LANDSCAPE ANALYSIS OF CURRENT HIV CURE TRIALS

Pre-CROI Community HIV Cure Workshop

March 3, 2019

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OVERVIEW OF TALK

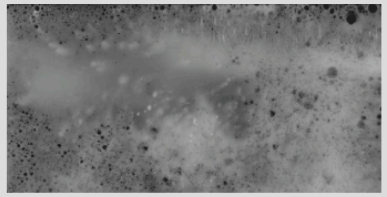
- Characteristics of survey and respondents
- Characteristics of current HIV cure trials
  - When will we see results?
- Survey data from study teams
  - Participant characteristics
  - Study development
  - Study enrollment
- Next steps & recommendations

PURPOSE OF THIS ANALYSIS

- Landscape analysis performed on behalf of Bill & Melinda Gates Foundation
- To better understand the current landscape of HIV cure clinical trials
  - What strategies are under consideration?
  - When can we expect results?
  - Where are studies happening?
  - What are participant demographics?
  - Future directions?

WHAT STUDIES WERE INCLUDED

- TAG maintains a listing of current HIV cure related trials
  - Phase I trials are not required to be registered, but most are voluntarily entered into the registry
- Cure-related = measures HIV reservoir or virus persistence, evaluations of immune responses that may control viral replication, or ATIs
- 113 of 128 studies are Phase I or II -- NIH Revitalization Act applies to Phase III studies (and pivotal Phase II or IV)



Research Toward a Cure Trials

DOWNLOAD:
This chart as a PDF

A listing of clinical trials and observational studies related to the research effort to cure HIV infection, mainly derived from the clinicaltrials.gov online registry. Click the trial registry identifier numbers for a link to the full clinicaltrials.gov entry containing detailed information on the trial design, enrollment criteria, principal investigators and location(s). It's important to appreciate that at the current time, none of these studies is expected to produce a cure for HIV infection—they represent research working toward that goal. Table 3 contains completed studies, with links to published or presented results where available. Changes from the previous update are highlighted in yellow. Additional information on current approaches in HIV cure research can be found in TAG's annual pipeline report and cure research fact sheet. Please send updates, corrections, or suggestions to Richard Jefferys at richard.jefferys@treatmentactiongroup.org.

February 19, 2019

Table 1. Current Clinical Trials

Trial	Trial Registry Identifier(s)	Manufacturer/ Sponsor(s)	Phase	Estimated End Date/Interim

http://www.treatmentactiongroup.

WHO WE SURVEYED

- 128 trials in TAG's report at the end of last year
  - Surveys sent to contacts listed in clinicaltrials.gov
  - 72 surveys completed
  - 7 declined to complete
- Collected additional information from clinicaltrials.gov listings*
  - Study procedures
  - Estimated completion date

