration
Erosion
Bleeding
Odor
Pruritus (Itch)
Burning
Stinging
Skin pain
Nail pain
Inflexibility

Item distillation

Identifying and removing synonymous items

Erythema/redness
Induration /thickness
Scale
Pustules
Body surface area
Location of lesions
~~Desquamation~~
~~Flaking~~
~~Shedding~~
Fissuring
Cracking
Skin pigment changes
Maceration
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Bleeding
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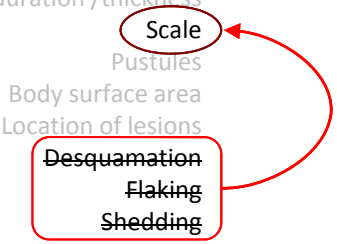
Skin pain
Nail pain
Inflexibility



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Inflexibility

Item organization:

Grouping items into larger domains

Primary cutaneous features

Secondary cutaneous features

Symptoms of psoriasis

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January 2013:
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Post meeting:
- Preliminary Delphi to generate items

DEVELOP CONCEPTUAL MODEL of DOMAINS/SUBDOMAINS

2nd IDEOM Meeting, Toronto, Ontario, Canada, July 2013:
- Further expansion and refinement of candidate items for domains/subdomains

Post meeting:

3rd IDEOM Meeting, Rome, Italy April 2014
- Presentation of first Delphi results

Post meeting:
- Revision of conceptual model to prepare for new Delphi

CONSENSUS PROCESS (DELPHI): to determine the CORE DOMAIN SET

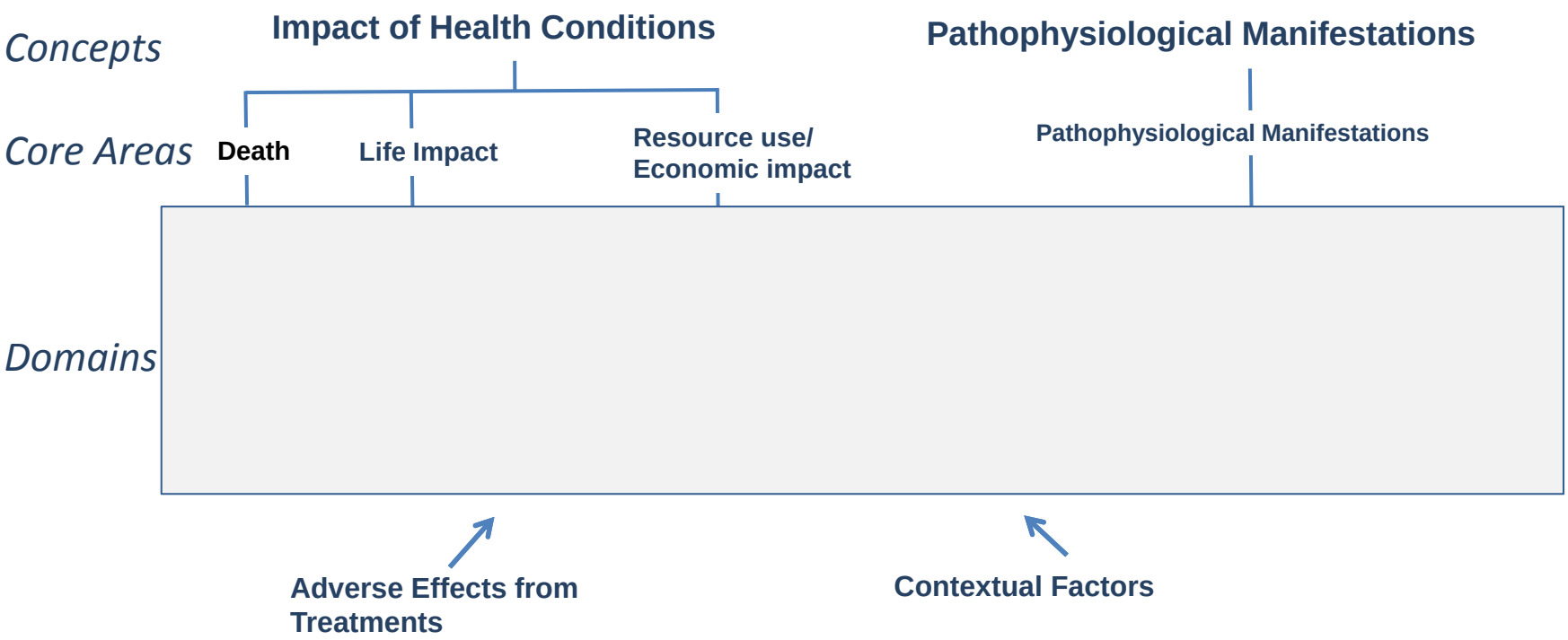
4th IDEOM Meeting, Washington, DC February 2015
- Presentation and vote on Core Domain Set
- Initiate determination of Core Measurement Set for psoriasis clinical trials

