THE ROCKEFELLER UNIVERSITY HOSPITAL
CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE


Measuring the Impact of Recruitment Efforts

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Study Accrual

- Many clinical trials fail to accrue
- Multiple calls for accountability in accrual
  - Evaluation KFC 2012; IOM 2013; NCATS PAR 2015
- No consensus metrics for “accrual success”
  - Recruitment Taskforce paper, Acad Med, 2014

Accrual Measures

Study Accrual

- Time to first enrollment
- Time to complete accrual
- *Timeliness* of accrual – Accrual Index

Multiple Factors Affect Accrual

Infrastructure and Data Capture

- Protocol Navigation *(Brassil et al CTS 2014)*

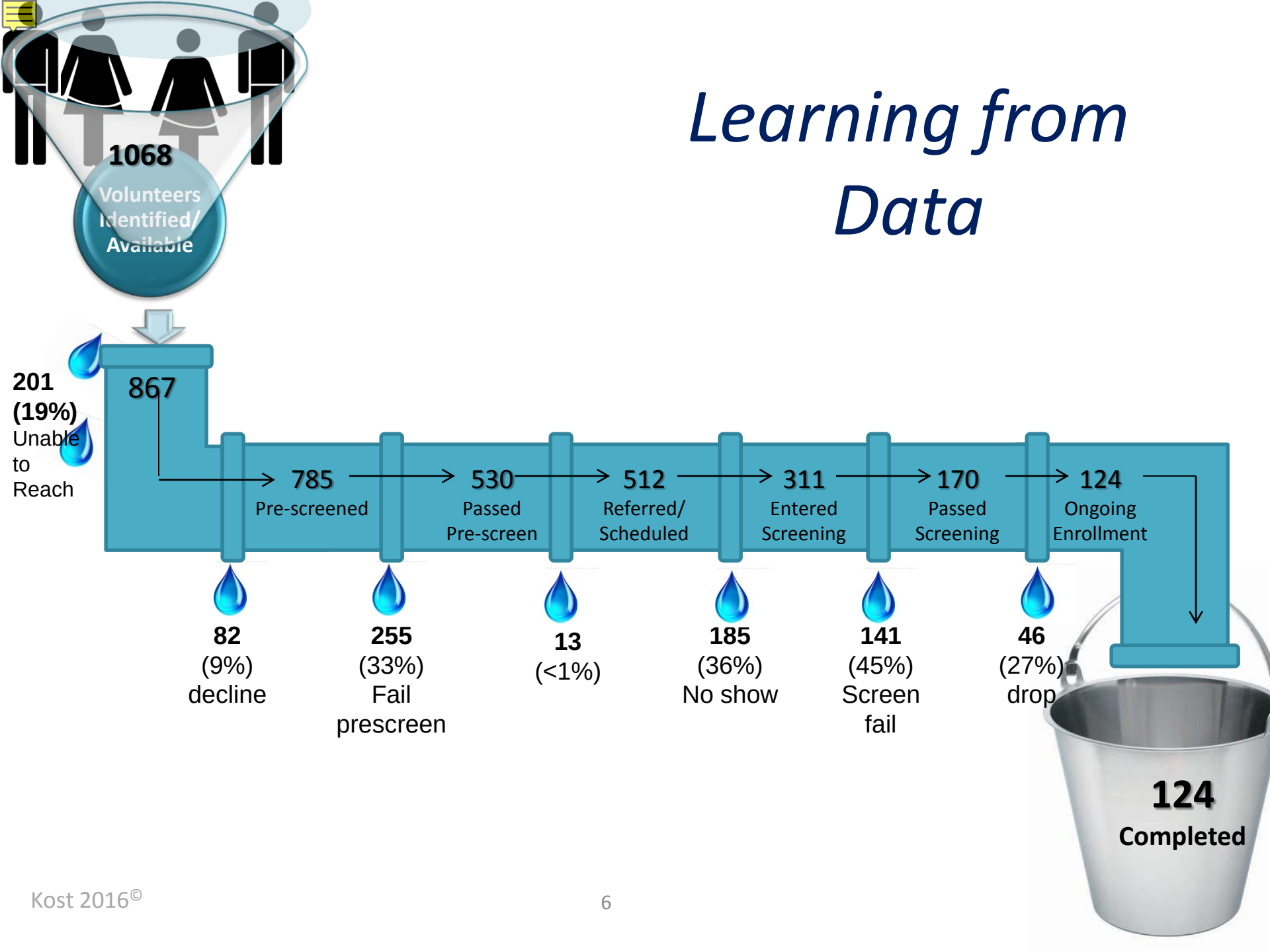
  --upstream Comprehensive Recruitment Consult

- Data Rich Recruitment Core, *(Kost et al CTS 2015)*

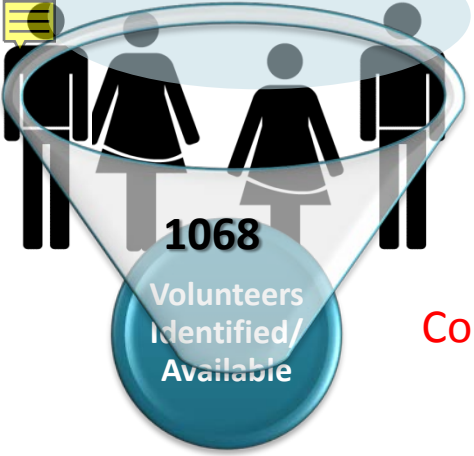
- Common platform for protocol writing, IRB, study management, subject management *(iRIS®)*

- Recruitment Management software *(Clinical Conductor®)*

Learning from Data



Learning from Data



Cohort Identification

Participant experience

201 (19%) Unable to Reach

867

785 Pre-screened → 530 Passed Pre-screen → 512 Referred/ Scheduled → 311 Entered Screening → 170 Passed Screening → 124 Ongoing Enrollment

Advertising, social media, capacity

82 (9%) decline

255 (33%) Fail prescreen

13 (<1%)