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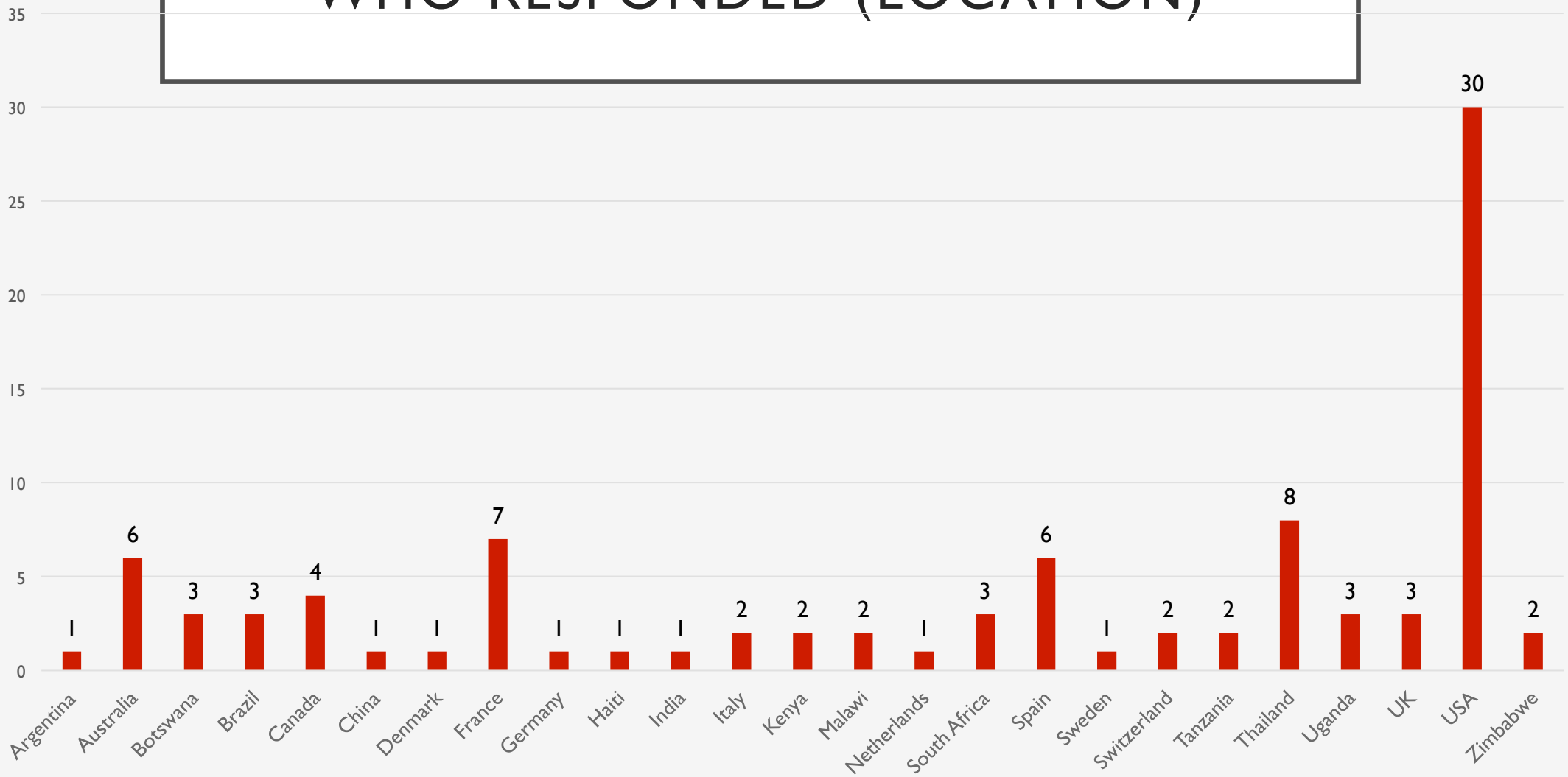
*clinicaltrials.gov listings are provided and updated by study teams and may not include all procedures

WHO RESPONDED

Trial categories represented in survey responses	
Adoptive immunotherapy	Imaging studies
Anti-inflammatory	Immune checkpoint inhibitors
Anti-proliferative	Latency reversing agents
Antibodies	mTOR inhibitors
Antifibrotic	Observational
Combinations	Proteasome inhibitors
Cytokines	Stem cell transplantation
Gene therapies	Therapeutic Vaccines
Gonadotropin-releasing hormone (GnRH) agonists	Treatment intensification/early treatment
Hormones	

WHO RESPONDED (LOCATION)



