



# Building and leveraging a multicenter registry

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Happy  
Birthday  
Kate!



# Disclosures

- Funding: PCORI, NIH, PERF, University of Michigan
- Honoraria: UpToDate
- Consultant: The Epilepsy Study Consortium
- Associate Editor: *Neurology*
- Board Member: *Pediatric Epilepsy Research Foundation (as of 7/1/21)*

Funding for  
the  
*Neonatal  
Seizure  
Registry:*



National Institute of  
Neurological Disorders  
and Stroke

## A word of caution

- NIH does not fund registries.
- The *NSR* name may become problematic.
- Don't use "registry" in your group name.



# Why are we here?

- PERC values collegial, collaborative, practice-changing research.
- What better way is there to do this than through multicenter data collection for [rare] diseases?
- Practice-changing research should ask questions people care about and answer those questions with rigor and efficiency.



*NSR shares these values.*

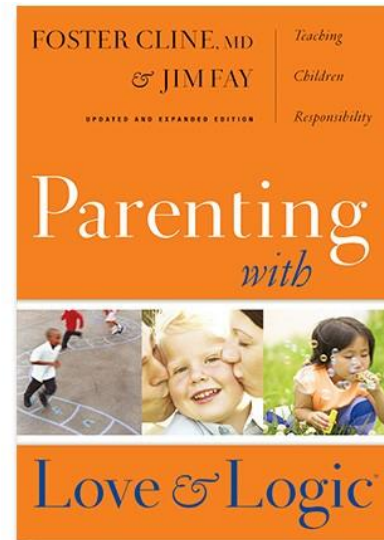
Lesson  
#1A:  
Research is  
a team  
sport.



<https://www.greatstate.co/blog/articles/user-research-as-a-team-sport---how-do-you-enable-your-team-to-play>

Lesson  
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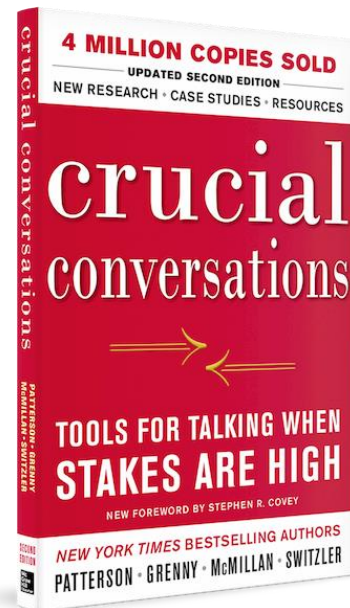
- Consider leadership training.
- If that isn't immediately available, draw on parenting skills.





Lesson  
#1A:  
Research is  
a team  
sport.

- Consider leadership training.
- Or read Crucial Conversations and/or Crucial Confrontations



Lesson #1B:  
You need to  
find your  
people.

FIND A  
GROUP OF PEOPLE WHO  
CHALLENGE AND INSPIRE YOU,  
SPEND A LOT OF TIME WITH THEM,  
AND IT WILL CHANGE  
YOUR LIFE.

AMY POELHER



Lesson #1B:  
You need to  
find your  
people.



# EEG Monitoring = for diagnosis.

- Most seizures in newborns are subclinical.
- Most unusual movements are not seizures.

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## ACNS GUIDELINE

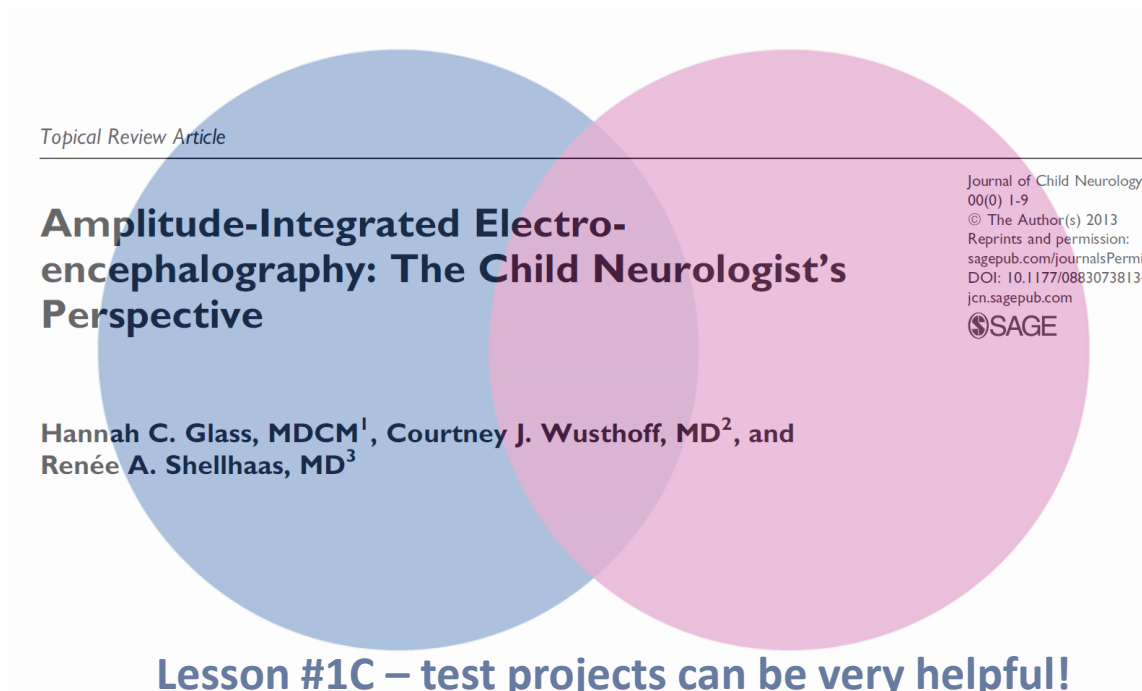
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### The American Clinical Neurophysiology Society's Guideline on Continuous Electroencephalography Monitoring in Neonates

