Advisory Panel on Rare Disease Winter 2015 Meeting

Arlington, VA
January 13, 2015 – 9:30 a.m. to 5:30 p.m. EST

Patient-Centered Outcomes Research Institute

Welcome and Plans for the Day

Bryan Luce, PhD, MBA, Chief Science Officer, PCORI

Marshall L. Summar, MD, Chair, Advisory Panel on Rare Disease, PCORI

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Housekeeping

- Today's webinar is open to the public and is being recorded.
- Members of the public are invited to listen to this teleconference and view the webinar.
- Anyone may submit a comment through the webinar chat function or by emailing advisorypanels@pcori.org.
- Visit www.pcori.org/events for more information.
- Chair statement on COI and confidentiality

Today's Agenda

Start Time	Item	Speaker
9:30 a.m.	Welcome and Plans for the Day	B. Luce M. Summar
9:45 a.m.	Evaluation of PCORI's Merit Review Process and Rare Disease Proposals	L. Forsythe
10:45 a.m.	Break	
11:00 a.m.	Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options Topic Prioritization	M. Summar U. Deshmukh
12:30 p.m.	Lunch	
1:30 p.m.	Clinical Trials in Rare Diseases: Starting from Scratch Even with Limited Resources	J. Connor
2:30 p.m.	Ad Hoc Advisory Panels on Rare Disease	B. Luce E. Djabali

Today's Agenda (cont.)

Start Time	Item	Speaker
3:15 p.m.	Break	
3:30 p.m.	Update about Collaboration with CTAP	B. Luce
3:45 p.m.	Compensating Patient Partners in Research	S. Schrandt
4:45 p.m.	Recap and Next Steps	B. Luce M. Summar
5:00 p.m.	Adjourn	

Meeting Objectives

- Discuss how rare disease projects are going through PCORI Merit Review to help PCORI fund more rare disease research.
- Participate in APDTO meeting during the discussion of a rare disease topic.
- Collaborate with the CTAP.
- Advise PCORI on compensating patient partners in research.

Analysis of PCORI Review of Applications on Rare Diseases

Laura Forsythe, PhD, MPH
Senior Program Officer, Research Integration and Evaluation Program

Vadim Y. Gershteyn, MPH
Program Associate, Research Integration and Evaluation Program

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Funded Projects on Rare Disease

- To date, PCORI has awarded **37** projects dealing with Rare Disease
  - 12 through Broad Funding Announcements
  - 3 Pilot Projects
  - 2 Pipeline to Proposal awards
  - 20 Networks (Patient Powered Research Networks and Clinical Data Research Networks)

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Rationale for Analysis

- Desire to understand whether applications on rare diseases fare differently than those on more common conditions in PCORI merit review and why
- Identify action steps for funding applications on rare diseases

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Evaluation Questions

- How many applications on rare diseases are reviewed, discussed and funded each cycle compared to the numbers of applications received on other conditions?
- Are applications on rare diseases less likely to be discussed at the in-person panels than applications on more common conditions? Why?
- Are applications on rare diseases less likely to be funded than applications on more common conditions? Why?

Methods

- Identified projects focused on rare disease
  - Submitted to broad PFAs
  - Cycles III (March 2013) through Spring 2014 (May 2014)
- Among those focused on rare diseases vs. all others
  - Compared the number received, discussed and funded
  - Compared criteria and overall scores

Applications Reviewed, Discussed and Funded

	Applications on Rare Disease			Applications on other conditions		
	Reviewed	**Discussed**	**Funded**	**Reviewed**	**Discussed**	**Funded**
Cycle III	14	10	4	395	170	48
August 2013	8	3	0	373	161	34
Winter 2014	9	7	2	266	130	21
Spring 2014	13	10	3	349	174	21
TOTAL	**44**	**30**	**9**	**1383**	**635**	**124**

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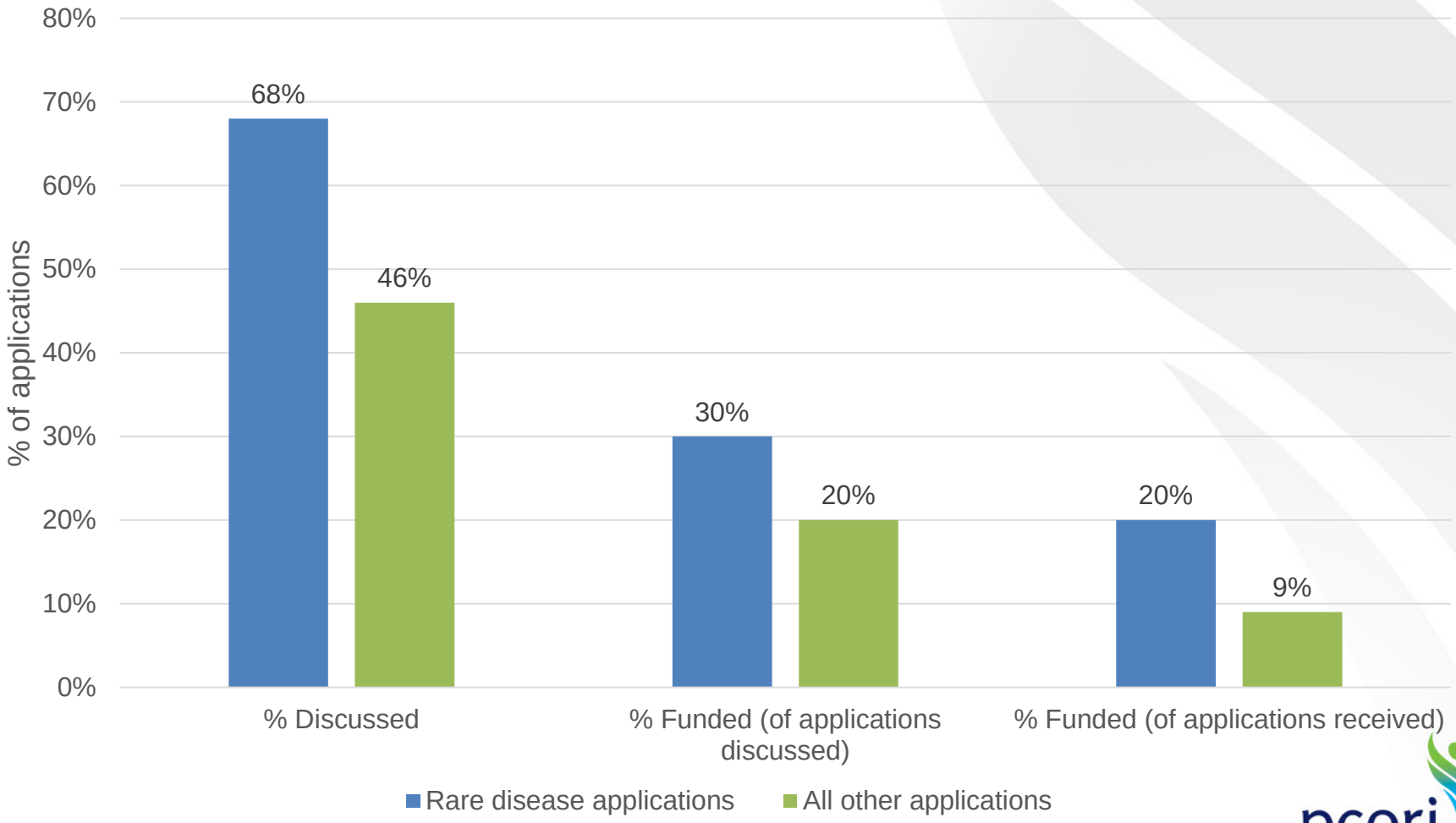
Likelihood of Discussion and Funding