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THE BIG PICTURE

Overview of all studies in TAG's listing

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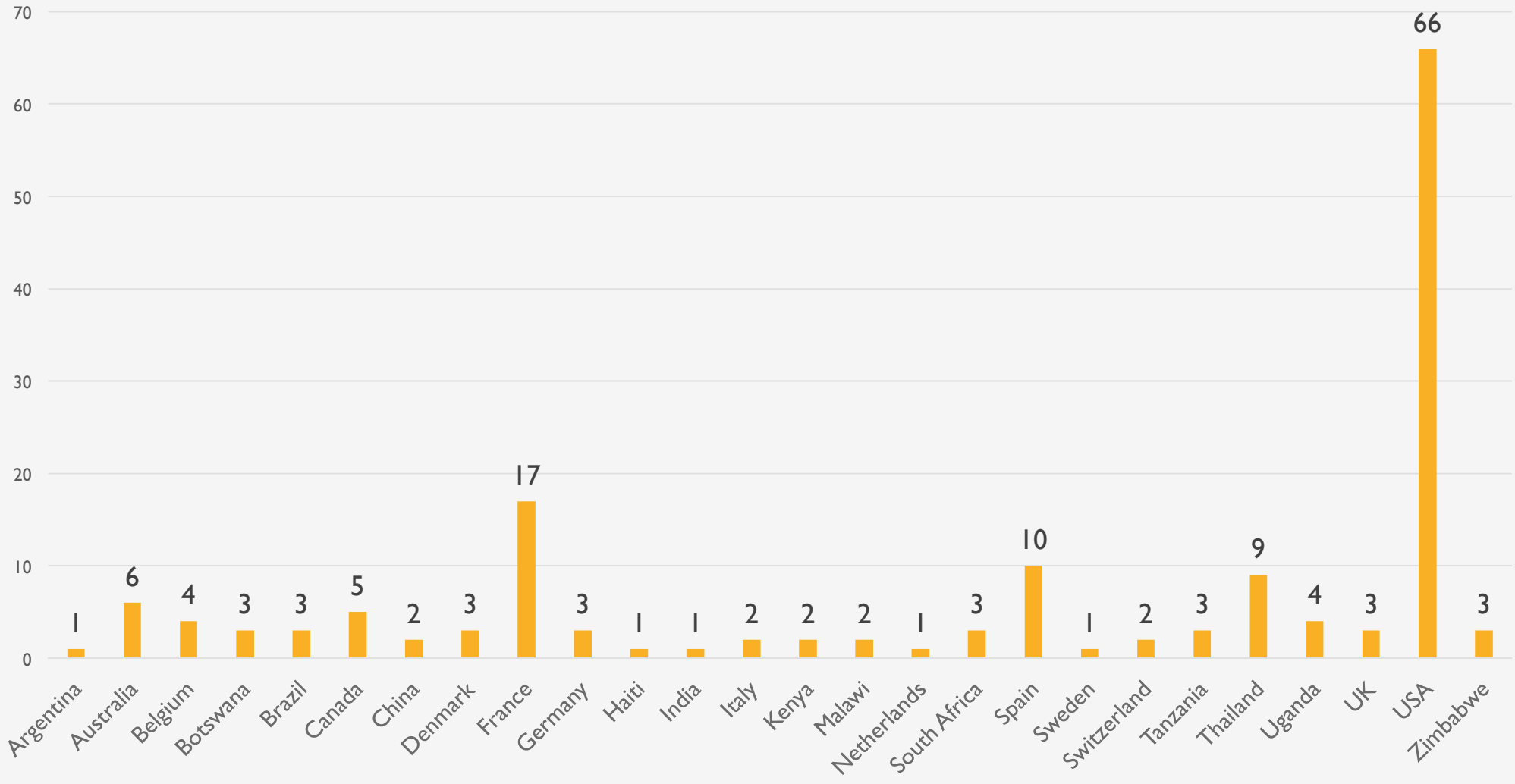
STUDY LOCATION



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TOTAL # OF PARTICIPANTS (ALL TRIALS)

Category	# of Studies	Avg # participants	Range	Total participants
Adoptive immunotherapy	1	12	---	12
Anti-inflammatory	3	66 (median 60)	30-110	200
Anti-proliferative	1	5	---	5
Antibodies	13	38 (median 34)	12-68	500
Antifibrotic	2	42 (median 42)	21-63	84
Antiretroviral therapy	1	36	---	36
Cannabinoids	1	26	---	26
Combinations	17	40 (median 30)	5-192	680
Cytokines	2	15 (median 15)	10-20	30
Dual Affinity re-targeting (DART) molecules	1	26	---	26
Gene therapies	8	16 (median 12)	6-40	132
Gene therapies for HIV positive people w/ cancers	8	8 (median 7)	3-18	69

TOTAL # OF PARTICIPANTS (ALL TRIALS)

Category	# of Studies	Avg # participants	Range	Total participants
Gonadotropin-releasing hormone (GnRH) agonists	1	52	---	52
Hormones	1	22	---	22
Imaging studies	2	7 (median 7)	5-10	15
Immune checkpoint inhibitors	4	46 (median 40)	20-84	184
Latency reversing agents	3	32 (median 28)	9-60	97
mTOR inhibitors	2	16 (median 16)	10-22	32
Observational	29	88 (median 50)	10-536	2571
Proteasome inhibitors	1	17	---	17
Stem cell transplantation	4	13 (median 12)	5-25	55
Therapeutic Vaccines	8	46 (median 39)	26-105	374
Toll-like receptor agonists	2	50 (median 50)	28-72	100
Treatment intensification/early treatment*	10	68 (median 65) 205 (median 72)	15-905	2054

TOTAL # OF INVASIVE PROCEDURES*

Study category	ATI	Lumbar Puncture	Leukapheresis/ HVBD	GALT biopsy	LN biopsy
Adoptive immunotherapy			1		
Anti-proliferative				1	
Antibodies	5	1	2	1	1
Antifibrotic		1		1	1
Antiretroviral therapy				1	
Combinations	4		3	1	1
Gene therapies	3		2	3	
Gene therapies for HIV positive people w/ cancers	6		2		
Immune checkpoint inhibitors		1			
Latency reversing agents			1		
mTOR inhibitors				1	
Observational	7	6	7	5	5
Stem cell transplantation	1	1	1		
Therapeutic Vaccines	3		2		
Toll-like receptor agonists	1				
Treatment intensification/early treatment	2			3	
Grand Total	**32**	**10**	**21**	**17**	**8**