185 (36%) No show

141 (45%) Screen fail

46 (27%) drop

Barriers, Incentives

Barriers, Incentives, capacity

Participant experience

Defining the Measures

Accrual Target

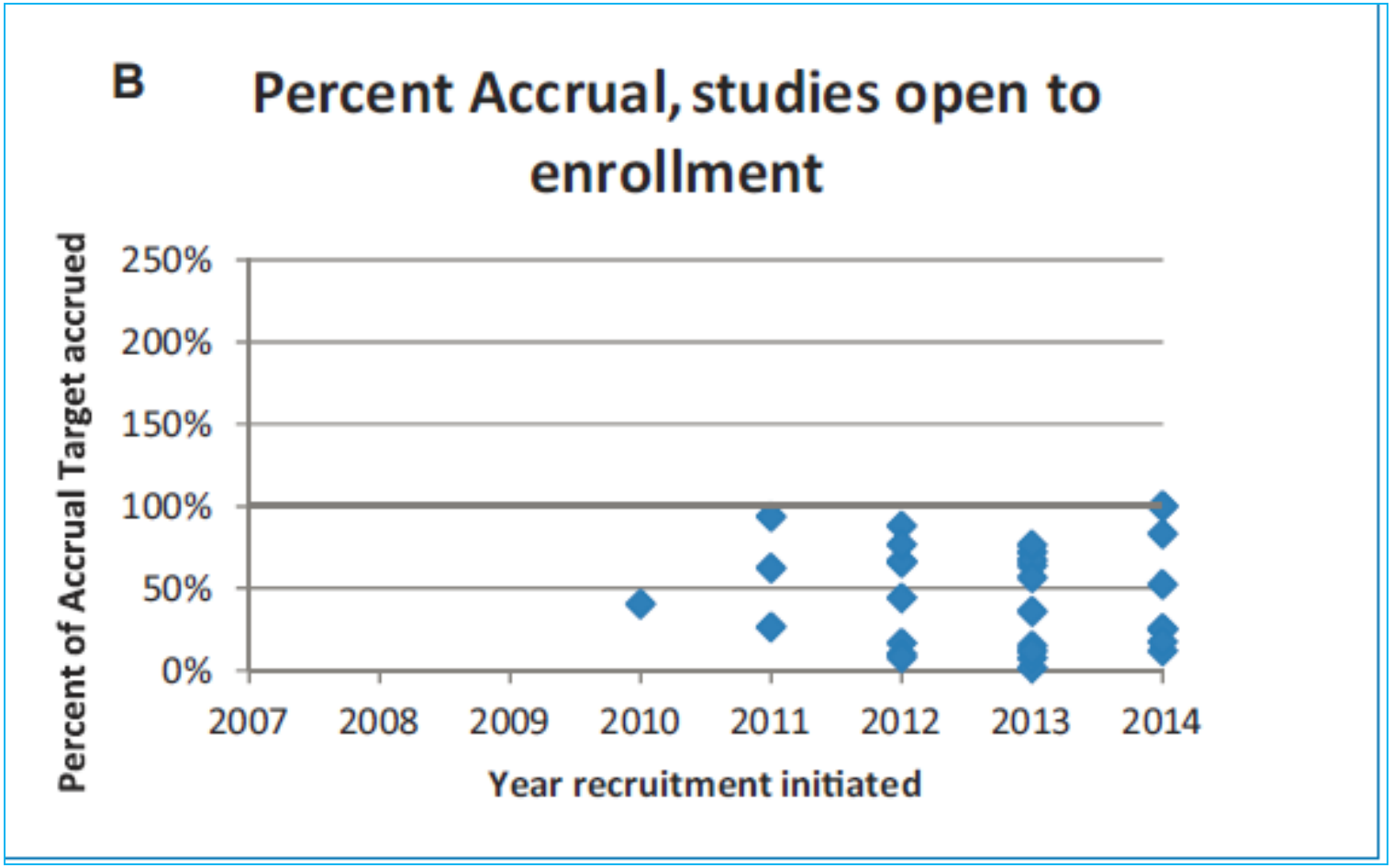
- # evaluable participants needed (sample size from power calculation)
- captured in protocol and recruitment plan in electronic IRB/study management system

Defining the Measures

Percent Accrual, at a specific time point

$$= \frac{\text{\# Evaluables accrued-to-date (on-study + completed)}}{\text{Accrual Target (Evaluables)}}$$

Percent Accrual Lacks Context



Corregano et. al. *Clin Transl Sci. 2015*

Defining Time as Context

Predicted Time to Accrual Completion (PTAC)

- Refined and justified with the research team:
  - 2007-2010: consider burdens/incentives
  - 2011-2012: add investigators' stated availability
  - 2013-2014: add LOA, vacations, delays for assay refinement, known August & December slow-downs, FDA review periods, competing protocols, grant deadlines, predictable delays

Justifying the PTAC, example

- Need 120 evaluable participants, criteria:HIV viral load, ART, CD4, nadir
- Prior study, similar population, screen/enroll = 3:1
  - Estimate need to screen, 120 x 3 = 360 volunteers
- Team can screen 10/week. Initial projection: 360/10 = 36 weeks
- Reality check:
  - Entire team attends national meeting: + 1 week
  - Head coordinator plans 2-wk vacation + 2 weeks
  - August slow-down in NYC recruitment + 2 weeks
  - Unit closes x 2 weeks over Xmas + 2 weeks
  - 3 wk FDA hold for each of 3 dose increases + 9 weeks

  REVISED: +16 weeks

Projected Time to Accrual Completion: 52 weeks

A new measure: Accrual Index (AI)

$$\frac{\text{Progress toward goal}}{\text{Fraction of enrollment period elapsed}}$$

$$= \frac{(\text{Evaluable Subjects Enrolled}/\text{Accrual Target})}{(\text{Days since recruitment start}/30)/\text{Projected Time to Accrual(mos)}}$$

How to interpret: $\frac{\text{2/3 accrued}}{\text{2/3 time elapsed}} = 1.0$; on-time accrual 

$\frac{\text{1/4 accrued}}{\text{1/2 time elapsed}} = 0.5$; < 1.0 = behind 

Accrual Index (AI)

$$= \frac{\text{(Evaluable Subjects Enrolled/Accrual Target)}}{\text{(Days since recruitment start/30)/Projected Time to Accrual(mos)}}$$

Example:

HIV study with 52 wk (12 month) PTAC, on day 150 , accrual includes 20 completed + 70 on-study:

$$\text{AI} = \frac{\text{(90 evaluable) / (120 accrual target)}}{\text{(150 days/30) / 12 month PTAC}} = \frac{.75}{.70} = 1.1$$

Data to track AI

Once:

- Sample size (evaluables in power calculation)
- Intended # to screen (data-driven estimate)
- Projected Time to Accrual Completion (PTAC)
- Date of recruitment start

For Updates:

- # participants (enrolled on-study + completed)
- Date of update

Three ways to use the AI

- A retrospective assessment of protocol accrual
- Case Studies – patterns?
- Real-time use in a Dashboard

