Welcome to IMMPACT-II

Initiative on **M**ethods, **M**easurement, &

Pain **A**ssessment in **C**linical **T**rials

Acknowledgement

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Endo Pharmaceuticals

Eli Lilly & Co.

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Johnson & Johnson

Merck & Company

NeurogesX, Inc.

Novartis Pharmaceuticals

Pfizer

Purdue Pharma

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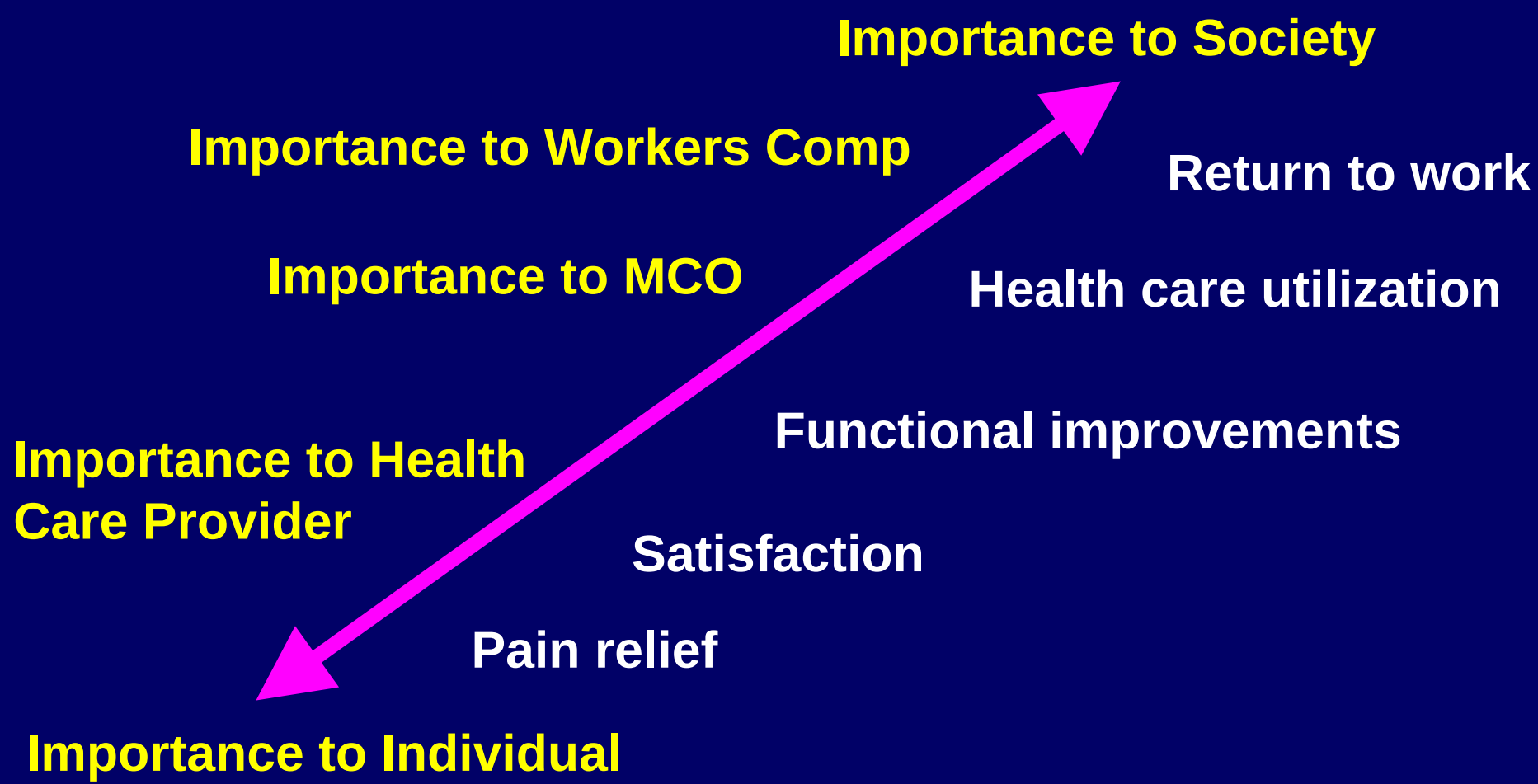
Criteria of Success, for Whom?



Simple Question(s) for IMMPACT

Is “this” treatment effective?

- On what outcomes?
- Measured in what way?
- Using what study design?
- Based on statistical & clinical significance?
- Compared to what alternatives?
- For whom?
- At what cost?