*Clinicaltrials.gov listings may be incomplete; these numbers may be higher

WHEN WILL WE HAVE RESULTS (ALL TRIALS)

ANTICIPATED RESULTS

- 38 trials are expecting to have results this year
- 29 trials expect results in 2020

Category	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034
Adoptive Immunotherapy					1													
Anti-inflammatory			1	1														
Anti-proliferative			1															
Antibodies		2	5	5	1													
Antifibrotic		2																
Cannabinoids			1															
Combinations		1	4	4	4	1	1											
Cytokines		1	1															
DART molecules				1														
Gene therapies	1		3	1					1						1			
Gene therapies w/ cancer			2	1	1		1								1			1

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Category	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034
GnRH agonists			1															
Hormones		1																
Imaging studies			2															
Immune checkpoint inhibitors			1	2														
Latency reversing agents		1	1	1														
mTOR inhibitors		2																
Observational	1	4	11	4		1	2		1									
Proteasome inhibitors				1														
Stem cell transplantation		2																
Therapeutic Vaccines		2	2	4														
Toll-like receptor agonists			1	1														
Tx intensification / early tx		4	1	3								1						

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PARTICIPANT CHARACTERISTICS

A STRONGLY WORDED DISCLAIMER

- Demographic information is incomplete –studies provided information "to date" – meaning participant demographics may change as trials fully accrue
- Trends should be interpreted cautiously, however—we are still able to identify areas where increased diversity is needed