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Average Preliminary Review Scores by Reviewer Type

	Scientist		Patient		Stakeholder	
	Rare disease	All other	Rare disease	All other	Rare disease	All other
Overall	4.5	5.0	3.7	4.2	4.0	4.3
Criterion 1	2.6	2.8	--	--	--	--
Criterion 2	4.1	4.4	**3.0 ***	**3.8 ***	3.5	3.9
Criterion 3	4.8	5.1	--	--	--	--
Criterion 4	3.4	3.8	**2.8 ***	**3.7 ***	3.3	3.8
Criterion 5	**3.2 ***	**4.1 ***	3.8	4.0	3.7	4.1

**p<0.05, statistically significant difference between applications on rare disease and all other applications*

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Average Final Overall Scores by Reviewer Type

Overall		Scientist		Patient		Stakeholder	
Rare disease	All other	Rare disease	All other	Rare disease	All other	Rare disease	All other
4.6 [1.7]	4.6 [1.6]	4.7 [1.8]	4.7 [1.7]	4.4 [1.6]	4.4 [1.6]	4.7 [1.6]	4.5 [1.6]

Note: Mean [standard deviation]

Summary

- PCORI receives a limited number of applications on rare diseases
- Applications on rare diseases are more likely to be discussed and funded than other applications
- Applications on rare diseases score as well or better than other applications

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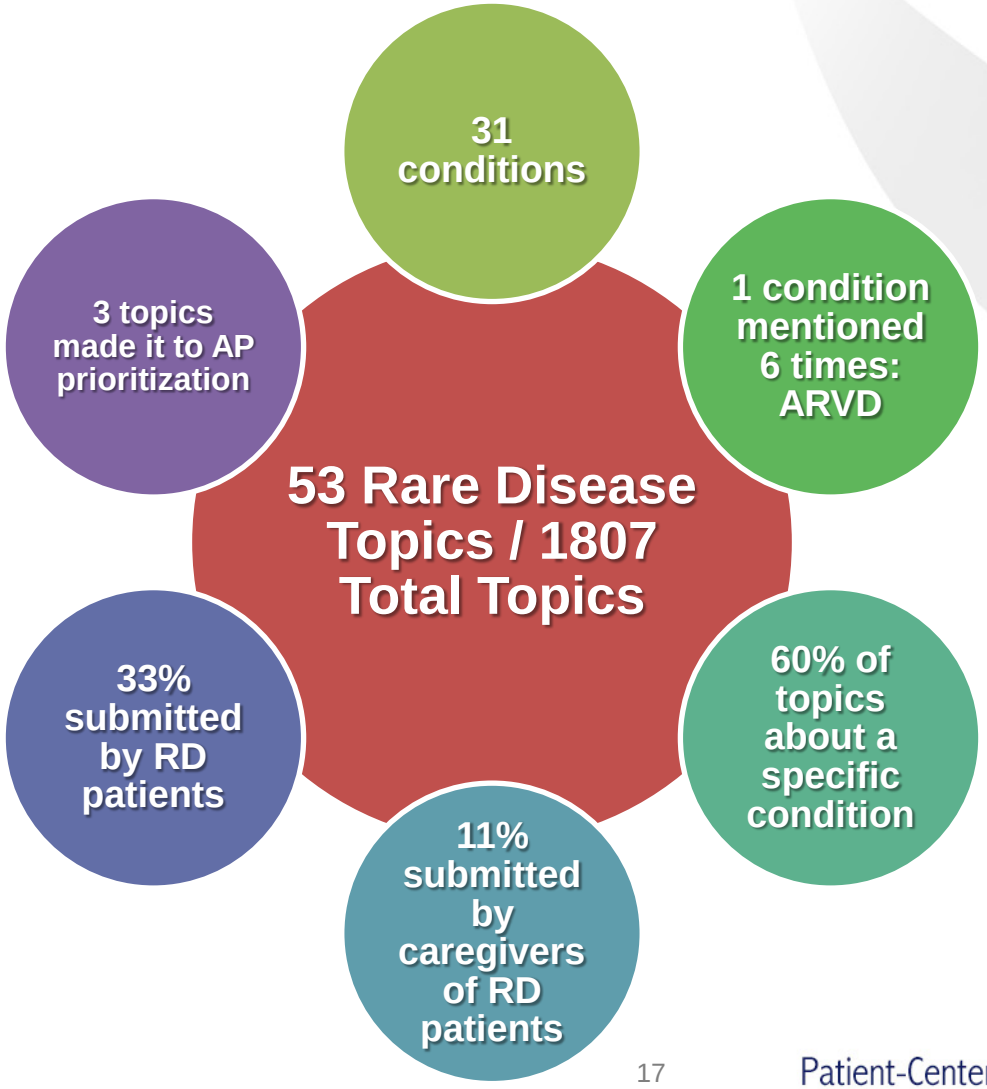
Summary of Submitted RD Topics



Discussion

- What are your reactions to the findings?
- What are the best action steps for facilitating funding of applications on rare diseases, given these findings?

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Break

10:45 – 11:00 a.m. EST

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Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options
Topic Prioritization

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Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options Topic Prioritization

- **Topic:** "Genetic Testing for Rare Diseases: Compare the effectiveness of genetic testing for select rare diseases in terms of patient care, treatment choices, and relevant clinical and patient-centered outcomes."
- **Topic Experts:**
  - Marshall L. Summar, MD, Chair, Advisory Panel on Rare Disease, PCORI
  - Uday Deshmukh, Member, Advisory Panel on Rare Disease, PCORI

Lunch

12:30 – 1:30 p.m. EST

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Clinical Trials in Rare Diseases: *Starting from Scratch, Even with Limited Resources*

Jason Connor, PhD
Member, Advisory Panel on Clinical Trials
Director and Senior Statistical Scientist, Berry Consultants

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Motivation

- Dying people don't have time or energy. We can't keep doing this one woman, one drug, one company at a time. Gracia Buffleben, Breast Cancer Advocate
- The tyranny of mathematics shouldn’t overwhelm the medical community’s ethical obligations about what’s best for the patient. Richard Royall, Emeritus Prof. John Hopkins
- No obstacle is insurmountable when our hearts are in the right place. Jenny Bowen, Half the Sky
- People think we’re unrealistic; they don’t know we’re crazy. Jim Kim, Partners in Health

Quiz

- Why were standard statistical methods invented?
- Who invented them?