"When the right thing can only be measured poorly, it tends to cause the wrong thing to be measured well. And it is often much worse to have good measurement of the wrong thing -- especially when, as is so often the case, the wrong thing will IN FACT be used as an indicator of the right thing -- than to have poor measurement of the right thing."

John Tukey, 1979

Primary Outcome Domains for Chronic Pain Clinical Trials: Consensus from IMMPACT- I

1. Pain (the pivotal outcome)
2. Physical functioning
3. Emotional functioning
4. Patients rations of improvement and satisfaction with treatment
5. Negative health states and adverse events
6. Patient disposition (including adherence to the treatment regimen, reasons for premature withdrawal from trial, and loss to follow-up

Supplemental Outcome Domains for Chronic Pain Clinical Trials: Consensus from IMMPACT- I

1. Role functioning (I.e., work and educational activities
2. Interpersonal functioning (relationships and activities)
3. Coping
4. Pharmacoeconomic measures and health care use
5. Biological markers
6. Clinician or surrogate ratings of global improvement
7. Neuropsychological assessment of cognitive & motor functioning
8. Suffering and other end-of-life issues

Objectives, Goals, & Scope of Meeting

I. Develop consensus on means for assessing each of the 6 core domains identified at IMMPACT – I meeting

II. Goals and scope of meeting

- A. Review means of assessing each of the 6 core domains
- B. Discuss advantages and disadvantages of methods recommended in commissioned paper
- C. Determine what methods or measures should be used to assess outcomes in pain clinical trials (publish manuscript)

III. Beyond scope of the current meeting

- A. Discussion of means of assessing supplemental domains
- B. Discussion of definition of clinical significance
- C. Discussion of design of clinical trials
- D. Discussion of primary endpoints & strategies for analyses of multiple end points

Tentative Agenda

Friday, April 11th (morning)

8:00 am - 8:45 am	Welcome, sponsorship, and faculty introductions, Objectives, goals and scope, update. D. Turk, R. Dworkin
8:45 am - 9:00 am	Reliability, validity, responsiveness R. Dworkin
9:00 am – 9:15 am	Pain Assessment: Overview, M. Jensen
9:15 am – 10:00 am	Pain Assessment: Discussion, M. Jensen, R. Dworkin
10:00am – 10:30 pm	Beverage Break

Tentative Agenda

Friday, April 11th (morning)

10:30 am - 11:00 am	Pain Discussion: Continued, M. Jensen, R. Dworkin
8:45 am - 9:00 am	Reliability, validity, responsiveness R. Dworkin
9:00 am – 9:15 am	Pain Assessment: Overview, M. Jensen
9:15 am – 10:00 am	Pain Assessment: Discussion, M. Jensen, R. Dworkin
11:00am – 11:15 am	Physical functioning, generic measures: Overview, G. Stucki

Tentative Agenda

Friday, April 11th (afternoon)

11:15 am - 12:00 noon Physical functioning, generic measures: Discussion, G. Stucki, D. Turk

12:00 noon - 1:00 0m Luncheon

1:00 pm – 1:30 pm Physical functioning, generic measures continued, G. Stucki, D. Turk

1:30 pm – 1:45 pm Physical functioning, pain specific: Overview , J. Haythornthwaite

1:45pm – 3:00 pm Physical functioning, pain specific: Discussion, J. Haythornthwaite, R. Dworkin

Tentative Agenda

Friday, April 11th (afternoon & evening)

3:00 pm - 3:30 pm	Beverage break
3:30 pm - 3:45 pm	Emotional functioning: Overview, R. Kerns
3:45 pm – 5:00 pm	Emotional functionig: Discussion, R. Kerns, D. Turk
6:45 pm	Charter transportation to off-site dinner departs from Willard (Meet in hotel lobby by 6:40)
7:00pm - 9:30 pm	Dinner at B. Smith's in Union Station

Tentative Agenda

Friday, April 11th (morning)

8:00 am - 8:45 am	Welcome, sponsorship, and faculty introductions, Objectives, goals and scope, update. D. Turk, R. Dworkin
8:45 am - 9:00 am	Reliability, validity, responsiveness R. Dworkin
9:00 am – 9:15 am	Pain Assessment: Overview, M. Jensen
9:15 am – 10:00 am	Pain Assessment: Discussion, M. Jensen, R. Dworkin
10:00am – 10:30 pm	Beverage Break

Tentative Agenda

Saturday, April 13th (morning)