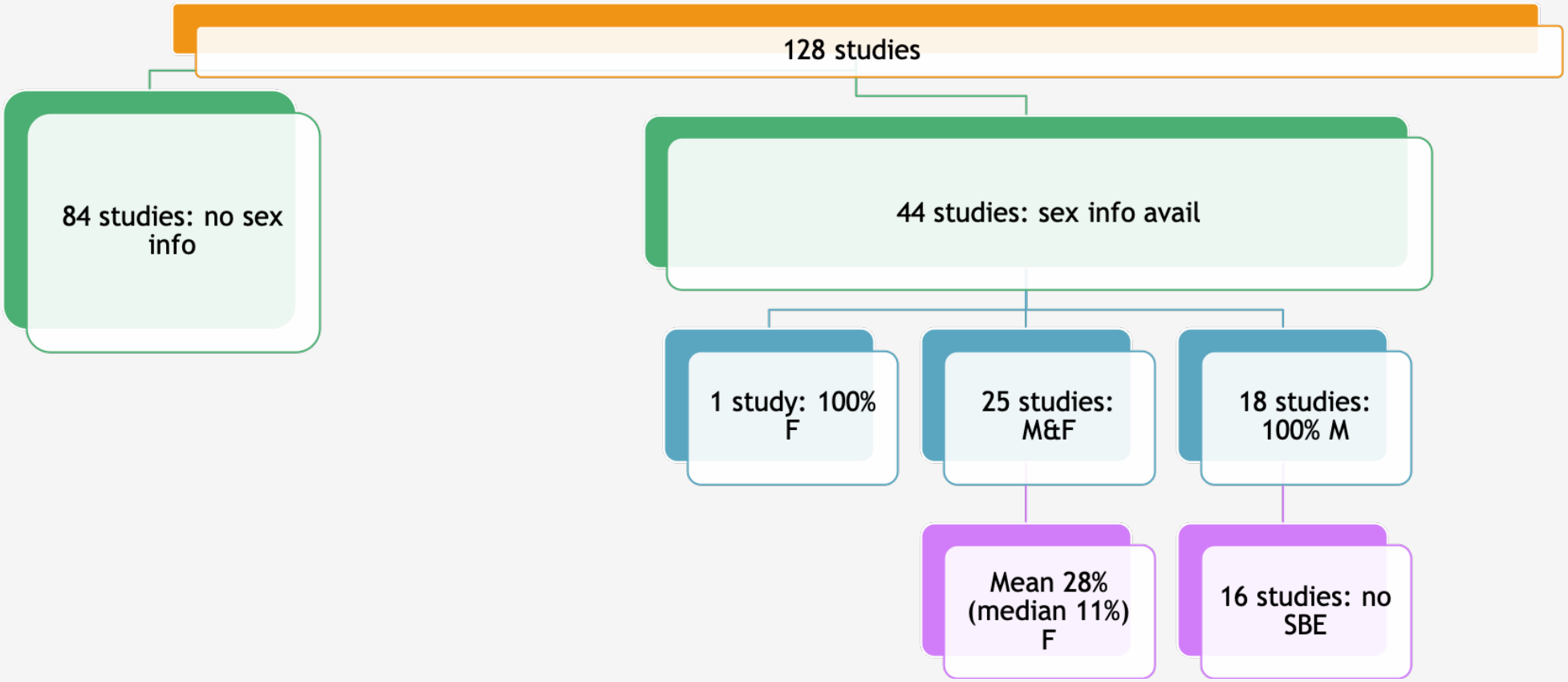
PARTICIPANT DEMOGRAPHICS

- Insufficient data to conduct analysis on racial and ethnic diversity in non-US and multinational studies
  - Data came largely from survey responses and some respondents were unable to provide all information
- In US-only studies, enrollment-to-date is:
  - 39% Black or African-American,
  - 52% White/Caucasian,
  - 16% Hispanic
- Insufficient data at this time to look for correlations or trends – hope to explore this domain in follow up analysis

APPROX. ENROLLMENT (TO DATE)

Category	% Male	% Female
Anti-inflammatory	100%	0%
Anti-proliferative	100%	0%
Antibodies	73%	27%
Antifibrotic	100%	0%
Combinations	79%	21%
Gene therapies	77%	23%
Immune checkpoint inhibitors	73%	27%
mTOR inhibitors	100%	0%
Observational	86%	14%
Proteasome inhibitors	100%	0%
Stem cell transplantation	75%	25%
Therapeutic Vaccines	96%	4%
Tx intensification/early tx	73%	27%
Grand Total	82.73%	17.27%