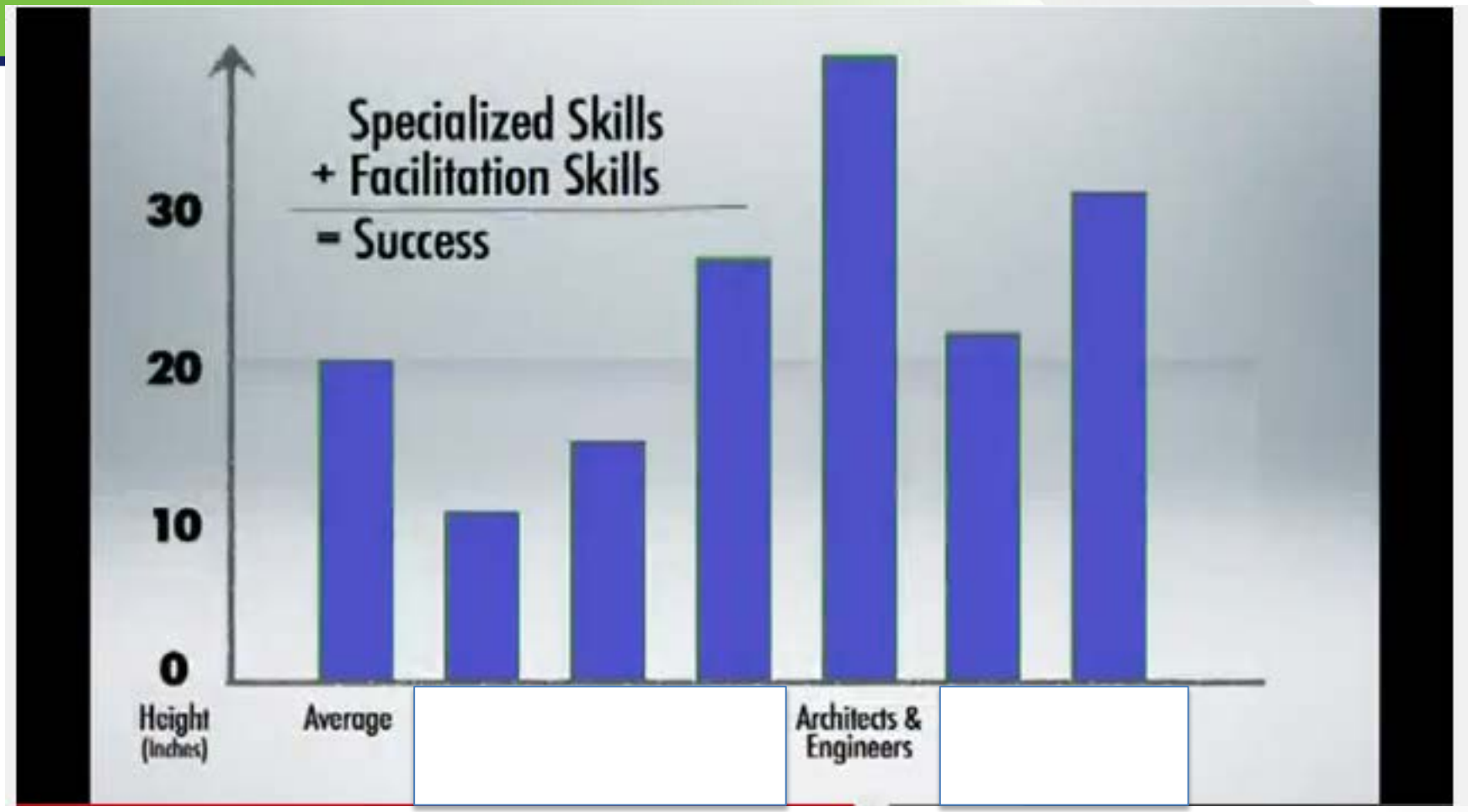
The Marshmallow Design Challenge

The Marshmallow Design Challenge
Peter Skillman

- 4-person team
- 18 minutes
- 20 pieces of raw spaghetti
- 1 meter of tape
- 1 meter of string
- 1 marshmallow

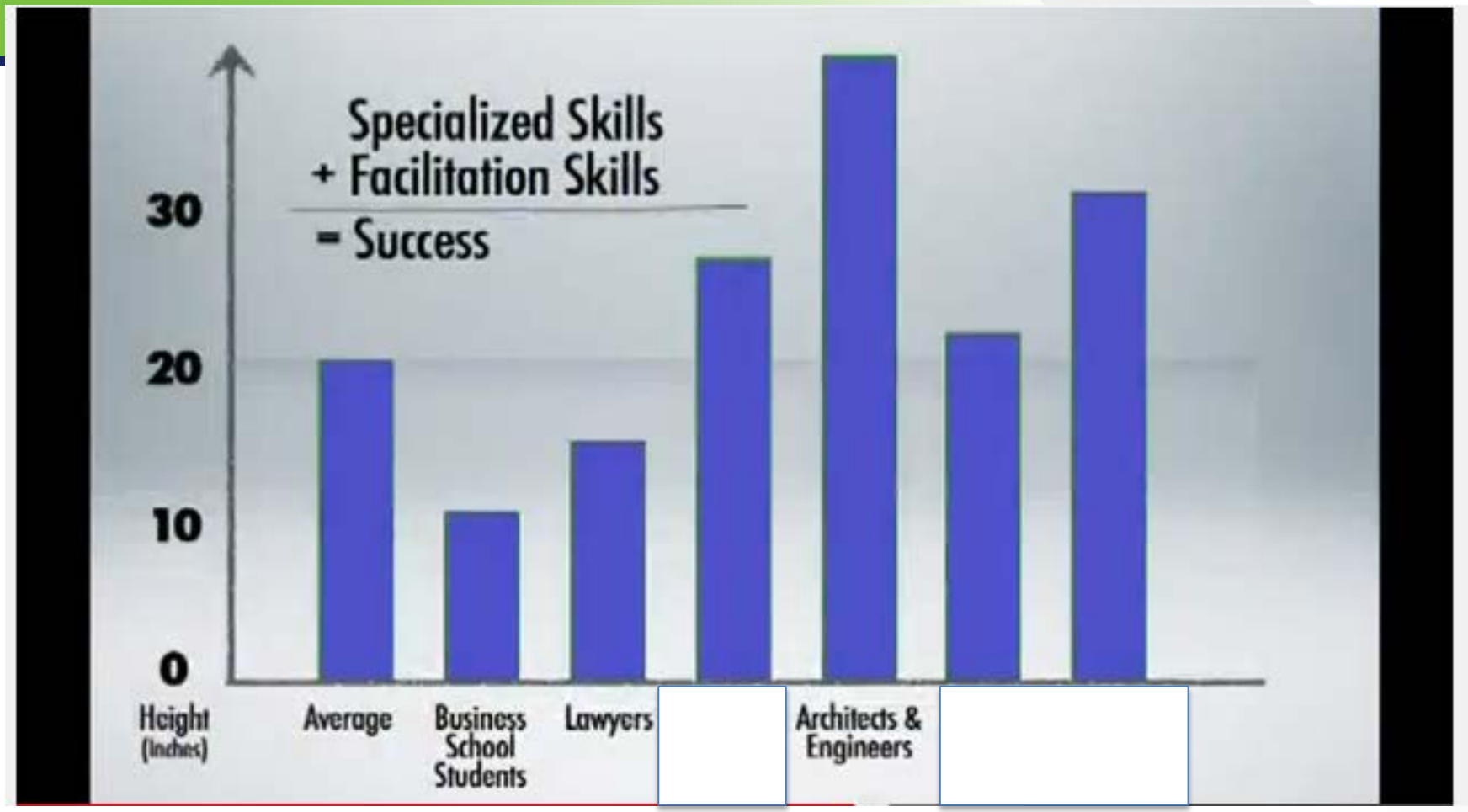
Peter Skillman Marshmallow Design Challenge
https://www.youtube.com/watch?v=1p5sBzMtB3Q