7:30 am - 8:00 am	Continental breakfast
8:00 am - 8:30 am	Pt global rating of improvement/satisfaction: Overview, J. Farrar
8:30 am – 9:30 am	Pt global rating: Discussion, J. Farrar, R. Dworkin
9:30 am – 10:00 am	Negative health states/events: Overview, N. Katz
10:00am – 10:30 pm	Negative health states/events: Discussion. N. Katz, D. Turk

Tentative Agenda

Saturday, April 12th (morning & afternoon)

10:30 am - 11:00 am	Beverage Break
11:00 am - 11:30 am	Negative health states/events, Discussion, N. Katz, D. Turk
11:30 am –11:45 am	Pt Disposition/CONSORT: Overview, D. Turk
11:45 am – 12:30 pm	Pt Disposition/CONSORT: Discussion, D. Turk, R. Dworkin
12:30pm – 1:30pm	Luncheon

Tentative Agenda

Saturday, April 12th (afternoon)

1:30 pm - 3:30 pm	Review and consensus on recommended measures, R. Dworkin, D. Turk
3:30 pm - 3:45 pm	Beverage Break
3::45 pm –5:00 pm	IMMPACT Future Directions, R. Dworkin, D. Turk

Endorsement of the CONSORT Statement

CONSORT

Consolidated **S**tandards

of **R**eporting **T**rials

CONSORT
Checklist of Items to include when reporting a randomized trial

Title and abstract

Introduction and background

Methods

- ✓ Participants
- ✓ Interventions
- ✓ Objectives
- ✓ Outcomes
- ✓ Sample Size
- ✓ Randomization
  - Sequence generation
  - Allocation concealment
  - Implementation
- ✓ Blinding
- ✓ Statistical Methods

Results

- ✓ Participant Flow
- ✓ Recruitment
- ✓ Baseline data
- ✓ Numbers analyzed
- ✓ Outcomes and estimation
- ✓ Ancillary analyses
- ✓ Adverse events

Discussion

- ✓ Interpretation
- ✓ Generalizability
- ✓ Overall evidence

Flow of Participants

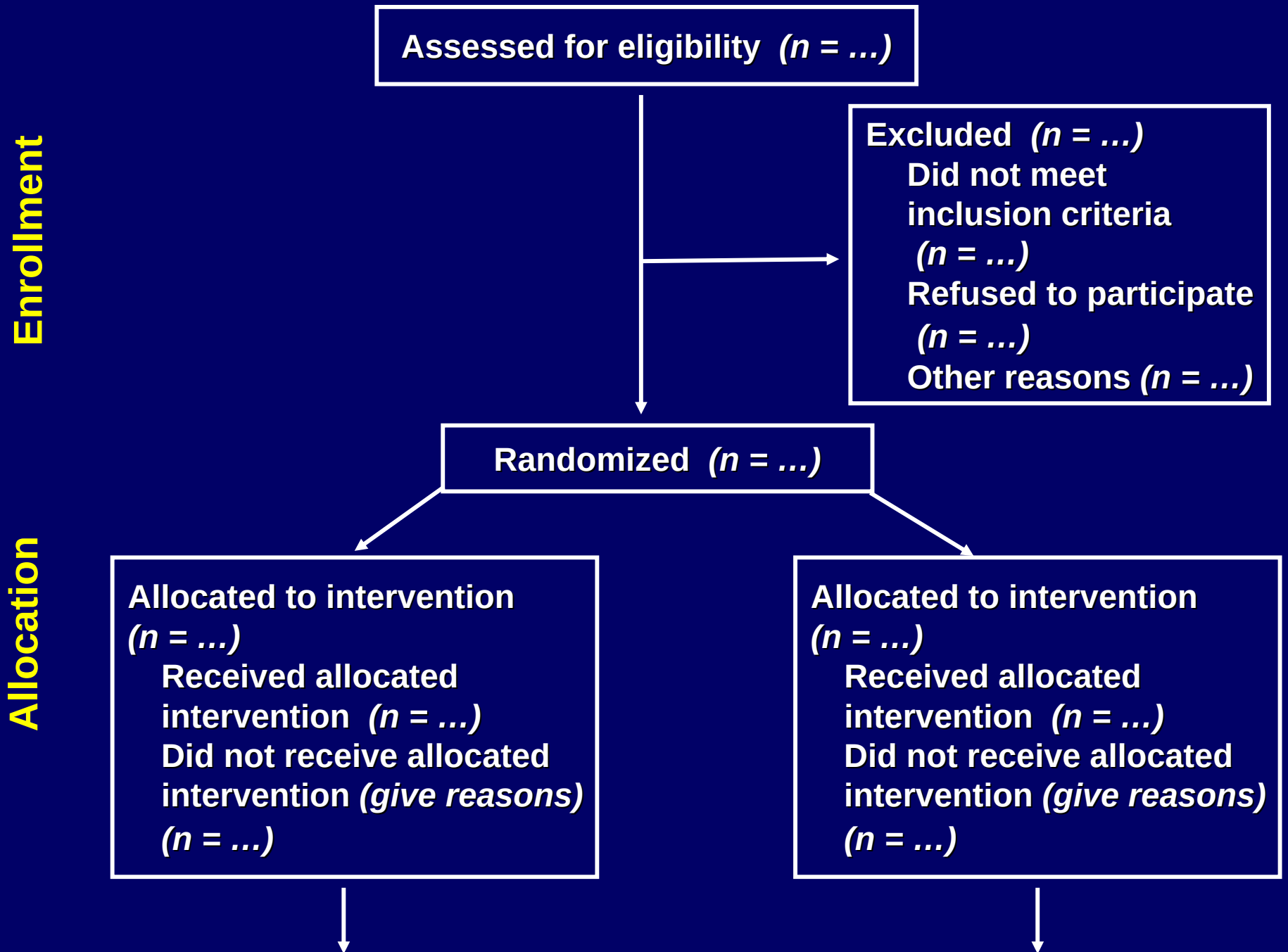
Stage	Number Included	Number Not Included
Enrollment	Pts. evaluated for enrollment	# did not me inclusion criteria # meet inclusion but declined tx.
Randomization	Pts. randomized	
Tx Allocation	Pts. who received tx. as allocated, by grp.	Pts. who did not receive tx.as allocated, by grp.