PARTICIPANT DEMOGRAPHICS

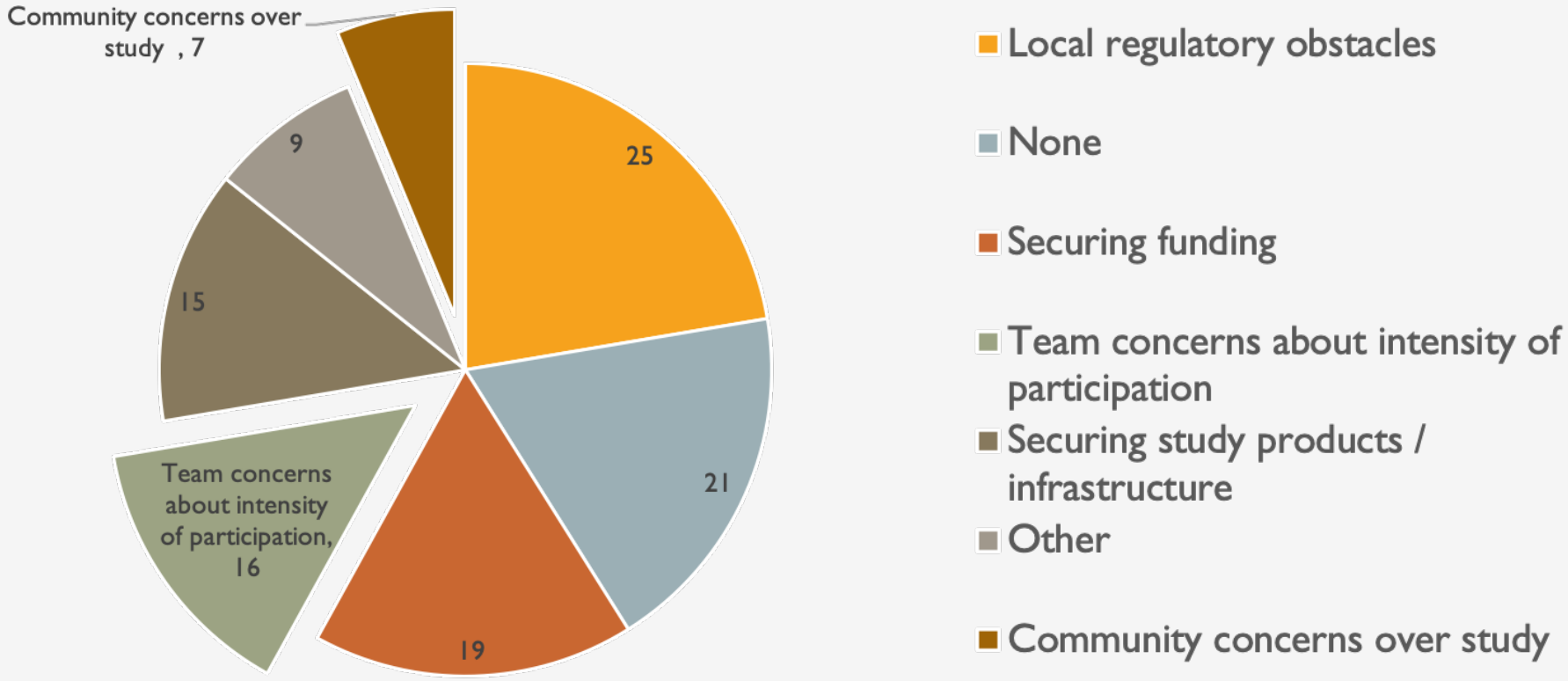


STUDY DEVELOPMENT

STUDY DEVELOPMENT (ALL SURVEYS)

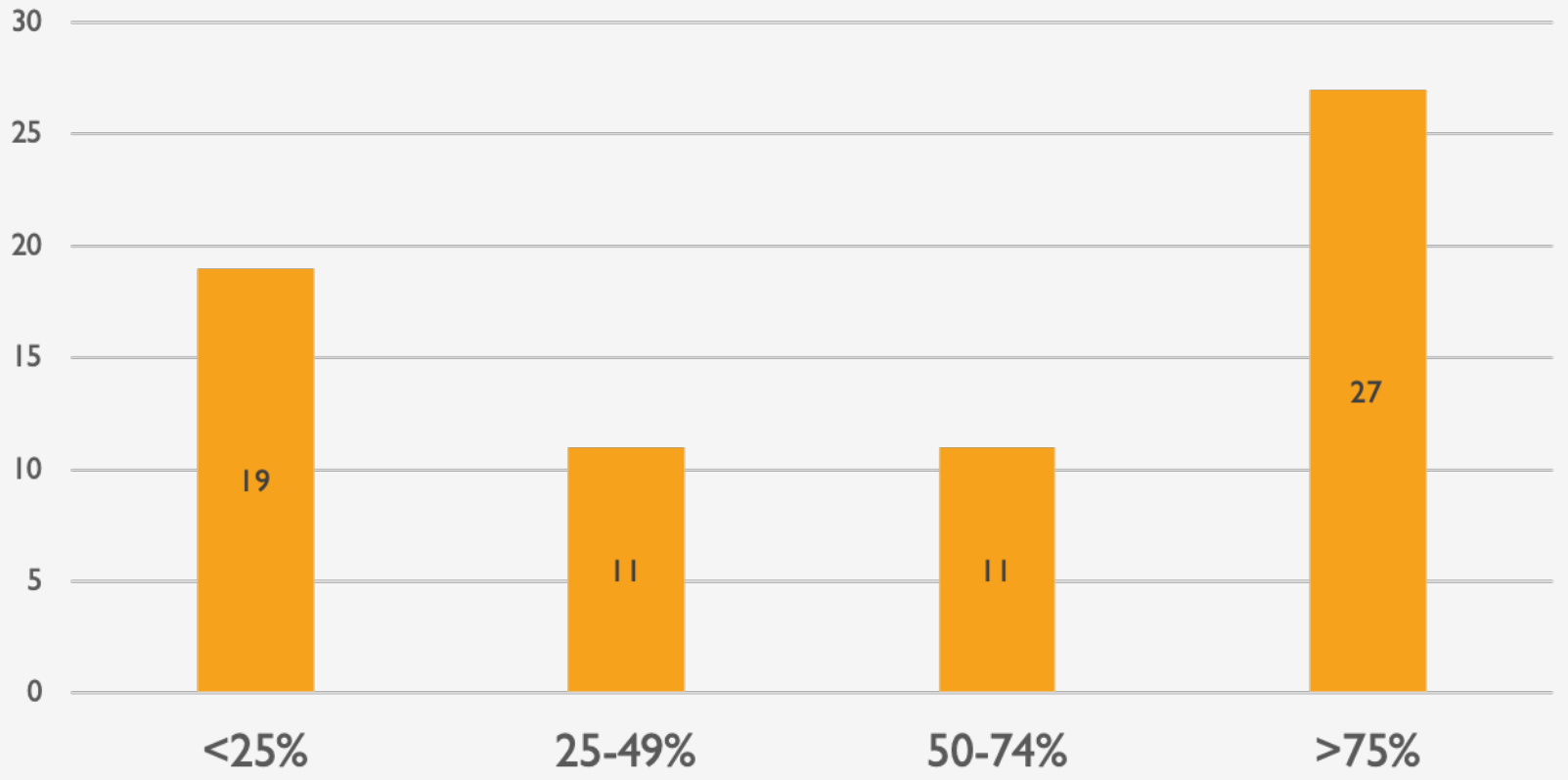
- 38 survey respondents specified that community representatives/advisory bodies were involved in study development
  - 22 of these indicated community was supportive/ enthusiastic about the concept
  - Most common community concerns were related to ATIs/drug resistance

