The Next Generation Learning Health System for Multiple Sclerosis (Next Gen-MS): Study design, demographics, and analysis of system-level variation in baseline characteristics.

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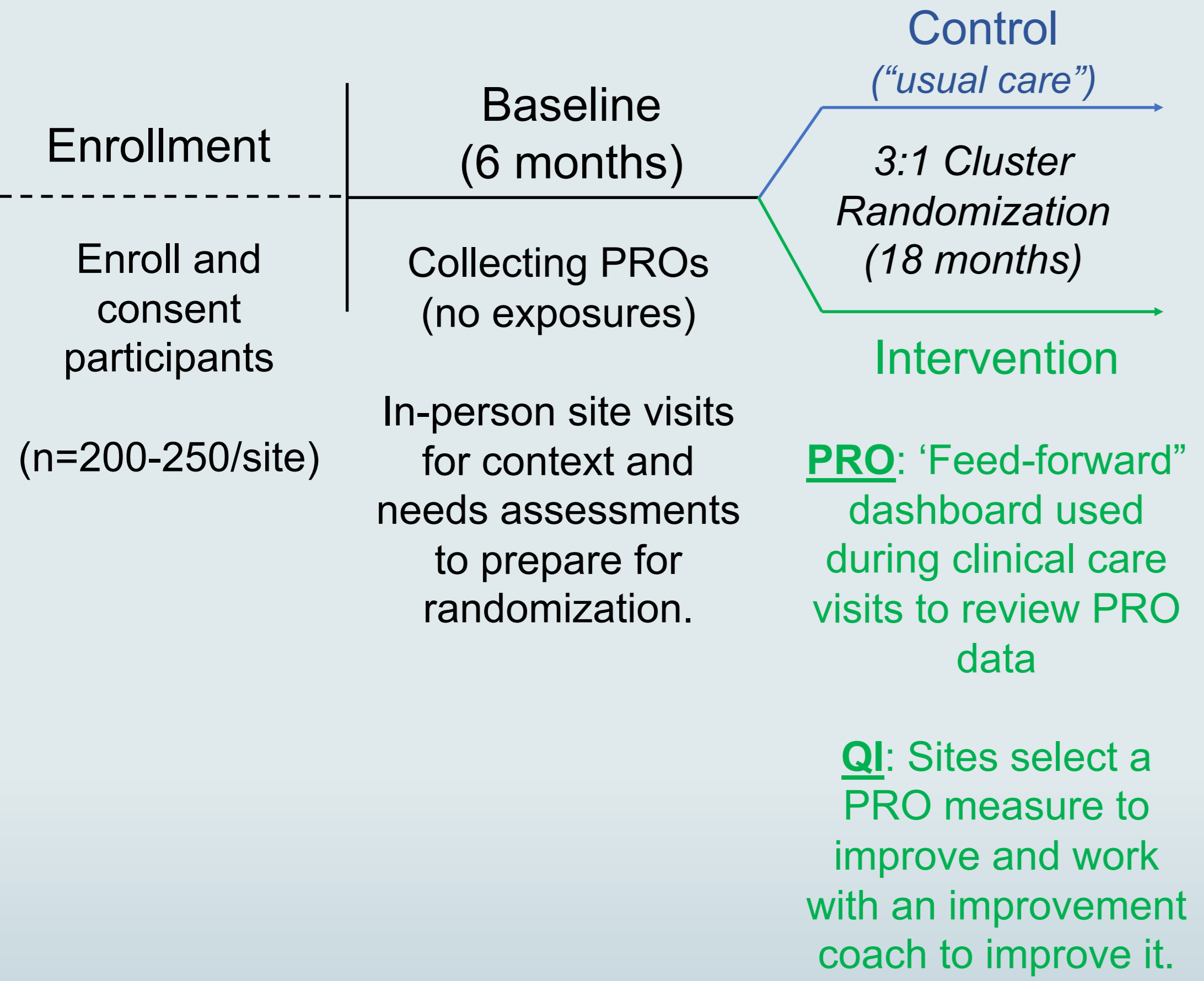
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INTRODUCTION

- Next Gen-MS is a hybrid improvement-implementation research learning health system for MS.
- Next Gen-MS is the first randomized multi-center study to test feed-forward Patient Reported Outcomes (PROs) informing MS care and system-level Quality Improvement (QI).
- Eight (8) MS care centers and approximately 2,000 persons with MS in the United States will participate in this study over three years.
- After reaching target recruitment and completing a six-month pre-intervention baseline observation period, sites will be cluster-randomized at a 3:1 ratio ("PRO + QI intervention" vs. "usual care" or control) and will be observed over an 18-month period.