Renée A. Shellhaas,\* Taeun Chang,† Tammy Tsuchida,† Mark S. Scher,‡ James J. Riviello,§ Nicholas S. Abend,||  
Sylvie Nguyen,¶ Courtney J. Wusthoff,# and Robert R. Clancy||

# At the same time...

- Hannah Glass & Janet Soul were working with (many others) on developing the Neonatal Seizure Treatment Trial group.





**C.S. MOTT  
CHILDREN'S HOSPITAL**  
MICHIGAN MEDICINE  
**Renée Shellhaas**



**UCSF Benioff Children's Hospital**  
San Francisco  
**Hannah Glass**



**Boston  
Children's  
Hospital**  
Until every child is well™  
**Janet Soul**



The Children's Hospital  
*of Philadelphia*®  
**Nicholas Abend**  
**Shavonne Massey**



**Children's  
National**™  
**Taeun Chang**



Cincinnati  
**Children's**™

**Cameron Thomas**



**Duke Children's**  
HOSPITAL & HEALTH CENTER  
**Monica Lemmon**



**Stanford**  
Children's Health | Lucile Packard  
Children's Hospital  
**Stanford**

**Courtney Wusthoff**



MassGeneral Hospital  
*for Children*  
**Catherine Chu**

Funding:  
PERF, PCORI, NIH

# Think about academic rank

All at the same stage = everyone hungry at the same time

Who are your senior advisers?

Who are your junior go-getters?

## Lesson #2 – start small



<https://clydestyle.org/2019/05/05/the-problem-with-low-hanging-fruit/>

**SIMPLE** questions are often the best.



# Lesson #3: Even simple projects need funding

- Focus on funded projects
- Or projects that are clearly designed to either:
  - Generate key preliminary data for a grant.
  - Generate a paper (not just an abstract) for a fellow or junior faculty member.



## Lesson #3: Even simple projects need funding

### **Be creative in your search for \$\$\$.**

- Department support for research coordinator
- Intramural awards
- Small resident/fellow grants (support your statistician)
- In kind resources (e.g. for statistics)
- Foundation grants
- Awards/grants from professional societies
- Ask your well-funded colleagues!
  - Ancillary study opportunities
  - Administrative supplements (e.g. designed to augment engagement and retention for scholars who come from URM)

# 1<sup>st</sup> funded project

- Enrolled EVERY baby with neonatal seizures at 7 excellent centers. – waiver of informed consent
  - Case Report Forms designed very carefully
    - Gather what we plan to analyze
    - Exclude information we don't have specific plans to use
    - Reviewed by many, many people to check for blind spots
    - Tested by investigators AND research coordinators
  - Not perfect. Not comprehensive. Just enough.

# 1<sup>st</sup> funded project

- NIH requires single IRB.
  - This will NOT save your sites time or energy.
  - Make sure to add a check-box for future contact/research.
- Data Use Agreements are necessary.
  - These take a LOT of time and energy.
  - And there are a lot of related acronyms.
  - Make friends with the data office managers.
  - Start early!
  - If you think there will be spin-off/ancillary proposals, then try hard to include these possibilities the FIRST time.

# 1<sup>st</sup> funded project

- Enrolled EVERY baby with neonatal seizures at 7 excellent centers. – waiver of informed consent
  - Most common etiologies: HIE, ICH, Stroke.
  - Neonatal epilepsies: 13% and usually genetic.
  - Preterm with seizures = risk for death.
  - Death = usually after decision to withdraw intensive care.
  - Best predictor of going home on anti-seizure medication = study center.
  - 6 published manuscripts (+ 2 in the works).



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  - **Best predictor of going home on anti-seizure medication = study center.**



# Next project: comparative effectiveness

Thought #1:  
This will take  
\$\$\$.