OBSTACLES DURING DEVELOPMENT (ACROSS ALL RESPONSES)



STUDY ENROLLMENT

CURRENT ENROLLMENT STATUS



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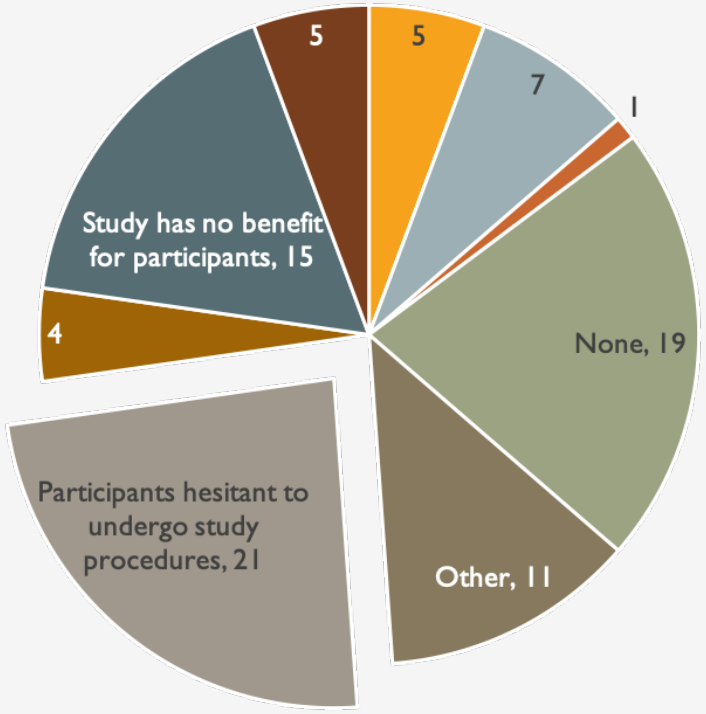
GENERAL TRENDS IN SURVEY RESULTS