The Marshmallow Design Challenge



Tom Wujec: Build a tower, build a team.
https://www.youtube.com/watch?v=H0_yKBitO8M

The Marshmallow Design Challenge



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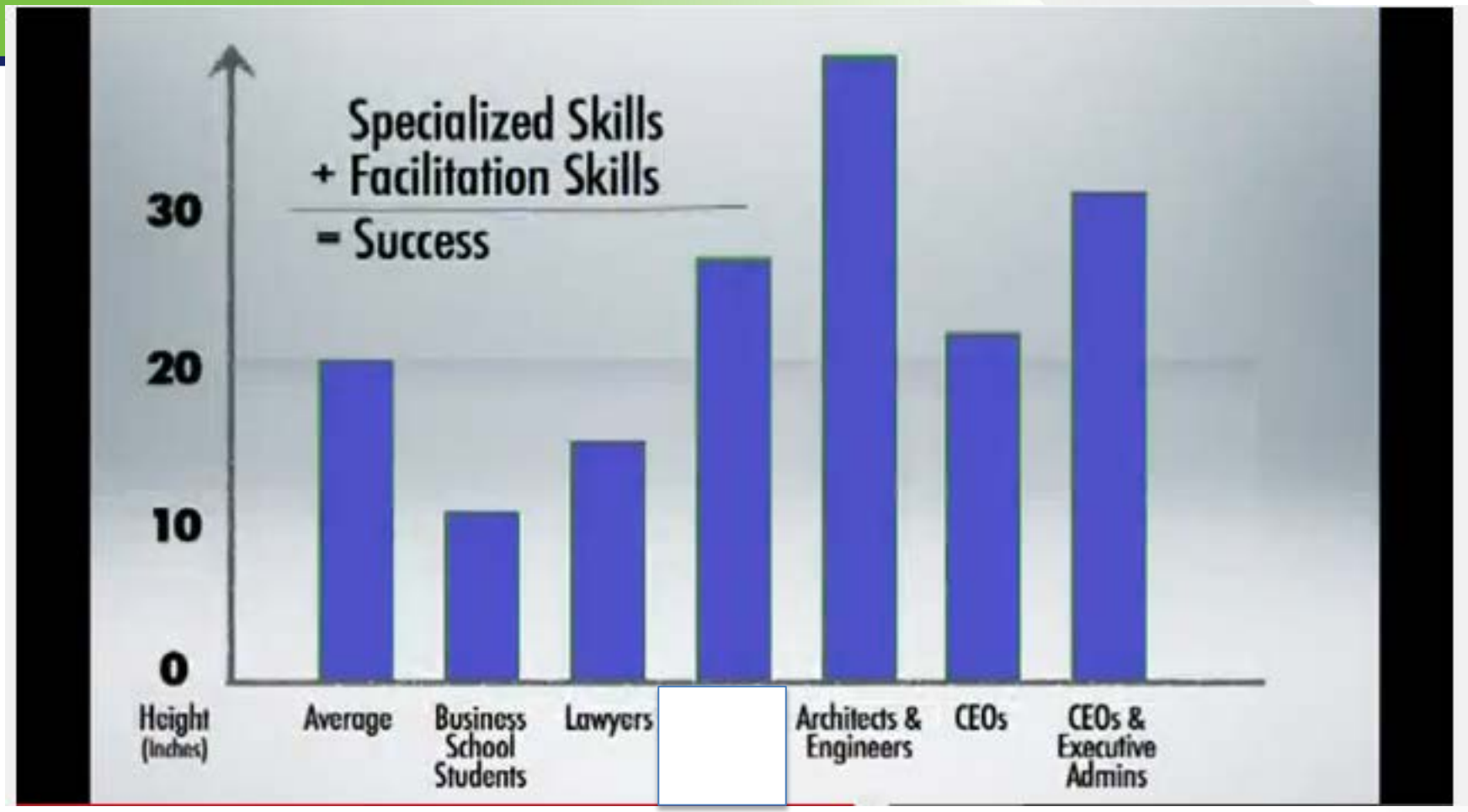

