



# Conducting a Multi-Site, Community-Based Pragmatic Trial: Study Design, Timeline, and Uncovered Barriers for MOBILITY



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## ABSTRACT

## BACKGROUND

## METHODS

## RESULTS

## CONCLUSIONS

## REFERENCES

**Objectives:** Compare and contrast MOBILITY (Metformin for overweight and obese children with bipolar spectrum disorders treated with second-generation antipsychotics) to other trials in terms of pragmatic versus explanatory design and outcomes, timeline from IRB submission to first patient enrolled, and barriers to recruitment/retention.

**Introduction:** Second-generation antipsychotics (SGAs) are effective for bipolar spectrum disorders (BSD), which commonly begin during childhood and adolescence. According to patients and their parents, weight gain is the most problematic side effect and often leads to medication non-adherence. Although recent clinical trials suggest metformin (MET) may mitigate weight gain associated with SGAs, there is a significant gap in the evidence base and widespread use of MET in this population. The overall aim of MOBILITY is to study the comparative effectiveness of MET and a simple healthy lifestyle intervention (LIFE) vs. LIFE alone on patient-centered outcomes for patients in community health settings in the Greater Cincinnati and New York City regions.

**Results:** PRECIS-2 score revealed this study has a pragmatic design. Timeline was similar to explanatory clinical trials, but design and barriers to recruitment/retention were different.

**Conclusions:** Conducting a multi-site patient-centered pragmatic trial is much different from an explanatory trial. As comparative effectiveness trials become more prevalent, understanding and adjusting for these differences will be paramount for success.

- Although recent clinical trials suggest MET may mitigate weight gain associated with SGA use<sup>2</sup>, there is a significant gap in the evidence base and widespread use of MET in this population. Pragmatic trials are designed to address this gap, yet there is a paucity of data regarding how to implement such a trial.

- Explanatory clinical trials aim to determine efficacy of an intervention under tightly controlled circumstances and may not predict improvement in health outcomes. Alternatively, pragmatic clinical trials seek to determine effectiveness of an intervention in “real world” or care as usual settings and bridge the gap from efficacy to applicability for clinicians and their patients.

- The PRECIS-2 (Pragmatic Explanatory Continuum Indicator Summary) tool helps researchers determine if their study design is consistent with the trial’s intended purpose (i.e. effectiveness v efficacy). The nine domains are scored on a continuum from very explanatory (1) to very pragmatic (5) and try to determine applicability to the intended community.

- A pragmatic study has broad inclusion and minimal exclusion criteria. MOBILITY’s inclusion criteria include anyone with the condition of interest (aged 8-17, any history of a bipolar spectrum disorder (BSD), overweight/obese, taking an SGA), while the exclusion criteria (prior intolerance/failed trial of MET, pregnancy, abnormal creatinine that would contraindicate MET use) are minimal. An explanatory trial with the same purpose might exclude co-morbid psychiatric diagnoses, require confirmation of diagnosis with a structured interview, and exclude those with adherence issues.

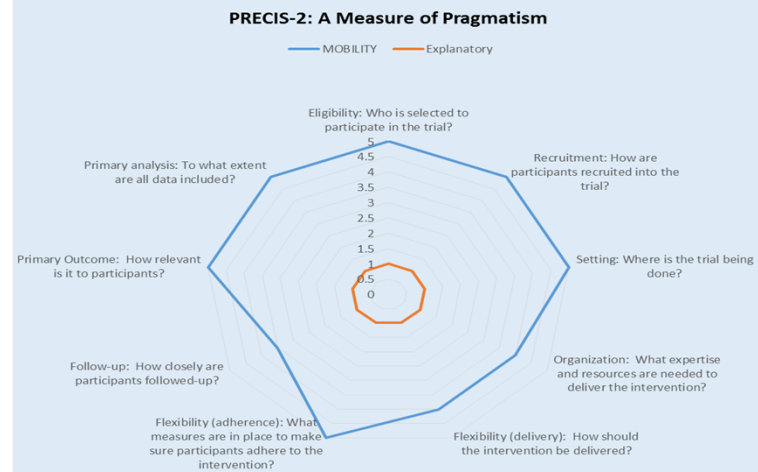
The MOBILITY team calculated the PRECIS-2 score, reviewed the IRB timeline, and gathered qualitative data regarding barriers in recruitment and retention.

**PRECIS-2 Score:** 4.2

**Timeline:** First IRB submission: July 30, 2015. First patient enrolled: November 5, 2015. Recruitment as of April 12: 121 patients from 18 community health centers.

**Recruitment barriers** unique to pragmatic trials as seen in MOBILITY: Limited research experience of community health center support staff and providers, limited staff time, limited awareness of intervention by community mental health providers, provider skepticism regarding research.

**Retention Barriers:** Transition from inpatient to outpatient settings.



- Conducting a multi-site patient-centered pragmatic trial is much different from an explanatory clinical trial in study design, and recruitment/retention, yet similar in timeline.
- Researchers should consider incorporating pragmatic trials to improve predictive validity.

- Loudon, K., Treweek, S., Sullivan, F., Donnan, P., Thorpe, K., Zwarenstein, M. (2015). The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ*, 350, 1-11, doi:10.1136/bmj.h2147
- Flodmark CE, Marcus C, Britton M. Interventions to prevent obesity in children and adolescents: a systematic literature review. *Int J Obes (Lond)*. 2006;30(4):579-589.

Domain	Eligibility	Recruitment	Setting	Organization	Flexibility (delivery)	Flexibility (adherence)	Follow-up	Primary Outcome	Primary Analysis
<b>Pragmatic</b>	Broad inclusion, anyone with condition of interest (5)	Recruit in usual care setting/minimal incentive	Community, multi-site	Making use of existing healthcare staff/resources	Implementation details left to providers, other interventions allowed	Patient compliance with intervention not enforced	Same frequency/length of visits as usual care, minimal data collection	Outcome meaningful to patients, measured as they would in usual care	An intent-to-treat analysis (in randomized studies) including all primary outcome data
<b>Explanatory</b>	Tight inclusion/broad exclusion (1)	Recruit in general community/media	Academic, single-site	Increasing resources/training/equipment	Specific protocol-driven directions/monitoring, no additional interventions	Withdrawal for non-compliance, measures to address non-compliance	Extensive data collection, longer/more frequent visits, unscheduled visits	Outcome less important to patients	As treated analysis, excludes non-compliant participants or providers
<b>Mobility</b>	5	5	5	4	4	5	3.5	5	5