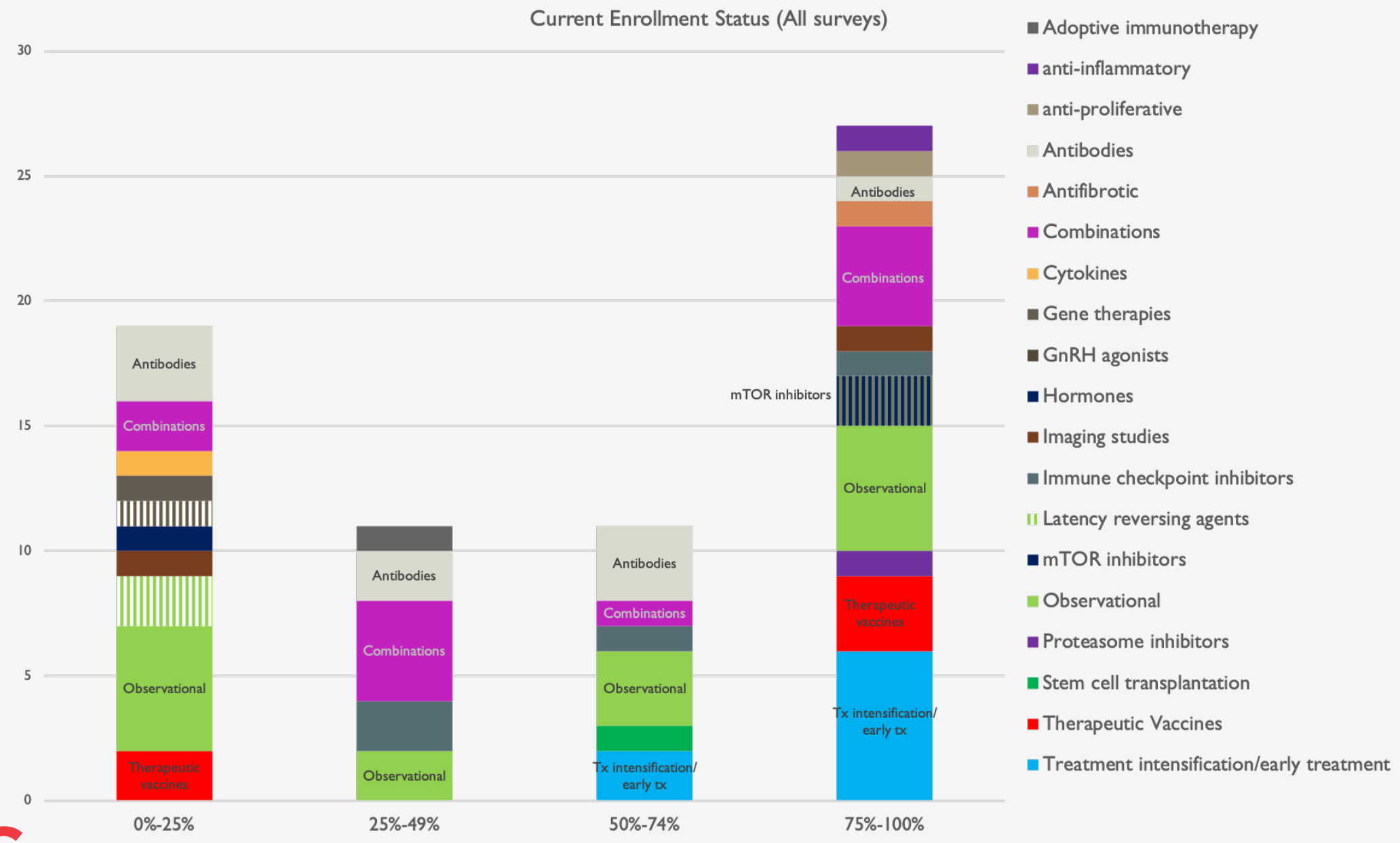
- Average length of enrollment: 20.3 months (median =15.5)
- Most participants will be enrolled in treatment intensification (1403);* observational (1006); combinations (541)
- Most common obstacles encountered during enrollment:
  - Participants are hesitant to undergo study procedures (N=21);
  - None (N=9);
  - Study has no benefits for participants (N=15)

*905 of these participants are pregnant women who are being enrolled in a trial of HIV treatment in newborns. The subset of newborns who are diagnosed with HIV infection is likely to be 5-10% of the total number of newborns. The babies who are not diagnosed with HIV infection will receive standard preventive HIV treatment and exit the trial 4-6 weeks postpartum

OBSTACLES TO ENROLLMENT (ACROSS ALL RESPONSES)



- Inclusion / exclusion criteria
- Participants nervous to jeopardize health
- Lab staff / facility access
- None
- Other
- Participants hesitant to undergo study procedures
- Providers are unwilling to refer participants
- Study has no benefit for participants



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OBSTACLES TO ENROLLMENT

- Regulatory obstacles are perceived as a barrier by study teams
- Strict exclusion/inclusion criteria slow enrollment
- Most commonly cited obstacle was participant hesitation around study procedures (28% of respondents)
  - ATIs can be scary and deter participation
  - Other invasive procedures can be scary and deter participation

AVERAGE LENGTH OF ENROLLMENT FOR STUDIES WITH INVASIVE PROCEDURES

- ATIs: 22.86 months (range 6-60 months)
- GALT/Colorectal biopsy: 24.7 months (range 9-60 months)
- Lumbar puncture: 26.67 months (range 18-38 months)
- LN biopsy: 28 months (range 24-36 months)

NEXT STEPS & RECOMMENDATIONS

NEXT STEPS

- Seeking publication, will also share writeup on TAGs site, social media
- Follow up with survey respondents Q3 2019
  - Participant characteristics
  - Enrollment obstacles
  - Role of incentives
  - Any observable relationship between participant demographics and trial location, trial category, funder, invasive procedures?

RECOMMENDATIONS

- Continue engaging with community to proactively address participants' concerns about trials
- Can sex (or gender) analysis be done across protocols?
- Keep clinicaltrials.gov entries up to date and comprehensive
  - A key source of information for community
- Increase education for referring providers and IRBs
- Qualitative research with sites & studies that met demographic enrollment targets to see what worked

THANK YOU!

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