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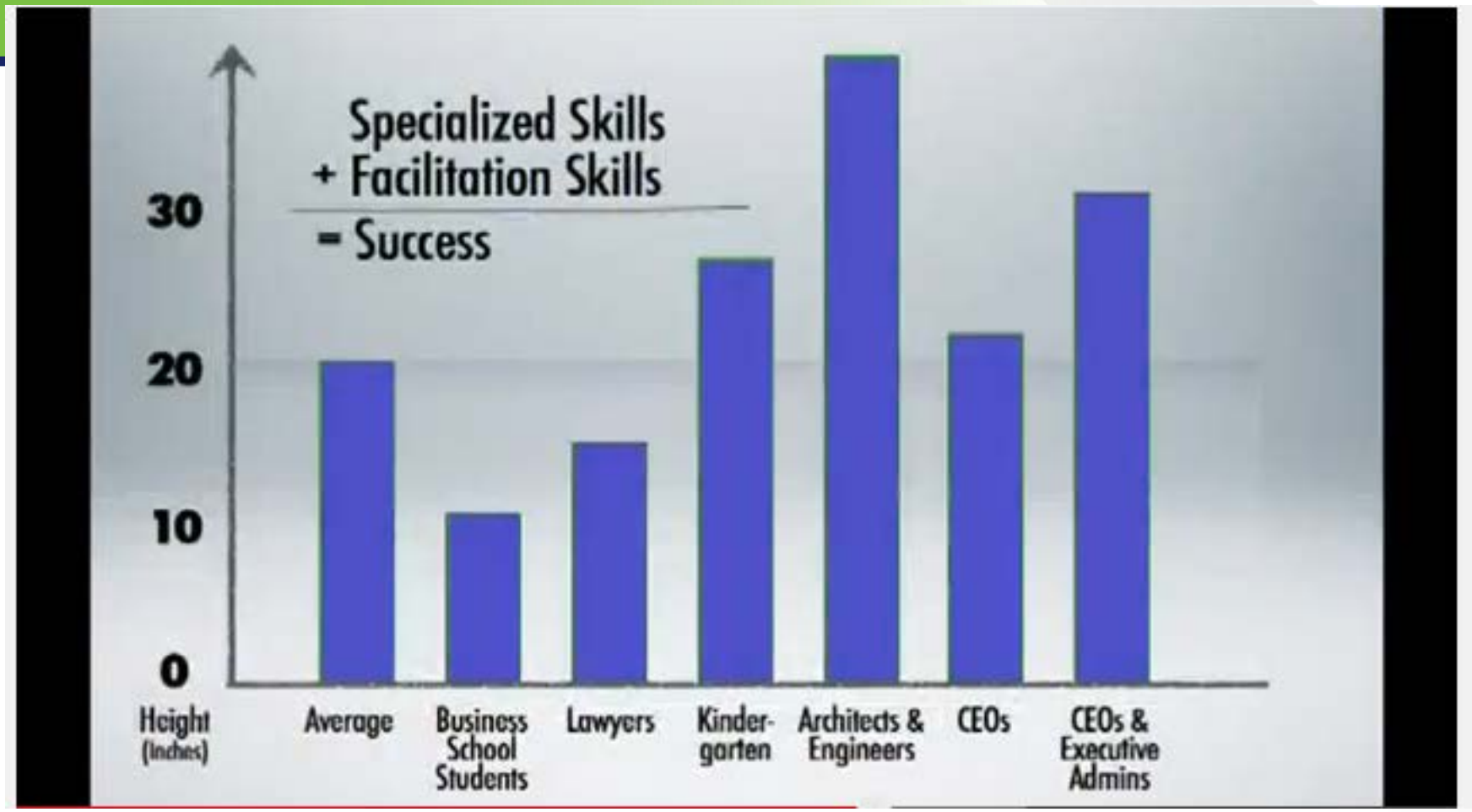

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The Marshmallow Design Challenge
Peter Skillman

- Kindergarteners
  - Don’t waste time seeking power
  - Don’t sit around talking about the problem
  - Try, fail, try, fail until time runs out
  - Grab stuff and try things
  - Usually keep the marshmallow on top when trying

- MBA grads
  - Spend a lot of time talking
  - Are trained to find the single best plan
  - Are trained never to fail
  - Put the marshmallow on top last
    (and often watch the whole tower collapse)

The Marshmallow Design Challenge
Peter Skillman

- You learn by doing
- Work in parallel
- Being first to market is usually bad
- Doing multiple iterations is good
- All projects have resource constraints

Marshmallow Design Challenge → Rare Disease Trials

- You learn by doing.
- Work in parallel.
- Being first to mar[illegible].
- Doing m[illegible] good.
- A[illegible] resource constraints.

Can We Do Rare Disease Trials by Trial & Error?

Marshmallow Design Challenge → Rare Disease Trials

- You learn by doing.
- Work in parallel.
- Being fir
- D
- A constraints.

Can We Do Rare Disease Trials by Trial & Error?

Absolutely !!!!!!!!!!

Example: ECMO Trial

- Extracorporeal membrane oxygenation
- Oxygenates babies' blood and gives underdeveloped lungs and heart time to heal or grow
- Historical survival rates = < 25%
- Michigan trial: Randomized play-the-winner strategy
  - Bartlett, *Pediatrics*, 1985, 76: 479~487

ECMO Trial: Randomization Rules

- Randomize first patient 1:1 to treatment
- If survives on treatment t, add 1 “t-colored” ball
- If dies on treatment t, add 1 other-colored ball
- Treat 10 patients this way

- Expected number patients treated with better treatment > 5, “ethical”

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50				

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO			

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived		

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived	1	2

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived	1	2
2	0.67				

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived	1	2
2	0.67	CMT	Died	1	3

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived	1	2
2	0.67	CMT	Died	1	3
3	0.75				

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived	1	2
2	0.67	CMT	Died	1	3
3	0.75	ECMO	Lived	1	4
4	0.80				

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived	1	2
2	0.67	CMT	Died	1	3
3	0.75	ECMO	Lived	1	4
4	0.80	ECMO	Lived	1	5
5	0.83				

ECMO Trial: Results

	Prob to ECMO	TRT	Result	Balls in Urn CMT	Balls in Urn ECMO
Start				1	1
1	0.50	ECMO	Lived	1	2
2	0.67	CMT	Died	1	3
3	0.75	ECMO	Lived	1	4
4	0.80	ECMO	Lived	1	5
5	0.83	ECMO	Lived	1	6
6	0.86	ECMO	Lived	1	7
7	0.88	ECMO	Lived	1	8
8	0.89	ECMO	Lived	1	9
9	0.90	ECMO	Lived	1	10
10	0.91	ECMO	Lived	1	11

ECMO Trial: Interpretation

- ECMO 9/9 CMT 0/1*
- * The 1 on CMT was the sickest of all patients
- As a statistician or a policymaker, do we have sufficient information to declare ECMO efficacious?

ECMO Trial: Interpretation

- ECMO 9/9 CMT 0/1*
- * The 1 on CMT was the sickest of all patients
- As a statistician or a policymaker, do we have sufficient information to declare ECMO efficacious?
- As a parent, would you dare *not* request ECMO for your premature baby?

ECMO Trial: Lessons

- Questions the trials designers should have asked before the trial:
  - How do we calculate a p-value?
  - Published p-values for this data

0.00049	0.051
0.001	0.083[F]
0.003	0.280
0.009	0.500
0.038	0.617
0.045	1.000
undefined	

  - *Statistical Science*, Nov 1989

ECMO Trial: Lessons

- Questions the trials designers should have asked before the trial:
  - How do we calculate a p-value?
  - Will the medical community believe our results?
  - Will we have enough data to sway opinions of people with a wide range of prior beliefs?
  - What are trial results likely to look like?
  - What if everyone is randomized to ECMO?
  - If CMT success = 30% and ECMO success = 90%
  - 6% chance all 10 patients will be randomized to ECMO

ECMO: Follow-up Trial

- Harvard Trial
  - Stage 1: randomize equally until 4 deaths in one arm
  - Stage 2: assign all to other arm until 4 deaths or stat sig.
  - 6/10 conventional therapy (60%)
  - 9/9 on ECMO (100%)
  - Then 19/20 on ECMO (97%)
  - *Pediatrics*, 1989, 84: 957-963
- Was this study design ethical?
- Do we have an irrational commitment to blinded RCTs?
- Do we have an irrational commitment to $p<0.05$?
- Does lack of $p<0.05$ mean equipoise until we see $p<0.05$?