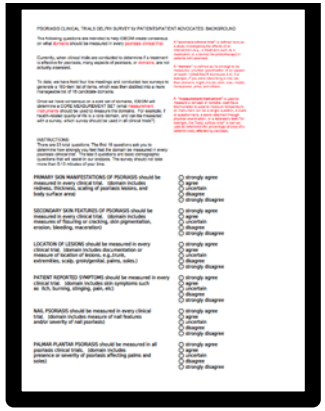
DETERMINATION OF Core Outcome Measurement Set

FOR CLINICAL TRIALs

5h IDEOM Meeting, Washington, DC February 2015
- Presentation of Delphi, voting on Core Domain Set

OMERACT framework





DELPHI SURVEY:
measured in **every** clinical trial?

Concepts	**Impact of Health Conditions**			**Pathophysiological Manifestations**
Core Areas	**Death**	**Life Impact**	**Resource use/ Economic impact**	**Pathophysiological Manifestations**
Domains	Death	Health-Related Quality of Life Treatment Satisfaction	Direct Cost Indirect Cost	Skin Activity Psoriatic Arthritis Activity Investigator Global Patient Global Patient reported symptoms

Adverse Effects from Treatments

Contextual Factors:
Social Behaviors Related to Psoriatic Disease

Unclassified, TBD

Cardiovascular Comorbidities

Delphi round 1

October 2015-January 2016

- 303 physician/scientists/stakeholders
  - 107 physician respondents
- 31 patients/patient advocates + up to 200 additional NPF members
  - 14 patient respondents (mostly IDEOM/NPF patient research partners)

Questionnaire

20 questions asking same question: should [domain] be measured in all clinical trials?

Scale used:

- ❑1: strongly agree
- ❑2: agree
- ❑3: uncertain
- ❑4: disagree
- ❑5: strongly disagree