OBJECTIVE

We present initial baseline descriptive statistics of site-level variation of socio-demographic characteristics and baseline PROs in participating sites.

METHOD

Prospective, 3:1 cluster-randomized at MS care center (site) level (6 month baseline, 18 months exposure).

Enrollment

Enroll and consent participants

(n=200-250/site)

Baseline (6 months)

Collecting PROs (no exposures)

In-person site visits for context and needs assessments to prepare for randomization.

Control ("usual care")

3:1 Cluster Randomization (18 months)

Intervention

PRO: 'Feed-forward' dashboard used during clinical care visits to review PRO data

QI: Sites select a PRO measure to improve and work with an improvement coach to improve it.

CONCLUSIONS

- Next Gen MS has demonstrated initial feasibility for recruitment and engagement and has completed initial analyses of baseline characteristics.
- We have observed significant system-level variation in baseline PROs between sites in psychiatric, cognitive, and quality of life domains.
- This sets a beginning foundation for subsequent study of the PRO + QI intervention to effect system-level changes in outcomes compared to usual care.

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RESULTS

- *A total of 1,104 participants have been recruited as of July 2023 across eight sites.*
- *Population mean age was 51.1 years (range: 21-83 years), 80% were females, 21% non-white, and 16% Hispanic or Other ethnicity.*
- *Over 50% were employed or self-employed.*
- *Education, employment, BMI, and income level varied widely among the population.*
- *Participants reported use of different DMTs and 12% reported no Disease Modifying Therapy (DMT) use.*
- *Participants reported approximately 84.1% with Relapsing-Remitting MS (RRMS).*
- *Over 91% of participants completed for baseline PROs which indicates high patient engagement.*
- *We observed that mean PRO scores for Patient Determined Disease Steps (PDDS) (1.8, SD=2.1), PROMIS Fatigue (55.2, SD=9.95) and Anxiety (52.4, SD=9.8) are marginally higher, while PROMIS Physical Function (43.4, SD=11.3) and Cognitive Function (45.4, SD=10.4) are marginally lower relative to the US general population.*
- *ANOVA analyses at 0.05 significance level reveals between site (system-level) variation in multiple PROs: PROMIS Fatigue (p<0.01), PROMIS Anxiety (p<0.05), PROMIS Cognitive Function (p<0.01), PHQ9 (p<0.01), and HRQoL (p<0.01).*

Table 1. Key sociodemographic characteristics (n = 1,104)

Sociodemographic Characteristics	n (%)	Sociodemographic Characteristics	n (%)
AGE		**HIGHEST EDUCATION LEVEL**	
Mean (SD)	51.1 (11.7)	Attended college but did not complete a degree	157 (14.2)
Median (Range)	51 (21-83)	Completed a Bachelors degree	324 (29.3)
SEX AT BIRTH		Completed a Doctoral or Professional degree	62 (5.6)
Female	888 (80.4)	Completed a Masters degree	230 (20.8)
Male	216 (19.6)	Completed an Associates degree	109 (9.9)
RACE		Did not finish high school	10 (0.9)
American Indian or Alaska Native	6 (0.5)	Graduated from high school	113 (10.2)
Asian	7 (0.6)	No response	99 (9)
Black or African American	185 (16.8)	**ANNUAL HOUSEHOLD INCOME**	
Native Hawaiian or Other Pacific Islander	2 (0.2)	$10,000-$49,999	189 (17.1)
Two or more races	33 (3)	$50,000-$99,999	294 (26.6)
White or Caucasian	773 (70)	$100,000-$199,999	259 (23.5)
No response	98 (8.9)	$200,000-$500,000	92 (8.3)
ETHNICITY		Above $500,000	26 (2.4)
Do not wish to disclose	24 (2.2)	Do not wish to disclose	144 (13)
Hispanic	38 (3.4)	No response	100 (9.1)
Not Hispanic	805 (72.9)	**EMPLOYMENT**	
Other	138 (12.5)	A homemaker	72 (6.5)
No response	99 (9)	A student	8 (0.7)
HANDEDNESS		Employed for wages	489 (44.3)
Ambidextrous	21 (1.9)	Military	2 (0.2)
Left	91 (8.2)	Out of work and looking for work	19 (1.7)
Right	893 (80.9)	Out of work but not currently looking for work	22 (2)
No response	99 (9)	Retired	153 (13.9)
BMI CATEGORY		Self employed	68 (6.2)
Healthy weight	313 (28.4)	Unable to work	172 (15.6)
Obese	410 (37.1)	No response	99 (9)
Overweight	267 (24.2)	**SMOKING STATUS**	
Underweight	15 (1.4)	Current Smoker	55 (5)
No response	99 (9)	Former Smoker	243 (22)
ALCOHOL USE		Never Smoked	681 (61.7)
No	386 (35)	Passive Smoker	26 (2.4)
Yes	619 (56.1)	No response	99 (9)
No response	99 (9)		