ECMO: Trial & Error Design by Simulation

```
p.ecmo <- 0.75;      p.cmt <- 0.25

group.vec <- NULL;    outcome.vec <- NULL
outcome <- matrix(nrow=100000, ncol=5)

for(s in 1:100000){
urn <- c(1,1)
for(pt in 1:10){
  group <- sample(c("C","E"), 1, prob=urn)
  result <- rbinom(1, 1, ifelse(group=="C",p.cmt, p.ecmo))
  if(group=="C"){
     if(result==1){
        urn[1] <- urn[1] + 1
     }else{
        urn[2] <- urn[2] + 1
     }
  }else{
     if(result==1){
        urn[2] <- urn[2] + 1
     }else{
        urn[1] <- urn[1] + 1
     }
}
group.vec[pt] <- group
outcome.vec[pt] <- result
}
tab <- table(factor(group.vec, levels=c("C","E")), factor(outcome.vec, levels=0:1))
outcome[s,] <- c(c(tab), fisher.test(tab, alternative='greater')$p.value)
print(s)
}
```

ECMO: Prospective Simulation

Operating Characteristics	CMT 25% ECMO 75%	CMT 25% ECMO 25%
Pr(All patients randomized to ECMO)	2.5%	0.04%
Pr(All patients randomized to CMT)	0.04%	0.04%
Pr(Majority to ECMO)	72%	36%
Pr(5 ECMO & 5 CMT)	14%	27%
Pr(Majority to CMT)	14%	36%
Pr(P-value < 5%)	12%	0.1%
Pr(# ECMO success > # CMT success)	89%	38%
Pr(# ECMO success ≥ # CMT success + 4)	59%	2.7%

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Power

Type I error

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Power

Type I error

ECMO Iterate Design

N	Decision Rule # ECMO Successes vs. # CMT Successes	Power when ECMO 75% CMT 25%	Type I error ECMO 25% CMT 25%
10	4 or more	59%	2.7%
10	3 or more	72%	8.1%

ECMO Iterate Design

N	Decision Rule # ECMO Successes vs. # CMT Successes	Power when ECMO 75% CMT 25%	Type I error ECMO 25% CMT 25%
10	4 or more	59%	2.7%
10	3 or more	72%	8.1%
15	4 or more	79%	5.9%
15	5 or more	71%	2.3%

ECMO Iterate Design

N	Decision Rule # ECMO Successes vs. # CMT Successes	Power when ECMO 75% CMT 25%	Type I error ECMO 25% CMT 25%
10	4 or more	59%	2.7%
10	3 or more	72%	8.1%
15	4 or more	79%	5.9%
15	5 or more	71%	2.3%
18	5 or more	80%	3.5%

ECMO Iterate Design

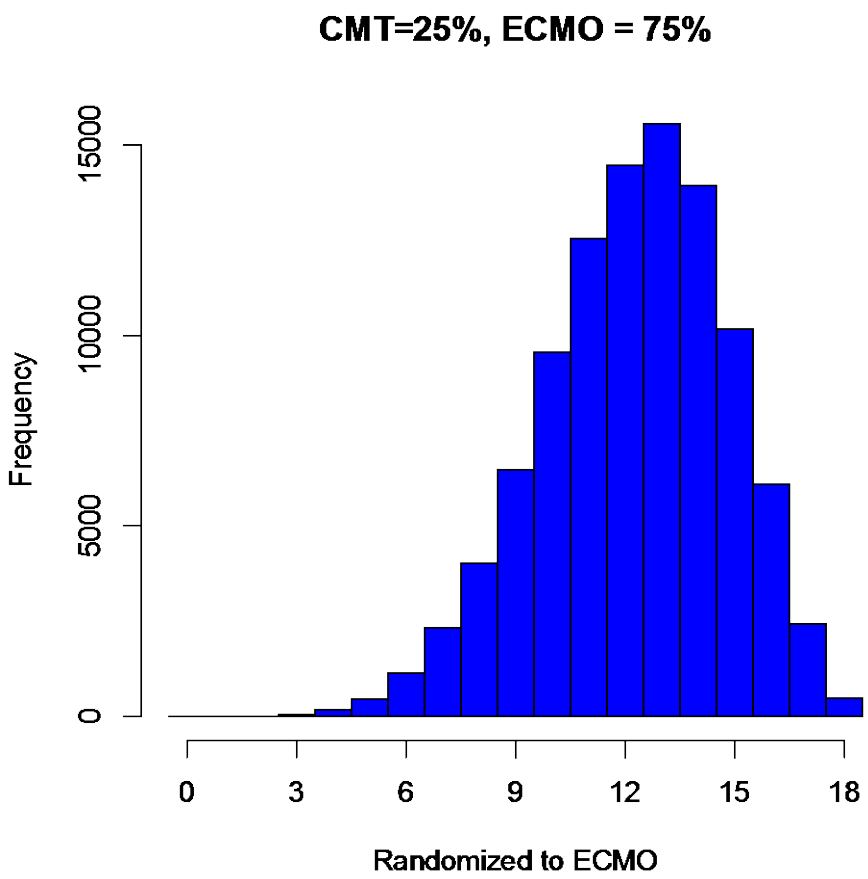
N	Decision Rule ECMO v CMT	Power 75v25	ECMO S/N	CMT S/N	T1error 25v25	ECMO S/N	CMT S/N
10	4 or more	59%	4.9 / 6.5	0.9 / 3.5	2.7%	1.25 / 5	1.25 / 5
10	3 or more	72%			8.1%		
↓	8 more patients		5.7 more ↓	2.3 more ↓		4 more ↓	4 more ↓
18	5 or more	80%	9.2 / 12.2	1.4 / 5.8	3.5%	2.25 / 9	2.25 / 9

