Novel Methods Leading to New Medications in Depression and Schizophrenia (NEWMEDS) Consortium: Lessons Learned on Improving Efficiency of RCT's on antipsychotic treatments

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NEWMEDS

Novel MEthods leading to NeW MEdications in Depression and Schizophrenia

One of the largest ever research academic-industry collaboration projects.

EFPIA companies: H Lundbeck A/S, Abbott, AstraZeneca AB, Eli Lilly and Company Ltd, Janssen Pharmaceutica NV, Novartis Pharma AG, Orion Corporation, Pfizer Limited, F. Hoffmann-La Roche AG, Institut de Recherches Servier

Universities: King's College London *(UK),* Karolinska Institutet *(Sweden),* The University of Cambridge *(UK),* Central Institute of Mental Health *(Germany),* CSIC *(Spain),* The University of Manchester *(UK),* Bar Ilan University (Israel)

SME's

Psynova Neurotech Ltd *(UK)*, deCODE genetics *(Iceland)*, GABO:mi *(Germany)*

NEWMEDS

Funding: Innovative Medicines Initiative Joint Undertaking (IMI JU). IMI JU is a public-private partnership between the pharmaceutical industry (represented by the European Federation of Pharmaceutical Industries and Associations, EFPIA) and the European Union (represented by the European Commission).

NewMeds Goal: Find new methods for development of drugs for schizophrenia and depression.

↳Todays presentation: Findings & lessons from NewMeds repository of antipsychotic randomized controlled trial (RCT).

Methodological Accomplishments

- **We have established a consortium that shares clinical trial data –coded patient/participant level data-- from industry and academia to examine precompetitive questions.**
- **Overcome challenges associated with establishing data sharing**
- **Pooled and mined data from studies that have sufficiently common experimental designs to have a reasonable chance of valid conclusions.**

Text borrowed from: Institute of Medicine, Washington, DC, August 2011, Cast as road map.

Schizophrenia Database

Data from: Astra Zeneca, Janssen, Lilly, Lundbeck, Pfizer

64 Industry sponsored studies
- **34 placebo controlled**
- **30 active comparator**
- **25,900 patients**
  - **16,105 study drug**
  - **7,119 active comparator**
  - **2,676 placebo**

1 NIMH sponsored study CATIE 1,493 patients

1 European Union sponsored study EUFEST 498 patients

Depression Database

Data from: Astra Zeneca, Lundbeck, Pfizer

26 placebo controlled Industry sponsored studies

8,053 patients

5,504 active drug

2,549 placebo

Additional data to arrive from Lilly.