Table 2. Use of DMTs (n = 973)

DMT	n (%)
Alemtuzumab	8 (0.82)
Cladribine	38 (3.91)
Dalfampridine	1 (0.10)
Dimethyl fumarate	53 (5.45)
Diroximel fumarate	38 (3.91)
Fingolimod	51 (5.24)
Glatiramer acetate	37 (3.80)
Interferon beta 1a IM	16 (1.64)
Interferon beta 1a SC	7 (0.72)
Interferon beta 1b	4 (0.41)
Intravenous immunoglobulin	10 (1.03)
Leflunomide	8 (0.82)
Methotrexate	1 (0.10)
Methylprednisolone	2 (0.21)
Monomethyl fumarate	1 (0.10)
Naltrexone	2 (0.21)
Natalizumab	84 (8.63)
Ocrelizumab	311 (31.96)
Ofatumumab	69 (7.09)
Ozanimod	20 (2.06)
Peginterferon beta 1a	6 (0.62)
Rituximab	9 (0.92)
Siponimod	14 (1.44)
Teriflunomide	63 (6.48)
No DMT	120 (12.33)

Table 3. Key PROMs

PROM	Count	Mean	std
PROMIS Fatigue (MS)	978	55.24	9.95
PROMIS Physical Function	960	43.37	11.32
PROMIS Anxiety	976	52.38	9.8
PROMIS Cognitive Function	968	45.45	10.43
PDDS	994	1.78	2.06
PHQ9 (Depression)	990	6.04	5.57
Wasson Health Confidence	983	7.37	2.22
HRQoL: Healthy Days	482	16.95	11.66
WPAI: Work Missed	516	0.06	0.17
WPAI: Impairment While Working	507	0.24	0.26

PROM= Patient Reported Outcome Measure

Table 4. PROM Variation

PROM	p
PROMIS Fatigue (MS)	* 0.000
PROMIS Physical Function (MS) 15a	0.168
PROMIS Anxiety 8a	* 0.024
PROMIS Cognitive Function 8a	* 0.000
PDDS	0.199
PHQ9	* 0.000
Wasson	0.333
HRQoL - Healthy Days	* 0.000
WPAI - Work Time Missed	0.477
WPAI - Impairment While Working	0.326

*Between site variation via ANOVA (p<=0.05).

Table 5. MS Subtype

MS Subtype	N (%)
Relapsing-Remitting MS (RRMS)	929 (84.1)
Secondary-Progressive MS (SPMS)	79 (7.2)
Primary-Progressive MS (PPMS)	36 (3.3)
Progression-Relapsing MS (PRMS)	3 (0.3)
Unknown/No Response	57 (5.2)

Figure 3. Baseline PRO Completion Rate (n = 1,063)

- WASSON: 92%
- WPAI: 89.1%
- PROMIS PHYSICAL FUNCTION (MS) 15A: 90.4%
- PROMIS FATIGUE (MS) 8B: 92%
- PROMIS COGNITIVE FUNCTION 8A: 91.1%
- PROMIS ANXIETY 8A: 92%
- PHQ9: 92.5%
- PDDS: 93.5%
- HRQOL: 86.8%

PRO completion rates greater than 90% indicate high patient engagement