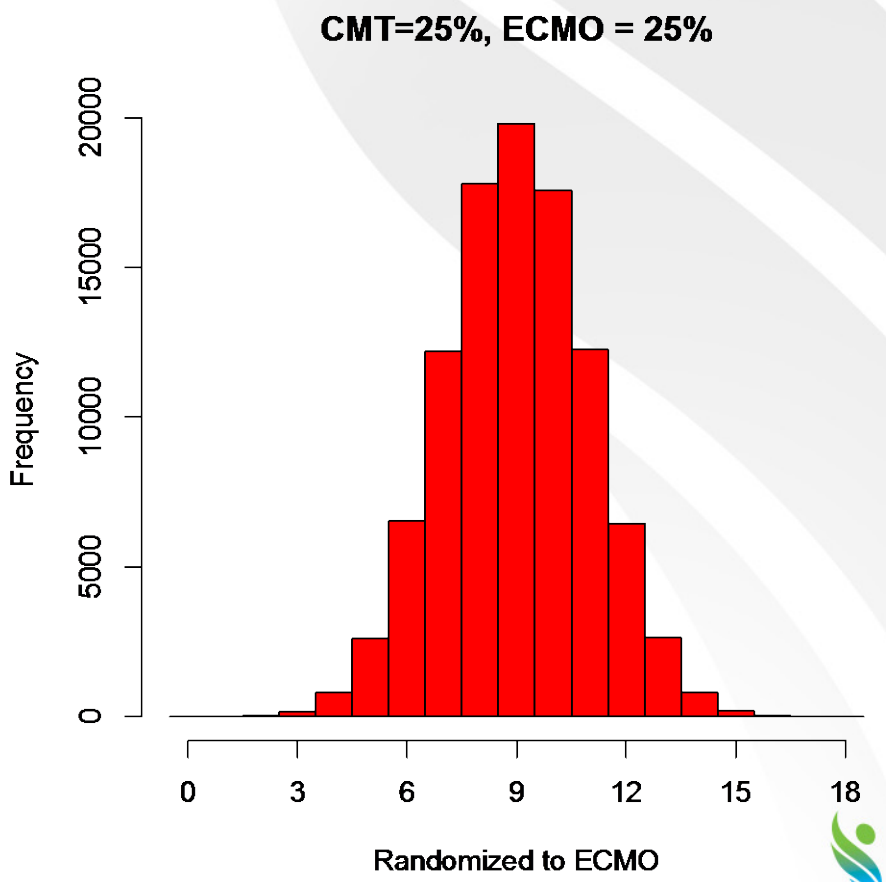
ECMO Iterate Design

N	Decision Rule ECMO v CMT	Power 75v25	ECMO S/N	CMT S/N	T1error 25v25	ECMO S/N	CMT S/N
10	4 or more	59%	4.9 / 6.5	0.9 / 3.5	2.7%	1.25 / 5	1.25 / 5
10	3 or more	72%			8.1%		
↓	8 more patients		5.7 more ↓	2.3 more ↓		4 more ↓	4 more ↓
18	5 or more	80%	9.2 / 12.2	1.4 / 5.8	3.5%	2.25 / 9	2.25 / 9

Standard trial with 18 patients has 58% power, 4.8% Type I error & always randomized half to CMT

ECMO with 18 Patients





In Summary I Believe We Should

Disclaimer: I am not a regulator or a payer; I'm not speaking for PCORI or Berry Consultants.

- Remember that current trialists were trained by people who were trained by people who had seeds as patients.
- Remember most statistical methodology is based on asymptotic theory.
- Remember most statistical methods are 'one size fits all' and don't fit well in our new world of personalized medicine
- Hire smart quantitative people with their heart in the right place.
  - People without bad habits; people who don't put dogma over decency
- Balance treating the next patient optimally with producing valuable long-term evidence.
  - This is in no way a part of current, 'accepted' statistical methodology
- Think much harder about tailoring a solution to each unique problem.
- Never have the first time we run a trial be the actual time we run the trial. Simulate trials under every possible scenario, iterate designs with doctors, patients, payers, regulators and other stake holders.

Take-Home Message

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We do research & clinical trials in hopes of eventually treating patients better.

So why not do clinical trials that treat patients better?

Ad Hoc Advisory Panels on Rare Disease

Bryan Luce, PhD, MBA
Chief Science Officer, PCORI
Emma Djabali
Project Assistant, Office of the Chief Science Officer, PCORI

Patient-Centered Outcomes Research Institute

What Does the Legislation Say?

- EXPERT ADVISORY PANEL FOR RARE DISEASE —

In the case of a research study for rare disease, the Institute shall appoint an expert advisory panel for purposes of assisting in the design of the research study and determining the relative value and feasibility of conducting the research study.

Same for CTAP:

- EXPERT ADVISORY PANELS FOR CLINICAL TRIALS —

The Institute shall appoint expert advisory panels in carrying out randomized clinical trials under the research project agenda under paragraph (2)(A)(ii). Such expert advisory panels shall advise the Institute and the agency, instrumentality, or entity conducting the research on the research question involved and the research design or protocol, including important patient subgroups and other parameters of the research. Such panels shall be available as a resource for technical questions that may arise during the conduct of such research.

What Does the Charter Say?

In the case of a research study for each rare disease, the RDAP shall assist PCORI in identifying experts to serve on a condition-specific ad hoc advisory panel to assist in:

- Evaluating
- Designing
- Conducting
- Determining the relative value and feasibility of conducting the research study

The chair of the RD panel will appoint:

- Members from the RDAP
- Other individuals with appropriate expertise in the rare disease to be studied

Charter of the Advisory Panel on Rare Disease – Approved by PCORI Board of Governors – November 18, 2013

How Is the CTAP Implementing the Mandate?

- Creation of trial-specific subcommittees for three large PCORI funded clinical trials:
  - Two Obesity Trials
  - PCORnet's Aspirin Trial
- These trial-specific subcommittees will report back to the CTAP's three overarching subcommittees and to the full CTAP to inform their broad guidance to PCORI.

Process and Management of CTAP Trial-Specific Subcommittees

- **Communication:** All communication between the CTAP subcommittee and the investigators of a project will go through program staff.

- **Nature of Advice:** Each Science Program will determine what the guidance needs are. The nature of advice solicited from the CTAP subcommittee could include, but is not limited to, issues associated with:
  - Statistical inference
  - Confounding
  - Complex methods
  - 'Usual care'
  - Sample size power
  - Alignment of trial components for cross-study analyses
  - Recruitment, accrual, and retention
  - Patient engagement
  - Review of DSMB reports

- **Member Selection:** To select subcommittee members, program staff are encouraged to ask the CTAP as well as other PCORI staff for recommendations.

Members

- The CTAP will infuse continuity by inviting the **merit reviewers**, and adding CTAP members and/or external experts as appropriate to form CTAP trial-specific subcommittees

Pre-Meeting Survey Results

- What type of assistance do you think the ad hoc panels should provide?
  - Specific RD expertise:
    - Issues relevant to specific RD research questions and clinical issues
    - Design of studies in specific populations
  - Pre-award:
    - Consultation during initial Advisory Panel prioritization
    - Merit review recommendations
  - Post-award:
    - Supporting staff in ongoing rare disease research issues
    - Developing methods that take into account outcomes meaningful to patients
    - Providing guidance based on sample size, known prevalence and incidence working with small or unknown patient population
    - Assisting researchers in accessing patients and raise research issues
    - Helping to disseminate findings
    - Providing oversight for consistency of projects to completion

Pre-Meeting Survey Results

- Should the focus of this assistance be pre- or post-award? Please explain.
  - 100% for both!
  - Examples of explanations:
    - Pre-award involvement can provide insight to help improve applications, including study design and topic review
    - Post-award involvement can help to sharpen applications to ensure success and guide ongoing study concerns, recruitment issues and other common pitfalls in rare disease research.