Flow of Participants (cont'd)

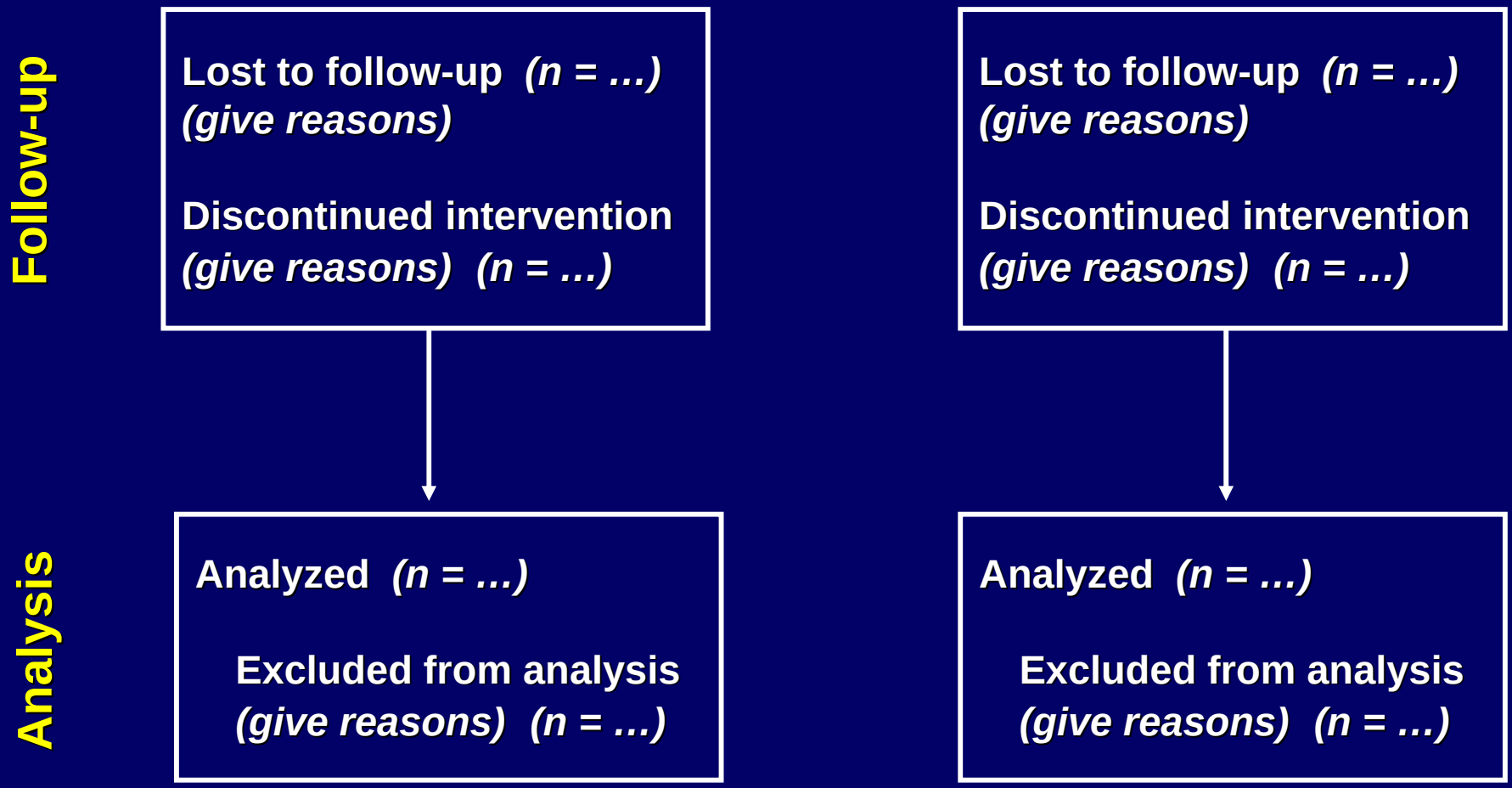
Stage	Number Included	Number Not Included
Follow-up	# completed tx as allocated, by group	# did not complete tx. as allocated, by grp.
	# completed f/u as planned, by grp.	# did not complete f/u as planned, by grp
Analysis	Pts.included in main analysis, by grp.	Pts. excluded from main analysis, by grp.