- Audience: investigators, recruiters, managers, leadership, sponsors

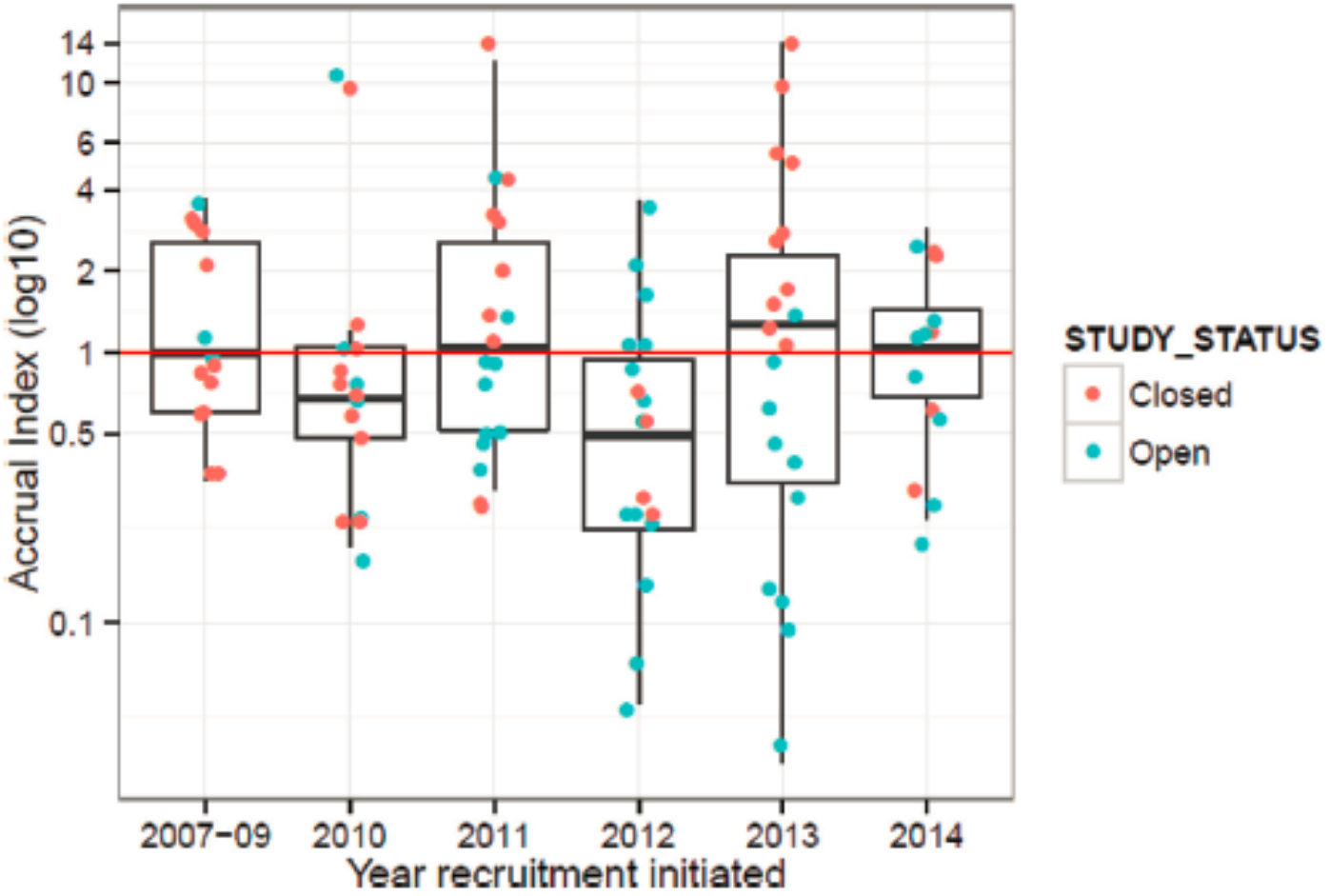
Characteristics of protocols 2007-2014

	Year in which recruitment was initiated					
	2007–2009*	2010	2011	2012	2013	2014
Protocols initiating recruitment	14	17	18	19	20	13
Accrual Target, median (range)	53 (4–500)	47.5 (5–500)	47.5 (5–500)	38 (5–300)	30 (10–180)	25 (8–80)
Projected Time to Accrual Completion in months, median (range)	13 (12–400)	12 (1–120)	12 (12–48)	12 (12–72)	12 (4–42)	12 (2–24)
CRROSS recruitment assistance provided	13 (93%)	9 (53%)	13 (72%)	9 (50%)	13 (65%)	13 (100%)
Protocols with placebo	2 (14%)	2 (12%)	4 (22%)	4 (21%)	0	2 (20%)
Protocols with direct benefits to subjects	4 (28%)	6 (36%)	3 (17%)	7 (41%)	4 (20%)	5 (39%)
DSMP risk						
0–Minimal	1	0	2	0	3	1
1–Low	6	6	5	3	6	3
2–Moderate	7	8	10	14	8	8
3–Significant	0	0	0	0	0	0

*Due to a low number of protocols initiating recruitment from 2007 to 2009, data from these years were grouped together.

Corregano et. al. *Clin Transl Sci. 2015*

Accrual Index



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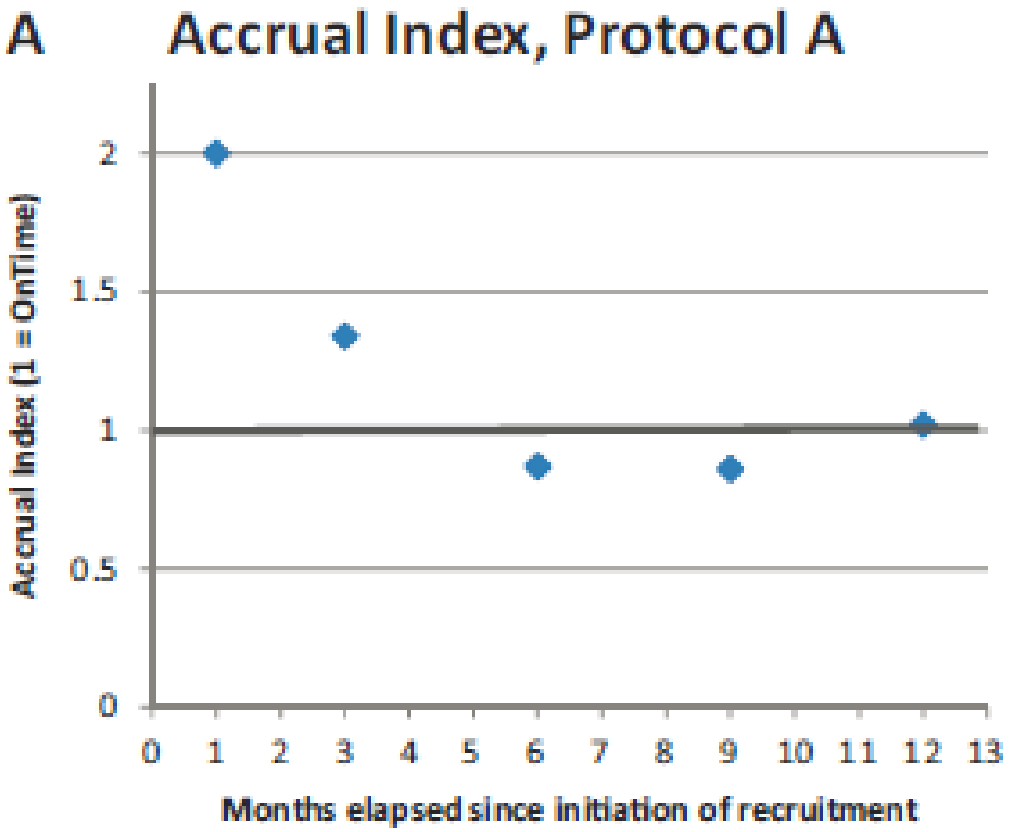