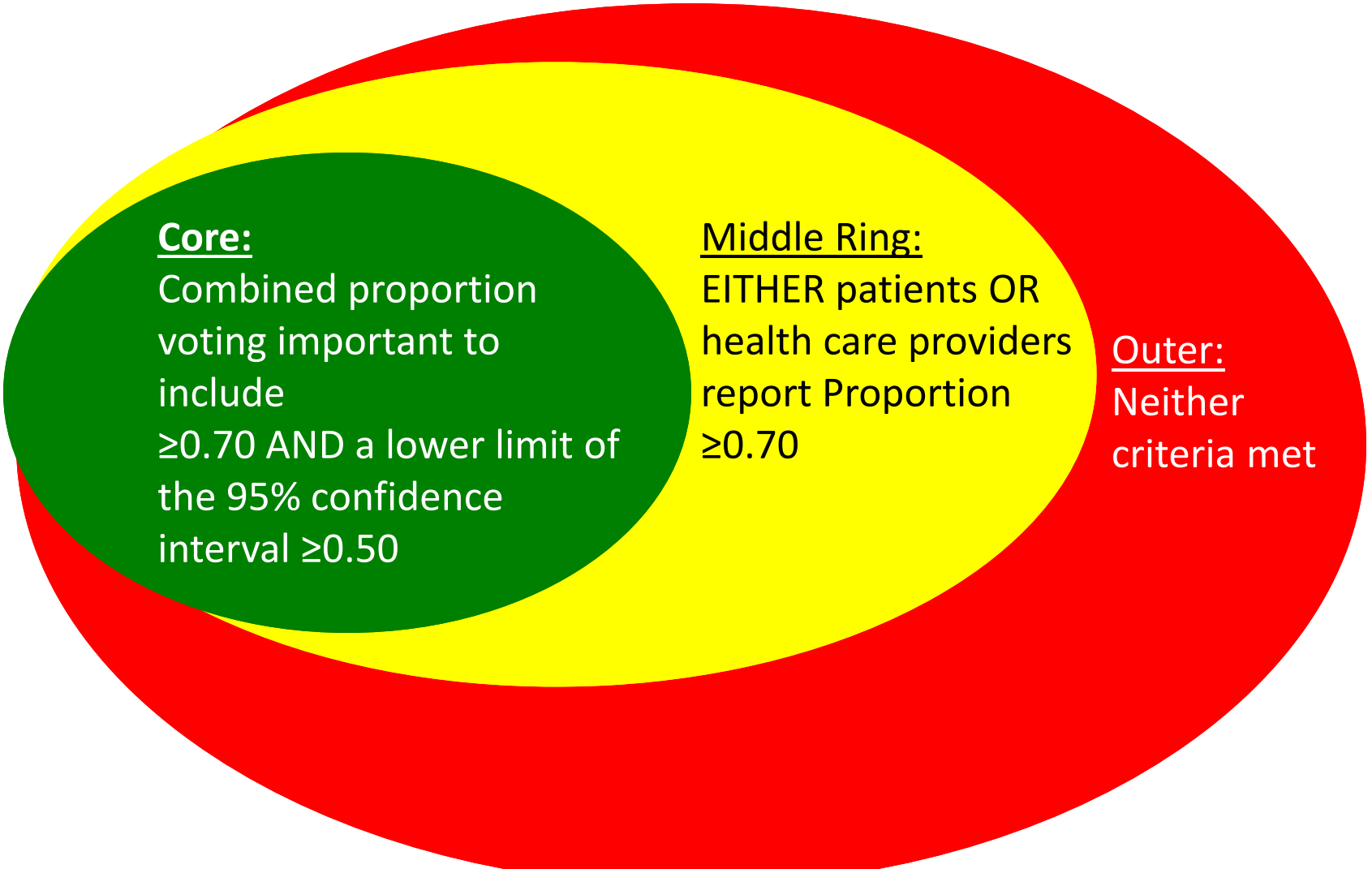
1&2: considered *important* to include as core domain

3: excluded from analysis

4&5: considered *not important* to include as core domain

Analysis:

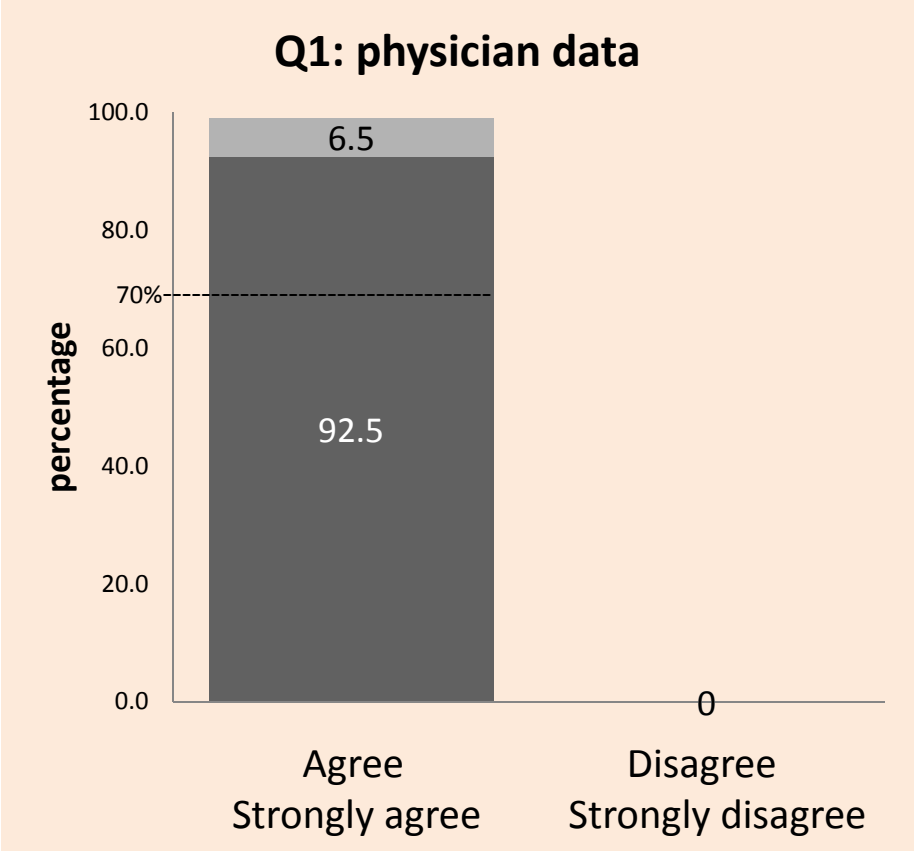
Based upon OMERACT "Onion Model"

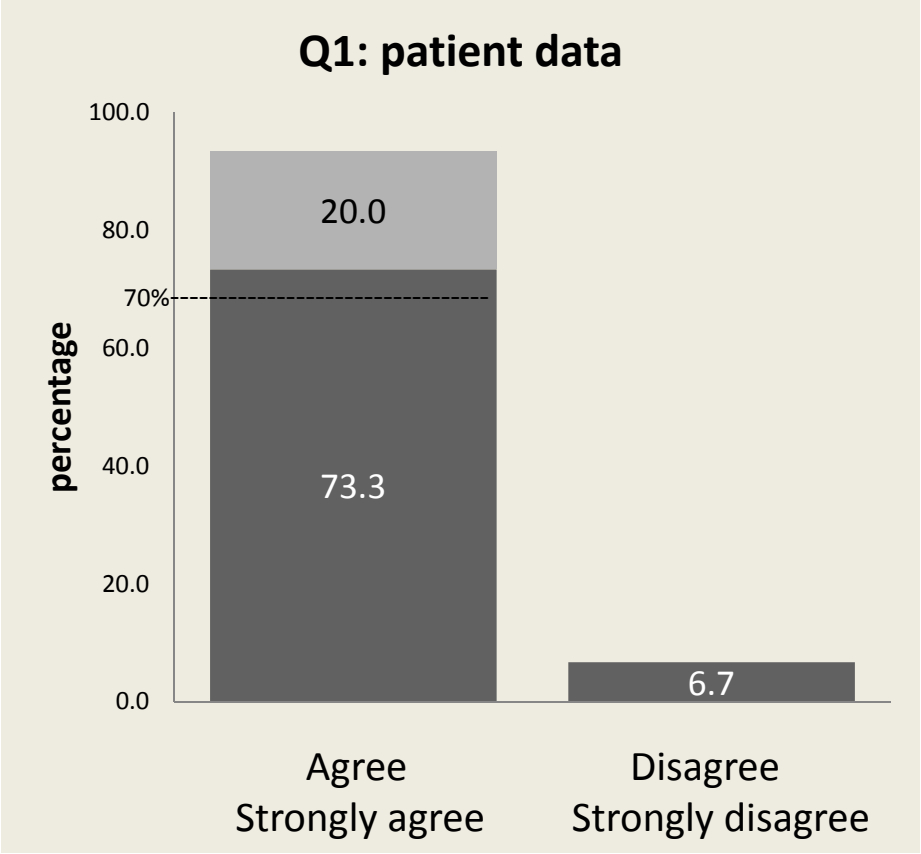


Gottlieb A, et al. J Am Acad Dermatol. 2015 Feb;72(2):345-8

Q1. PRIMARY SKIN MANIFESTATIONS OF PSORIASIS should be measured in every clinical trial.