Pre-Meeting Survey Results

- Should we form one ad hoc panel per rare disease project or group them together? If grouped, then how?
  - 7/9 responded “Multiple studies --> One ad hoc advisory panel”
  - Grouping options:
    - Subspecialties, or adult vs pediatric
    - Research form
    - Therapeutic areas, say broadly, oncology, immunology, cardiovascular, etc., with some having more than one subgroup
    - Pathophysiological pathways
    - Case by case basis
  - How many members should each ad hoc advisory panels have?
    - Average: 6

Pre-Meeting Survey Results

- How often should the ad hoc advisory panels report back to the full RDAP?
  - Each RDAP meeting – 4 responses
  - Once every two RDAP meetings – 1 response
  - Once a year – 2 responses
- What should be the content of the ad hoc advisory panels' reports to the full RDAP?
  - Pre-award:
    - High level of grants considered and results of review and awards and follow up
  - Post-award:
    - Aim of research
    - Type of assistance that was sought
    - Develop best practices across the ad hoc panels
    - Lessons learned in research design
    - Review or CER evaluation for RD

Pre-Meeting Survey Results

- Other Comments:
  - The aim should be to have few ad hoc panels to address shared issues in rare disease research.
  - These panels should not be a barrier or burden to applicants and researchers, but an assistance.
  - Create a process that is consultative and supportive.
  - Continue to learn from the process and modify as needed.

Break

3:15 – 3:30 p.m. EST

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Update about Collaboration with CTAP

Bryan Luce, PhD, MBA
Chief Science Officer, PCORI

Patient-Centered Outcomes Research Institute

Existing Collaboration

- Dinner on October 6, 2014 – Discussion points:
  - Lack of data – No need for different standards of evidence, but instead need for specific ways of interpreting different types of evidence.
  - Ways of improving patient engagement (e.g., shorter consent forms)
  - Decision of simulation analysis
  - Focus on most important outcomes (cross-cutting?)
- Jason Connor's presentation to full RDAP on January 13: Clinical Trials in Rare Diseases: Starting from Scratch Even with Limited Resources
  - Report back to CTAP the next day with Marshall Summar

Future Collaboration

- CTAP Subcommittee on Recruitment, Accrual, and Retention (RAR) to
  - Inform PFAs and related review criteria;
  - Guide PCORI monitoring of funded contracts by providing technical assistance and support; and
  - Provide additional direction regarding the engagement of healthcare stakeholders around recruitment, accrual, and retention.
- Commitment:
  - Reviewing materials (including funded award proposals)
  - Participating in up to three teleconferences a year
  - Sign a non-disclosure agreement

  →Appropriate stipend

- Volunteers? One RDAP representative preferred

Future Collaboration (cont.)

- Joint subcommittees/ad hoc advisory panels to provide technical assistance to rare disease clinical trials?
- CTAP to help RDAP produce guidance on how to perform rare disease research once the landscape review is performed?

SOW of Landscape Review

- Rare disease registry standards/guidance
- Rare disease minimal datasets; rare disease data standards
- Rare disease bio specimen collection standards/guidance
- Guidance on the type of evidence and standards needed when new treatments are introduced to the rare disease world
- Evidence grading systems for rare disease research

Compensating Patient Partners in Research

Suzanne Schrandt, JD

Deputy Director, Patient Engagement, PCORI

Patient-Centered Outcomes Research Institute

Activity to Date

- Engagement Rubric
- Application Guidance
- Engagement Officers
- PCORI Pilot Projects
- Patient Engagement Advisory Panel Subcommittee on Compensation Draft Framework on Compensation

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The Engagement Rubric

The rubric is intended to provide guidance to applicants, merit reviewers, awardees, and engagement/program officers (for creating milestones and monitoring projects) regarding patient and stakeholder engagement in the conduct of research. It is divided into four segments:

Planning the Study

Conducting the Study

Disseminating the Study Results

PCOR Engagement Principles

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Engagement Principles

4. PCOR ENGAGEMENT PRINCIPLES:

Reciprocal Relationships: *Describe the roles and decision-making authority of all research partners, including patient an*

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- Reciprocal Relationships
- Co-learning
- Partnership
- Trust
- Transparency
- Honesty

Examples of how to demonstrate this in your proposal:

- Compensation for patient partners is included in the budget at an appropriate level.
- Meetings are held at a time and in a location that that accommodates patient and stakeholder partners. Compensation is provided for transportation and related expenses.
- Accommodations are made to encourage the full engagement of a diversity of patient and stakeholder partners, and the research team includes a diversity of members. For example, a

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Engagement Principles

4. PCOR ENGAGEMENT PRINCIPLES:

Reciprocal Relationships: *Describe the roles and decision-making authority of all research partners, including patient and stakeholder partners.*

Examples of how to demonstrate this in your proposal:

- Explain how decision-making is made within your research team, including the decision-making authority that patient and stakeholder partners have and in what circumstances

Partnership;

- *Describe how the time and contributions of patient partners are valued and demonstrated in fair financial compensation, as well as reasonable and thoughtful time commitment requests*

communication with patients, led by patient instructors).

Partnership: *Describe how the time and contributions of patient partners are valued and demonstrated in fair financial compensation, as well as reasonable and thoughtful time commitment requests.*

Examples of how to demonstrate this in your proposal:

- Compensation for patient partners is included in the budget at an appropriate level.
- Meetings are held at a time and in a location that that accommodates patient and stakeholder partners. Compensation is provided for transportation and related expenses.
- Accommodations are made to encourage the full engagement of a diversity of patient and stakeholder partners, and the research team includes a diversity of members. For example, a

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Engagement Principles

Real World Examples;

- *Compensation for patient partners is included in the budget at an appropriate level.*
- *Meetings are held at a time and in a location that that accommodates patient and stakeholder partners. Compensation is provided for transportation and related expenses.*
- *Training and educational opportunities are provided, for patient and stakeholder partners such as training in human subjects protection.*
- *Training is provided for researchers such as instruction in better communication with patients, led by patient instructors.*

- Accommodations are made to encourage the full engagement of a diversity of patient and stakeholder partners, and the research team includes a diversity of members. For example, a

Guidance: Applicant FAQs

How much compensation should we provide patient partners? Can there be different levels of compensation?

PCORI does not specify the compensation for patient partners or other team members. According to the Engagement Rubric, "Time and contributions of patient partners are valued and demonstrated in fair financial compensation, as well as reasonable and thoughtful time-commitment requests." It is very important that the patient partners' contributions be valued as highly as contributions from other team members. Because compensation can take many forms, you may want to ask your patient partners what they regard as equitable. For example, patient partner compensation may be included in the budget at market rates for consultants. Each project is different, and patients may receive different levels of compensation—particularly when they are providing different levels of input.

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Guidance: PFAs and Application Guidelines

Personnel Costs: In addition to noting the base salary for each scientific/technical staff, you must note the base salary for each employee patient or stakeholder partner of your research team, if these members are not accounted in Section B: Consultant Costs.

Consultant costs apply to those individuals who will dedicate time to the project neither as an employee of the applicant organization nor under a subcontract agreement as a member of contracted staff. Payments to non-employee patient and stakeholder representatives should be included.

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Engagement Officers

- Milestone negotation
- Kick-off and interim calls
- Other conversations and guidance

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Patient Engagement Advisory Panel

- Subcommittee on compensation
- Draft compensation framework

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Discussion

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Recap and Next Steps

Bryan Luce, PhD, MBA
Chief Science Officer, PCORI

Marshall L. Summar, MD

Chair, Advisory Panel on Rare Disease, PCORI

Patient-Centered Outcomes Research Institute

Adjourn

Thank you for your participation!