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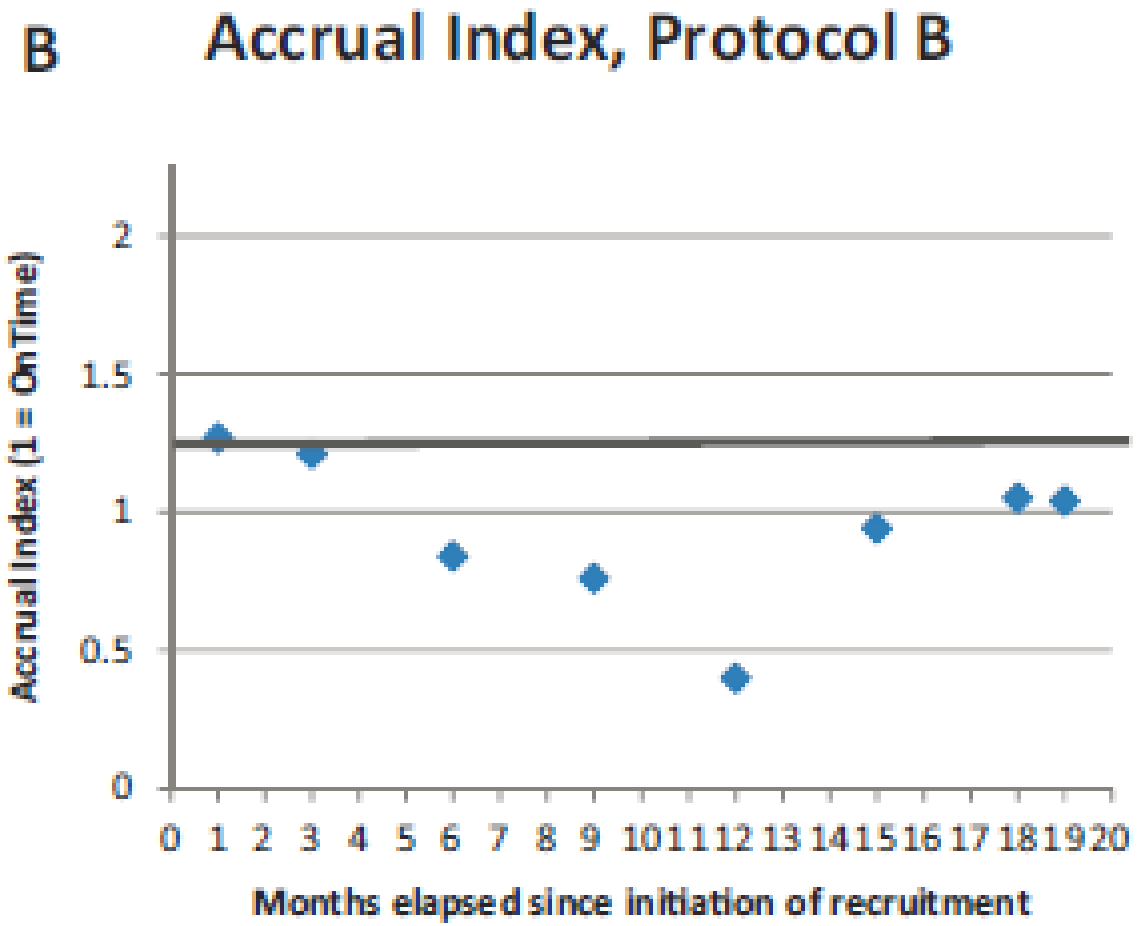

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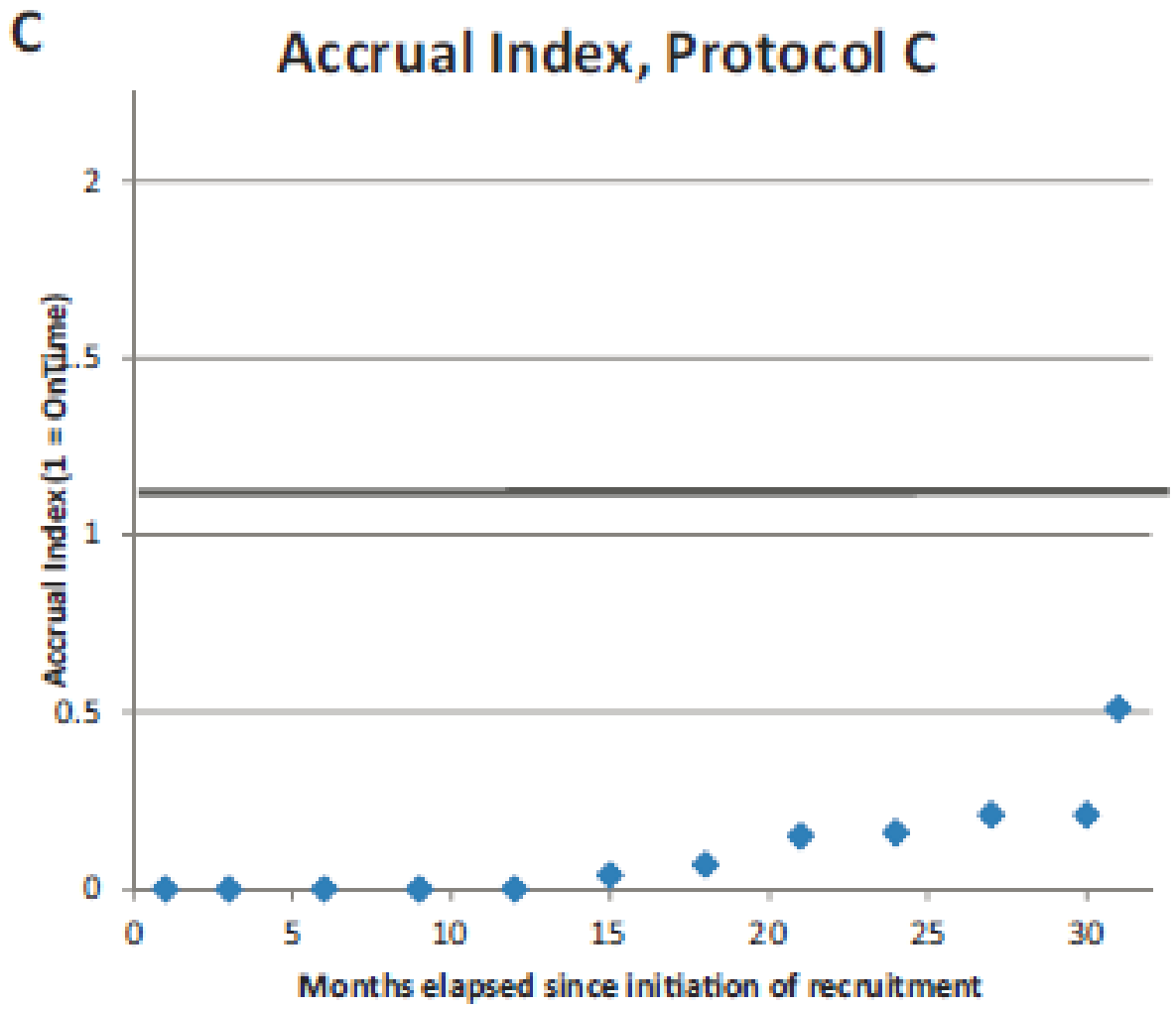