(domain includes redness, thickness, scaling of psoriasis lesions, and body surface area)





Question 1: primary skin manifestations

Meets consensus as core domain

- 96% combined agreement
  - **Physicians:** 99.1%
  - **Patients:** 93.3%

Determined by weighting physicians and patients equally

- **95% CI:** 0.93-1.00
- **Standard Error:** 0.017

Outcome	N_MD	Yes_MD	No_MD	N_Pts	Yes_Pts	No_Pts	pY_MD	pY_Pts	pY	pN_MD	pN_Pts	pN	SE(pY)	95%lclY	95%uclY
q1	107	106	0	15	14	1	0.99	0.93	0.96	0.00	0.07	0.03	0.017	0.93	1.00

Flag of Mali

primary skin manifestations
patient reported symptoms
Treatment Satisfaction
HRQOL
Investigator Global
Patient Global

Q3: location of skin lesions
Q6: palmar-plantar psoriasis
Q7: scalp psoriasis

Death: an outcome measured in every clinical trial – no questions about this

Q2: secondary skin manifestations
Q5: nail psoriasis
Q8: Inverse psoriasis
Q9: Genital psoriasis
Q10: Guttate psoriasis

Q12:PsA symptoms

Q20: CVD

Q11: PsA signs

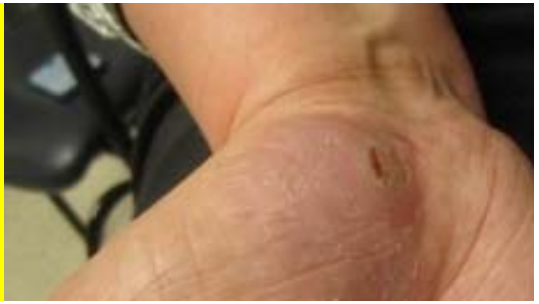
Q17:Direct Cost
Q18:Indirect Cost
Q19: Work Productivity

Core domains per Delphi 1 with no further discussion

- Primary skin manifestations (signs)
- Patient reported symptoms
- Treatment satisfaction
- HRQOL
- Investigator/Physician Global Assessment
- Patient Global Assessment

- Next move: take to Measurement Set Working Group to select candidate measures

Secondary skin manifestations



- 100% patient agreement that this should be core domain
- Physicians didn’t meet consensus criteria
- No validated instrument in use

Location of Lesions Scalp Psoriasis Palmar-plantar psoriasis	**Nail psoriasis** **Inverse psoriasis** **Genital psoriasis** **Guttate psoriasis** **cardiovascular co-morbidites**

- Very similar consensus scores hovering around 70% consensus (combined)
  - Physicians did not meet consensus
  - Patient did meet consensus

- Likely are CONTEXTUAL factors
  - Inclusion criteria
  - Effect modifiers (e.g. biologic naïve or not, obesity)

- Reword questions: If present in patient with plaque psoriasis, **should it be measured?**

Work Productivity
Direct Cost
Indirect Cost

- Neither combined/individual met consensus
- Entertained idea of “participation” instead of work productivity as domain to reassess

Next steps

- Domains that clearly met consensus:
  - establish Work Group for Measurement Sets
- Domains not meeting consensus -> Delphi 2:
  - Present physician and patient data
  - secondary skin manifestations: and how it should be handled (core or research agenda)
  - Participation instead of work productivity/cost
  - Tease out core vs. contextual factor
- Start work on CLINICAL PRACTICE CORE DOMAINS

Thank you!

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