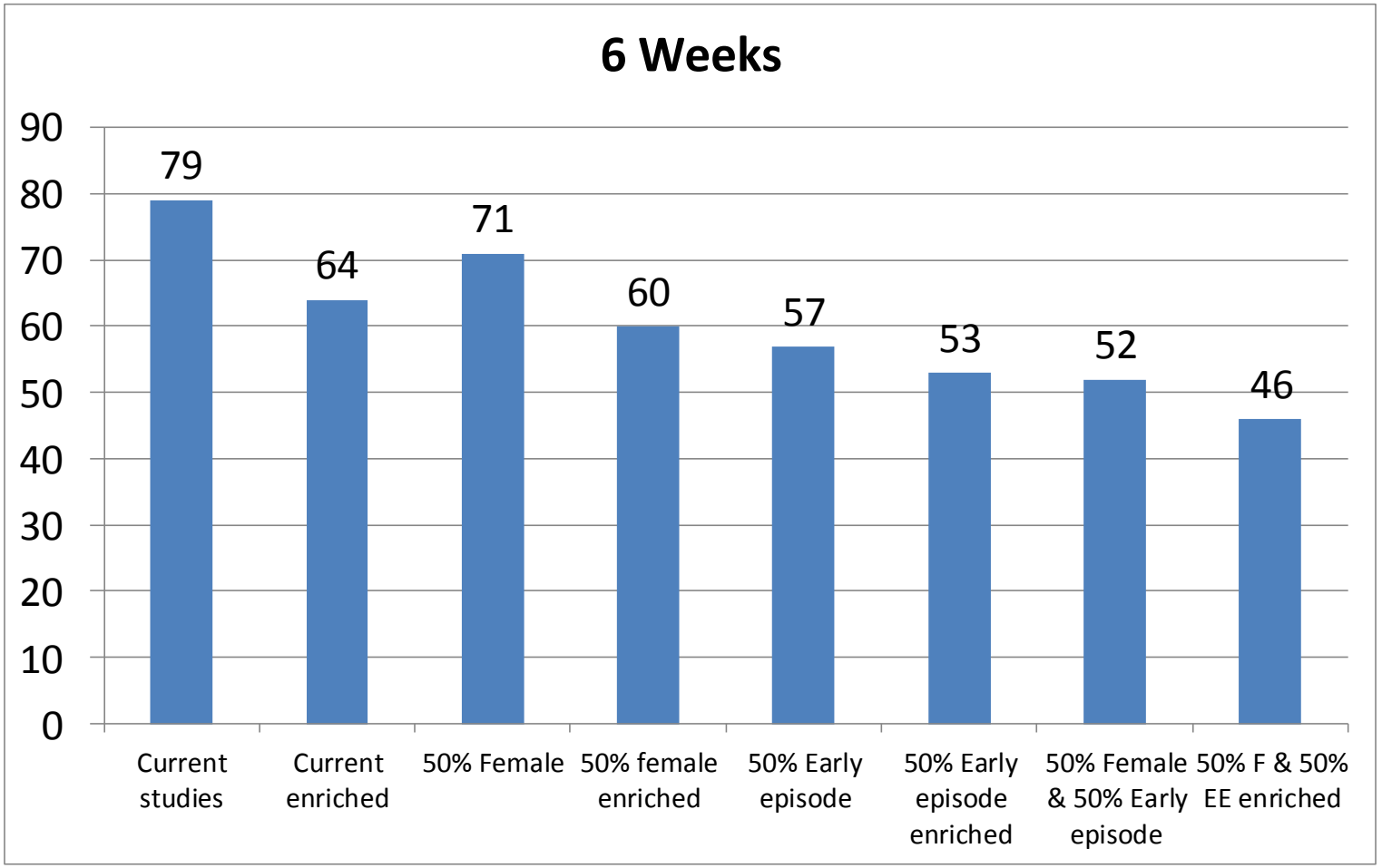
Major findings

Placebo-controlled antipsychotic studies

- Efficacy results at 4 weeks almost the same as at week 6.
- Females show more pronounced differentiation from placebo than males, primarily driven by lower placebo effect in females.
- Patients with a later onset of disease show more pronounced improvements, irrespective of their allocation to active or placebo, but differentiation from placebo is not affected by age of onset.
- Patients age ≤ 30 with ≥ 4 years of illness show highest active vs. placebo differentiation.
- Patients with both prominent positive and negative symptoms show the most pronounced active-placebo differentiation.
- Impact of above characteristics contribute independently.

- Persons just meeting symptom eligibility criteria are not overrepresented but show a somewhat lower active-placebo differentiation than the rest of the study population.
- The use of benzodiazepines does not affect the treatment results, active-placebo differentiation.
- Active-placebo differentiation differs per geographical area, considerably more differentiation in Eastern Europe than North America.

Sample sizes needed per arm (90% power, p of .05)



Current=70% female; 20% early episode; 40% enriched
Enriched=prominent positive and negative symptoms
Note: Per patient cost 6wk study $70,000-$100,000

Implications of findings on future drug development

- Trials of 4 weeks duration.
- Representative / enriched populations, particularly in Proof of Concept trials.
- More efficient trial designs
- Data informed regulatory policy and new studies
- Paradigmatic shift: data sharing as ethical imperative

**Limitation: Some findings may not be applicable for new compounds with different mechanisms of action.

Personal experiences

Facilitators

- Commitment of companies to partner with external funding around *precompetitive* challenges.
- Recognition by industry that drug discovery was becoming more difficult.
- Need for clear message, ongoing support from top
  - Ideal partner from top management.
- Previous relationships
- Peer pressure among companies
- Active collaboration regarding formulating research questions and interpreting data.

Challenges

- Locating data
  - Changes in corporate structure
  - Acquisitions
- Competing for internal resources and priorities
- Change in personnel
- Complexity of data storage, disparate systems
  - Differences within companies and between companies and over time.
- Data controllers and extent of cooperation.
  - Compartmentalization of companies.
- HIPA
- Concerns of legal departments
  - Ethical benefits of data sharing

Future

What if all trials were stored in a uniform way and patient level data routinely entered into data bank?

Who is best positioned to do this?

How does data sharing or un-willingness to share data impact the risk benefit ratio of conducting a study?

Our experience is that the common good can be greatly enhanced by sharing data.