Corregano et. al. *Clin Transl Sci. 2015*

Accrual Index Dashboard: Fields

Field	Set-up versus Updated	Source	Definitions
Study name	Set-Up	Protocol (in iRIS)	Text
Study enrollment status	One time entry	Study team or iRIS	Open/closed to enrollment
Accrual Target (evaluables)	Set-Up	Protocol (in iRIS)	sample size from power calculation
Date: Data update	Regular update required	Recruitment Staff	Date data updated
Date: Enrollment Open	One time entry	Study team or iRIS	Date recruitment may begin
Date: Enrollment Closed	One time entry	Study team or iRIS	Date last enrolled participant signs ICF
Date: First enrolled	One time entry	iRIS	Date ICF signed for first participant
Time to first enrolled (days)	Formula	Formula	=DAYS360([@[Enrollment Open Date]],[@[First Patient,First Visit Date]])
Predicted evaluables/yr	Set-Up	Protocol (in iRIS)	text
PTAC - predicted time to accrual completion (mos)	Set-Up	Protocol (in iRIS)	text defined/justified in Recruitment Plan
Time elapsed at update (mos)	Formula	Formula	=DAYS360([@[Enrollment Open Date]],[@[Accrual data update Date]])/30
Current Accrued Evaluables	Regular update required	iRIS	# on study + # completed
Previous Accrual Index	Formula	Previous dashboard update	populate values from previous update
Current Accrual Index	Formula	Formula	=((accrued evaluables/accrual target) *(PTAC/Time elapsed at update))
Slope of change Accrual Index	Formula	Formula	=(current AI/previous AI)/# months since update
% PTAC elapsed	Formula	Formula	=(Time elapsed at update/PTAC)*100

AI Dashboard

Study Name	Status	AI past month	AI current month	AI Trend (slope)	Percent PTAC elapsed
Protocol M	Open	↓ 0.33	↓ 0.22	↓ -0.11	7%
Protocol X	Open		→ 0.94		8%
Protocol S	Open		↑ 1.22		8%
Protocol R	Open	↑ 2.40	↑ 2.00	↓ -0.40	25%
Protocol N	Open	↑ 1.88	↑ 2.11	↑ 0.23	26%
Protocol T	Open	↑ 1.60	↑ 1.12	↓ -0.48	42%
Protocol L	Open	↑ 1.07	↑ 1.04	↓ -0.03	46%
Protocol Q	Open	↓ 0.50	↓ 0.70	↑ 0.19	46%
Protocol K	Open	↑ 1.89	↑ 1.57	↓ -0.31	50%
Protocol G	Open	↓ 0.36	↓ 0.30	↓ -0.06	75%
Protocol V	Open	↓ 0.80	↓ 0.86	→ 0.06	117%
Protocol W	Open	↓ 0.64	↓ 0.53	↓ -0.12	133%
Protocol H	Open	↓ 0.70	↓ 0.70	→ 0.00	133%
Protocol Z	Open	↓ 0.64	↓ 0.64	→ 0.00	133%

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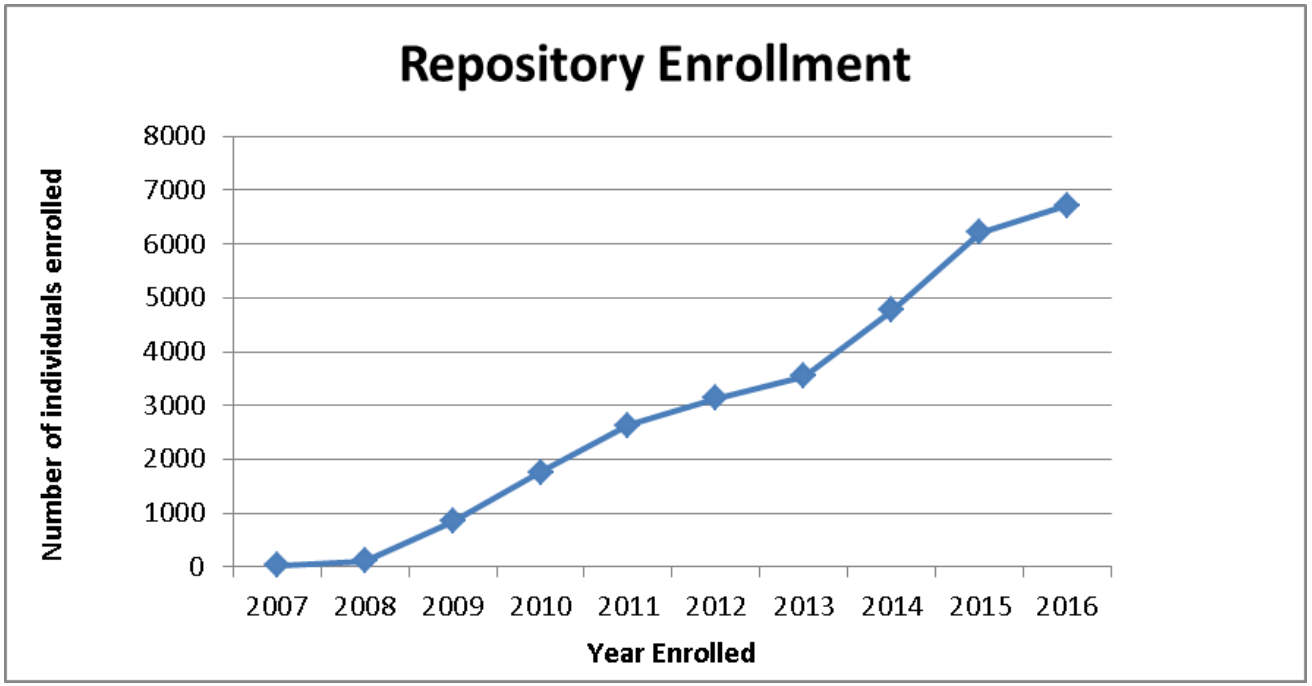
Accrual Index Dashboard Report