CONSORT

Flow Diagram


Assessed for eligibility (n = …)
Excluded (n = …)
Did not meet inclusion criteria (n = …)
Refused to participate (n = …)
Other reasons (n = …)
Enrollment
Randomized (n = …)
Allocation
Allocated to intervention (n = …)
Received allocated intervention (n = …)
Did not receive allocated intervention (give reasons) (n = …)
Allocated to intervention (n = …)
Received allocated intervention (n = …)
Did not receive allocated intervention (give reasons) (n = …)

Cont'd


Follow-up
Lost to follow-up (n = …)
(give reasons)
Discontinued intervention
(give reasons) (n = …)
Lost to follow-up (n = …)
(give reasons)
Discontinued intervention
(give reasons) (n = …)
Analysis
Analyzed (n = …)
Excluded from analysis
(give reasons) (n = …)
Analyzed (n = …)
Excluded from analysis
(give reasons) (n = …)

PATIENT DISPOISITION

Requirements for Positive Outcomes in Clinical Trials

1. Treatment must have a positive impact on condition or symptoms

2. Patient must follow the prescribed regimen

Different Forms of Nonadherence

- Failure to follow treatment as prescribed –
  - too little,
  - too much,
  - different schedule,
  - use of concomitant treatments
- Missed appointments

Factors Related to Nonadherence

- **Patient variables** (e.g., disposition, forgetfulness, confusion, apathy, pessimism, beliefs, expectations)
- **Disease or disorder variables** (e.g., stability of symptoms)
- **Treatment variables** (e.g., complexity of treatment regimen, inadequate instructions, size of pills, taste, side effects)
- **Relationship variables** (e.g., inadequate communication)

Methods to Measure Nonadherence

- ✓ Interview, clinical ratings
- ✓ Self-report, Self-monitoring behavior and symptoms
- ✓ Pill counts
- ✓ Tallies of refills
- ✓ Marked-sign techniques (inactive or false marker embedded in treatment package)
- ✓ Biochemical indicators (e.g., chemical tracers)
- ✓ Record of appointments

Concomitant treatments initiated during a trial from a trials often reflect inadequate pain relief or distressing, uncontrolled side effects.

Reasons why subjects in clinical trials may be lost to follow-up:

- Inadequate pain relief
- Adverse events
- Dissatisfaction with trial personnel
- Resolution of symptoms
- Change of living circumstances

In addition to CONSORT detailed information about each of the following should be reported:

- **Protocol violations** -- number and nature(e.g., use of prohibited medications, unauthorized dose change)
- **Concomitant treatment** – e.g., all medication, unscheduled visits for health care
- **Nonadherence** -- reasons and prevalence of each type
- **Premature withdrawal** – reasons and prevalence of each type
- **Loss to follow-up** – reasons and prevalence of each type

Assess the PERSON . . .

Not just the

PAIN!!!