	Study Name	Status	Accrual Target, evaluables	Last AI	Current AI	Slope of change, AI	Current Evaluables	Percent PTAC elapsed
2	PTL1	Closed	48	⇑ 1.78				29%
3	PTL2	Closed	10	⇑ 2.43				41%
4	PTL3	Closed	154	⇑ 12.16				10%
5	PTL4	Closed	10	⇑ 1.51				73%
6	PTL5	Closed	20	⇑ 5.73				28%
7	PTL6	Closed	20	⇑ 14.00				10%
8	PTL7	Closed	150	⇑ 1.07				95%
9	PTL8	Closed	15	⇑ 2.24				44%
10	PTL9	Closed	20	⇑ 4.00				38%
11	PTL10	Closed	15	⇑ 1.64				53%
12	PTL11	Closed	35	⇑ 1.94				42%
13	PTL12	Closed	30	⇑ 2.87				31%
14	PTL13	Closed	8	⇑ 1.45				69%
15	PTL14	Closed	8	⇑ 2.44				59%
16	PTL15	Closed	30	⇑ 1.00				27%
17	PTL16	Closed	120	⇑ 2.00				50%
18	PTL19	Open	100		⇑ 1.32	⇑ 1.32	11	8%
19	PTL20	Open	75		⇑ 8.64	⇑ 8.64	54	8%
20	PTL21	Open	16		⇑ 8.25	⇑ 8.25	11	8%
21	PTL22	Open	70	⇑ 3.26	⇑ 4.46	⇑ 1.20	52	17%
22	PTL23	Open	500	⇒ 0.97	⇑ 2.09	⇑ 1.12	235	23%
23	PTL24	Open	100	⇓ 0.52	⇓ 0.55	⇓ 0.03	16	29%
24	PTL25	Open	300	⇑ 1.14	⇑ 1.18	⇓ 0.04	143	40%
25	PTL26	Open	80	⇓ 0.56	⇓ 0.45	⇓ -0.11	15	42%
26	PTL27	Open	10	⇑ 2.62	⇑ 2.60	⇓ -0.02	13	50%
27	PTL28	Open	110	⇑ 1.41	⇑ 1.35	⇓ -0.06	74	50%
28	PTL29	Open	20	⇓ 0.50	⇓ 0.90	⇓ 0.40	10	56%
29	PTL30	Closed	180	⇓ 0.02	⇓ 0.02	⇓ 0.00	3	72%
30	PTL31	Open	25	⇓ 0.36	⇓ 0.32	⇓ -0.04	6	75%
31	PTL32	Open	12	⇑ 1.00	⇒ 0.91	⇓ -0.09	10	92%
32	PT343	Open	48	⇓ 0.30	⇓ 0.40	⇓ 0.10	18	93%
33	PTL35	Open	360	⇓ 0.32	⇓ 0.31	⇓ -0.01	104	94%
34	PRL36	Open	8	⇑ 1.36	⇑ 1.63	⇓ 0.27	13	100%
35	PTL37	Open	40	⇓ 0.65	⇓ 0.68	⇒ 0.03	27	100%
36	PTL38	Open	25	⇓ 0.38	⇓ 0.36	⇓ -0.02	9	100%
37	PTL39	Open	140	⇑ 1.19	⇑ 1.27	⇒ 0.08	192	108%
38	PTL40	Open	30	⇓ 0.68	⇓ 0.74	⇒ 0.06	26	117%
39	PTL41	Open	68	⇓ 0.11	⇓ 0.13	⇒ 0.02	11	125%
40	PTL42	Open	50	⇓ 0.06	⇓ 0.06	⇒ 0.00	4	133%
41	PLT43	Open	36	⇓ 0.54	⇓ 0.54	⇒ 0.00	27	139%
42	PTL44	Open	61	⇓ 0.57	⇓ 0.56	⇓ -0.01	49	144%
	PTL45							

Measuring Other Recruitment Efforts

- Registries/repositories – enrollment yield
- Advertising - effectiveness
- Call management - impact
- Participant Experience
  - protections, satisfaction, operations, retention, re-enrollment, word of mouth

Research Volunteer Repository



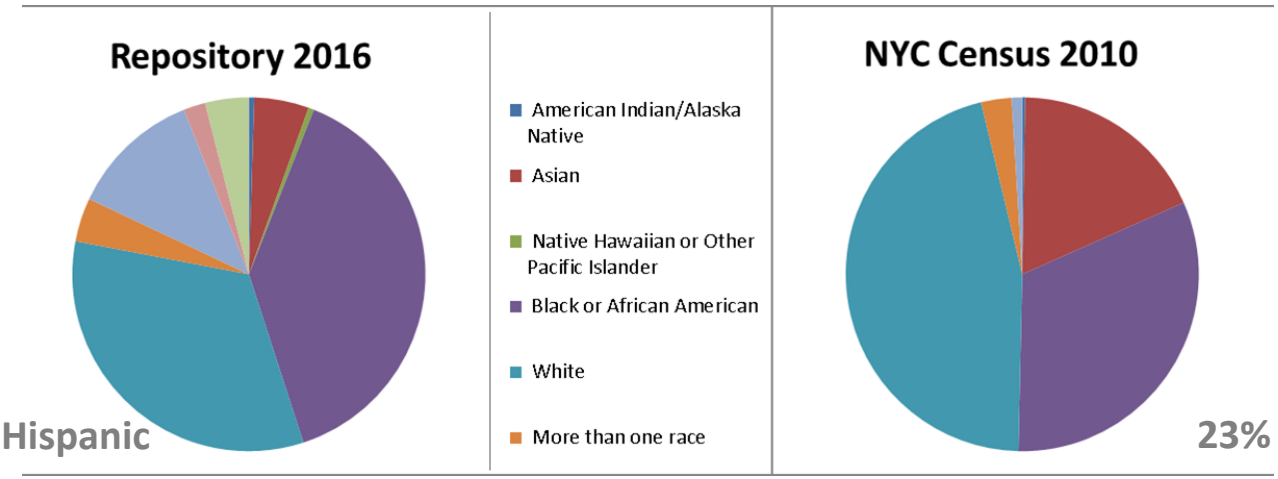
- Positive informed consent
- 23% of Repository members have enrolled in/completed ≥1 study; 85% retention in the studies
- Of those reached via queries, 50% enrolled; 92% retained in the studies

Research Volunteer Repository

Age, race, ethnicity

Results

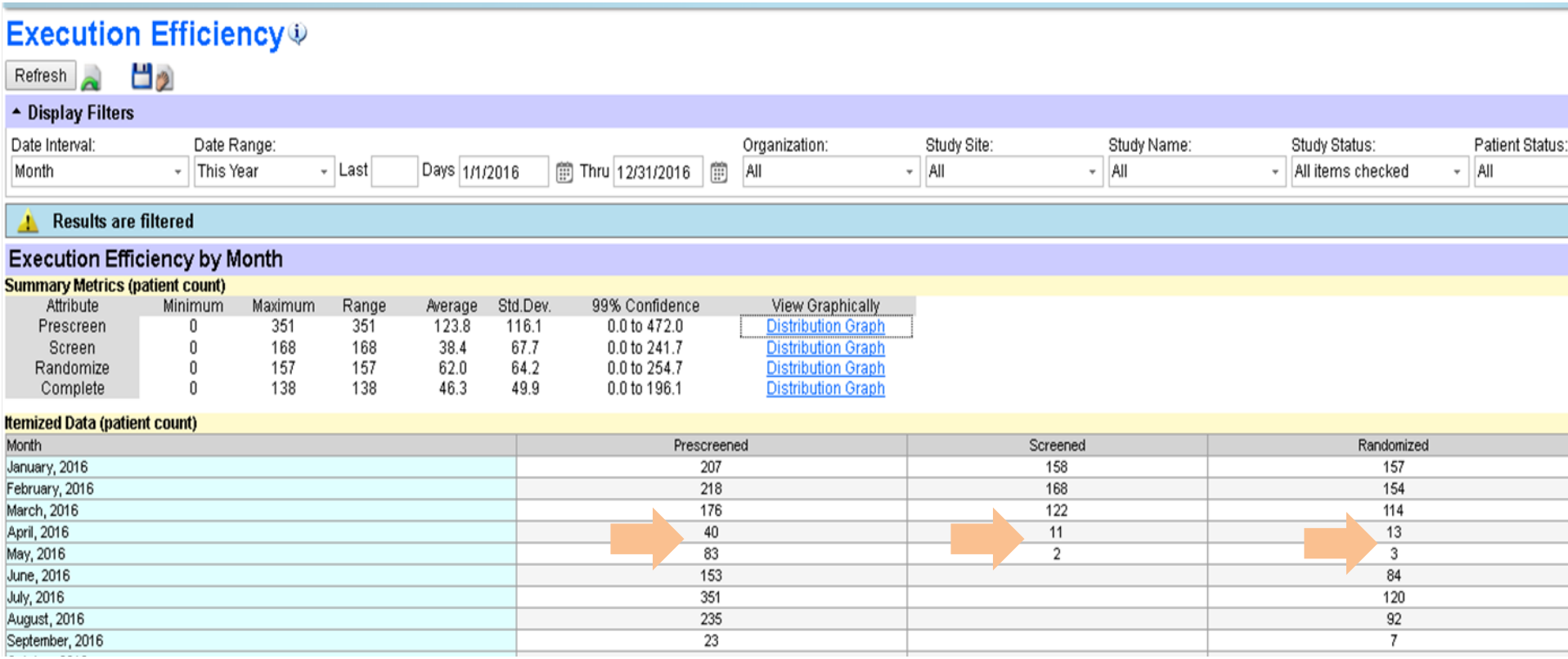
Group	Count	Percent	Bar Chart
Age 0 < 10	0	0.0	
Age 10 < 20	17	0.2	
Age 20 < 30	927	13.4	
Age 30 < 40	1348	19.6	
Age 40 < 50	1314	19.1	
Age 50 < 60	1771	25.7	
Age 60 < 70	991	14.4	
Age 70 < 80	273	4.0	
Age 80 < 90	88	1.3	
Age 90 < 100	17	0.2	
Age 100 < 110	0	0.0	
Age 110 < 120	0	0.0	
Not Available or < 0	147	2.1	
Total	6893	100.0	



20% Hispanic

23% Hispanic

Recruitment Core Call Management



Execution Efficiency

Refresh

Display Filters

Date Interval:	Date Range:						Organization:	Study Site:	Study Name:	Study Status:	Patient Status:
Month	This Year	Last		Days	1/1/2016	Thru 12/31/2016	All	All	All	All items checked	All

Results are filtered

Execution Efficiency by Month

Summary Metrics (patient count)

Attribute	Minimum	Maximum	Range	Average	Std.Dev.	99% Confidence	View Graphically
Prescreen	0	351	351	123.8	116.1	0.0 to 472.0	Distribution Graph
Screen	0	168	168	38.4	67.7	0.0 to 241.7	Distribution Graph
Randomize	0	157	157	62.0	64.2	0.0 to 254.7	Distribution Graph
Complete	0	138	138	46.3	49.9	0.0 to 196.1	Distribution Graph

Itemized Data (patient count)

Month	Prescreened	Screened	Randomized
January, 2016	207	158	157
February, 2016	218	168	154
March, 2016	176	122	114
April, 2016	40	11	13
May, 2016	83	2	3
June, 2016	153		84
July, 2016	351		120
August, 2016	235		92
September, 2016	23		7

- CRROSS recruitment core prescreen/scheduling provided: Jan – mid-March;
- Services discontinued by research team: mid-March
- Late May, PI called to complain about lag in recruitment
- CRROSS recruitment services resumed: June

Advertising

Advertising campaigns to recruit HIV infected individuals, on/off ART, for Phase I/II trials

Media	Number of ads placed	Responses	Callers passing prescreen	Callers enrolling	Yield Response /enrolled	Cost per individual enrolled
Grindr	51	220	174	85	2.6	$ 240
Repository Query	0	108	20	10	10.8	$ 0
Word of Mouth	0	84	62	37	2.3	$ 0
Metro	45	67	275	89	0.8	$ 461
Provider Query	0	47	38	28	1.7	$ 0
Radio	5	29	23	10	2.9	$1,261
Village Voice	3	5	4	4	1.3	$ 813
Pandora	4	4	3	1	4.0	$5,001

GEOGRAPHIC DISTRIBUTION OF HIV

FIGURE 4.1: Poverty level, NYC 2009-2013

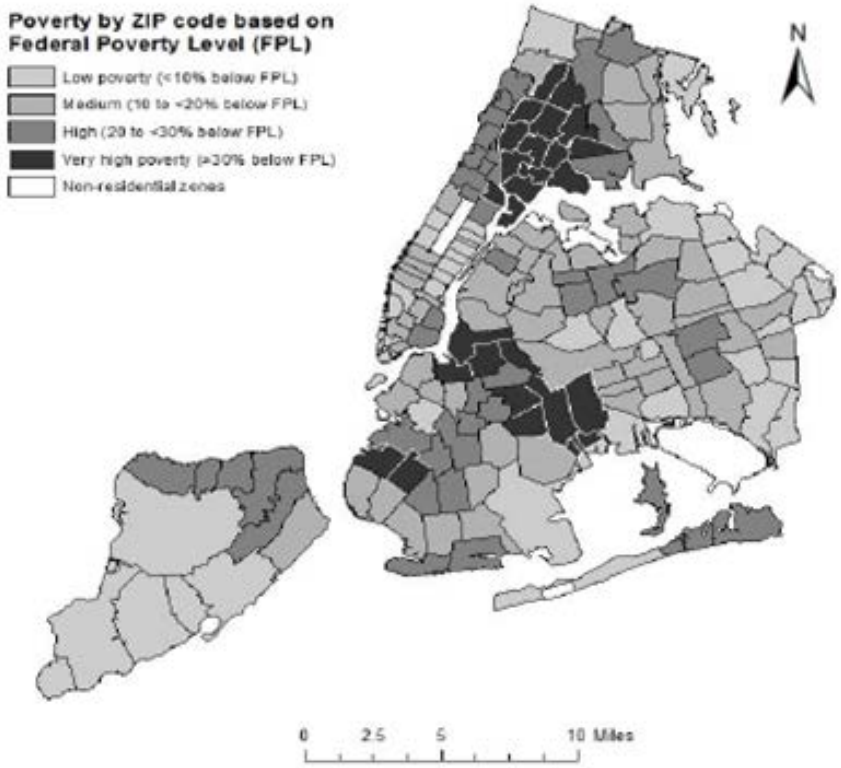
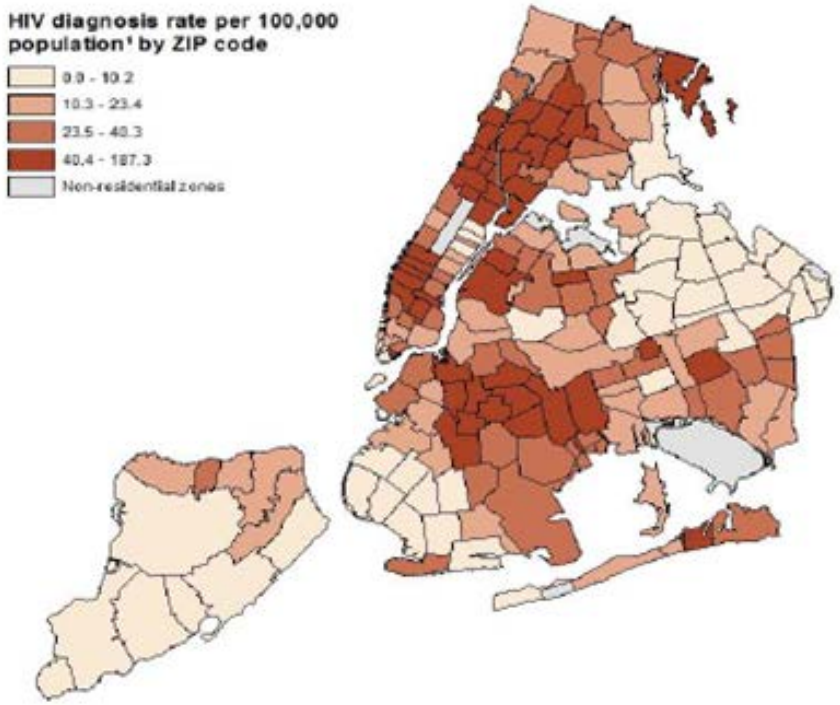
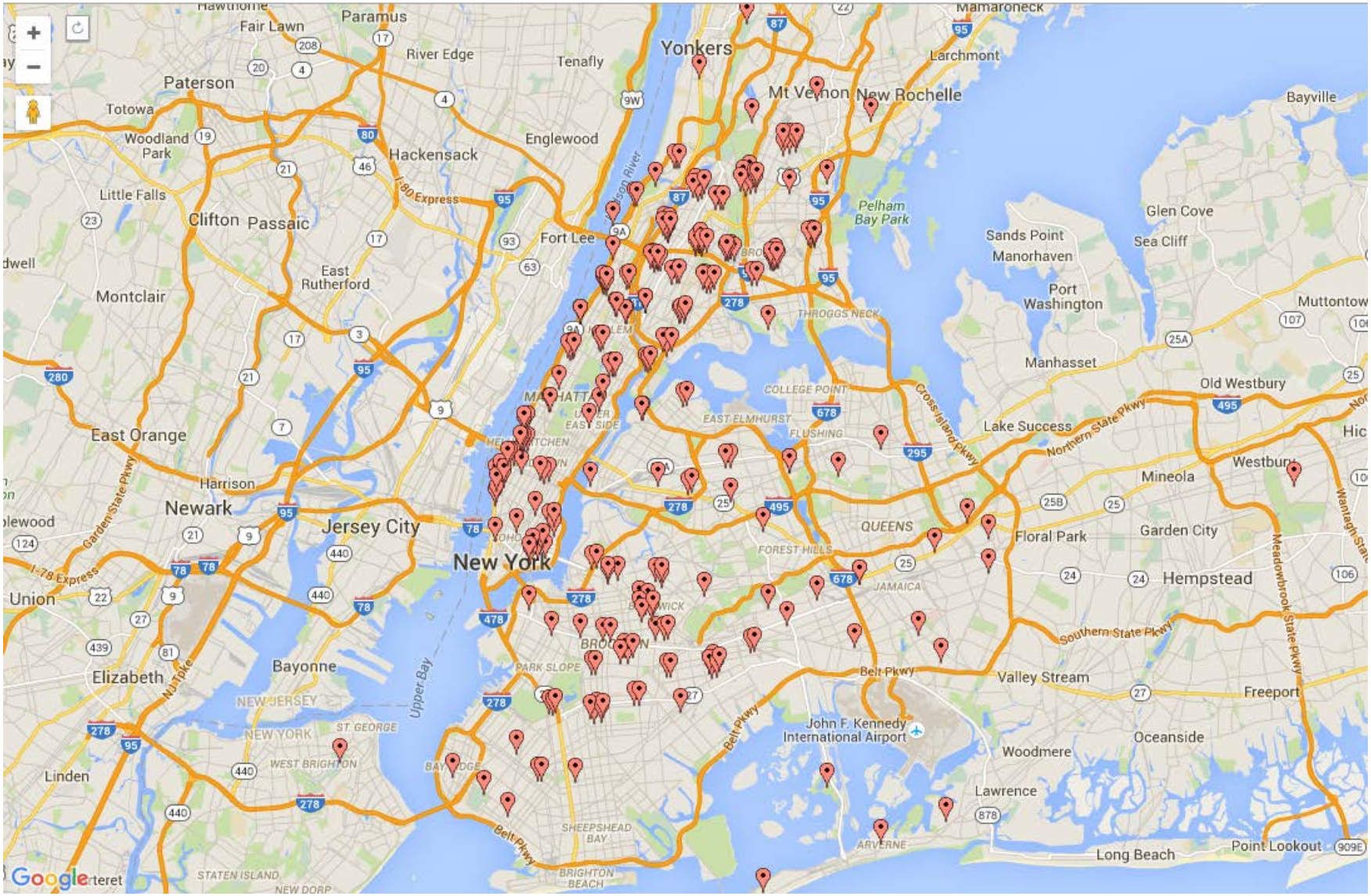


FIGURE 4.2: HIV diagnosis rates, NYC 2014



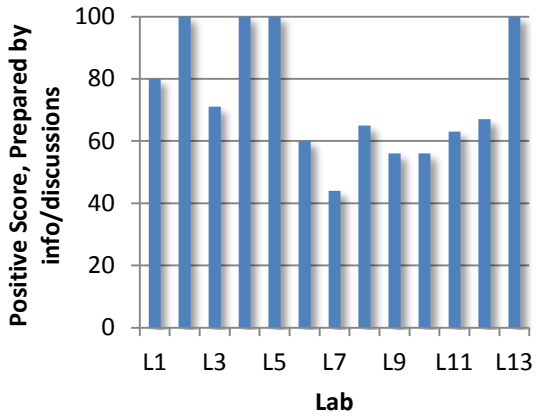
ZIP codes in the Chelsea-Clinton, Central Harlem-Morningside Heights and East Harlem neighborhoods had the highest HIV diagnosis rates in 2014 (Figure 4.2). In 2014, ZIP codes in Chelsea-Clinton, West Queens and Central Harlem-Morningside Heights had the highest HIV prevalence (Figure 4.3), and ZIP codes in the South Beach - Tottenville, Flushing-Clearview and Rockaway neighborhoods had the highest mortality among people with HIV (Figure 4.4). Many ZIP codes with high HIV diagnosis rates were also among those with highest poverty rates (Figure 4.1), including those in Central Harlem-Morningside Heights, East Harlem and East New York. However, ZIP codes in the Chelsea-Clinton neighborhood were the exception with the highest HIV diagnosis rates but relatively low poverty and mortality rates.

Geographic distribution of HIV-positive participants enrolled; by zip code; Batchgeo



Participant experience

- Research Participant Perception Survey
  - Validated at 15 NIH supported sites, robust, reliable,
  - Overall rating, "Would recommend", motivation to join, stay, leave study, consent, trust, etc.
  - Opportunity to identify better performers, better practices



- Shorter RPPS –
  - Validated, reliable
  - *Flash*: compensation impacts response, reliability , ratings
  - Backbone survey; menu of add-in questions
    - Will be available with analysis handbook

Kost 2011, Yessis 2012, Kost 2013, Kost 2014

Measuring the Impact of Patient and Stakeholder Engagement

- From our Community Engaged Reseach Navigation Program (CEnR-Nav) process – Track
  - Stakeholder characteristics, participation
  - Stakeholder generated themes/suggestions
  - Incorporation of stakeholder recommendations
  - Analysis of recruitment outcomes +/- stakeholder input

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