Thought #2:  
We need to  
expand our  
network.

Stakeholder engagement is required by PCORI.  
Parent well-being is outside our area of expertise.  
We need more statistical support & study design expertise.

Lesson #4:  
Sometimes  
you need to  
broaden  
your  
horizons –  
*develop & use  
connections!*



Photo credit: Peter Shellhaas



Ronnie Guillet,  
MD, PhD

PROPHENO trial PI  
Consultant  
extraordinaire





A walk in  
the park...



# Meaningful stakeholder engagement.



Contents lists available at [ScienceDirect](#)

Pediatric Neurology

journal homepage: [www.elsevier.com/locate/pnu](http://www.elsevier.com/locate/pnu)

Original Article


## **Seizures and Antiseizure Medications are Important to Parents of Newborns With Seizures**

Elizabeth Hill MD<sup>a,\*</sup>, Hannah Cranley Glass MD, MAS<sup>b,c,d</sup>, Kelli Kelley<sup>e</sup>,  
Marty Barnes<sup>f</sup>, Stephanie Rau MD, BS, CCRP<sup>a</sup>, Linda S. Franck RN, PhD<sup>g</sup>,  
Renée A. Shellhaas MD, MS<sup>a</sup>

# Continual Parent & Stakeholder Input



- A parent from each study site
- Representatives from advocacy organizations
- Monthly meetings (paid)



## NSR Parent and Stakeholder Involvement in a Multicenter Study of Continued Anticonvulsants after Resolution of Neonatal Seizures

M Barnes, H Glass, K Grant, L Grossbauer, E Hill, T Barako, J Guerriero, D Annis, K Pawlowski, G Ma, K Monteras, S Rau, B Bailey, E Rogers, M Lemmon, L Franck, and RA Shellhaas for the Neonatal Seizure Registry

### Objective

Continued anticonvulsants after resolution of neonatal seizures is a PCOR-funded randomized comparative effectiveness study. This multicenter study is designed to assess the impact of short versus prolonged treatment with anticonvulsants after acute symptomatic neonatal seizures on (1) neurodevelopmental outcomes, (2) the incidence of epilepsy, and (3) parent/family well-being. Our objectives are to: (1) establish the Parent and Stakeholder Advisory Panel; (2) recruit parents and parent/proxy voluntary research active partners in all stages of the research design; (3) disseminate study findings.

### Methods

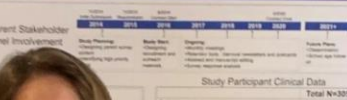
Participants are 325 children with acute symptomatic neonatal seizures (resolutions in infancy age < 12 weeks) enrolled at 4 children's hospitals in 8 sites: Boston Children's Hospital, Illinois Children's Hospital, Johns Hopkins Children's Hospital, Children's National Medical Center, Nemours Children's Hospital, Seattle Children's Hospital, Texas Children's Hospital, and Boston Children's Hospital.

### About the Parent and Stakeholder Advisory Panel

- Each parent/proxy research active partner will receive a 2-page letter to inform them of the study.
- The advisory panel will meet regularly to discuss study issues.
- The advisory panel will provide input on study design, recruitment, and dissemination of results.

### Results

#### Timeline of Parent Stakeholder Advisory Panel Involvement



#### Study Participant Clinical Data

	Total N=325
Secure etiology:	
- Hypoxic-ischemic Encephalopathy	130 (43%)
- Ischemic stroke	85 (26%)
- Intracranial hemorrhage	42 (13%)
- Other	47 (14%)
Initial treatments:	
- Phenytoin	274 (84%)
- Levetiracetam	18 (6%)
- Phenobarbital	3 (1%)
- No loading dose given	10 (3%)
Home on anti-seizure medication:	
- AEDs only	197 (61%)
- AEDs + medication	198 (61%)
- No AEDs	184 (57%)
- AEDs + Levetiracetam	37 (11%)

### Results (cont)

#### Ongoing Parent and Stakeholder Advisory Panel Contributions

- Participate actively in data analysis discussions and manuscript preparation for parent survey results (manuscript examining neonatal time point open ended questions submitted in July 2015; manuscript for neonatal time point quantitative survey data is being drafted).
- Developed, drafted and published 'Seizures and Antiepileptic Medications are Important to Parents of Children with Seizures', E Hill et al Pediatric Neurology 2017 Feb 87-84.
- Assist with drafting and editing biannual newsletters to inform study participant families about study progress, presentations, manuscripts in progress.
- Available to discuss the importance of the study with enrolled participants to encourage ongoing participation.
- Assist with ancillary study development and conduct including Risk for Infantile Spasms after Acute Symptomatic Neonatal Seizures (NSR-GSNM), funded by Pediatric Epilepsy Research Foundation.
- Ongoing contributions to NSR R01 follow-up study proposal.

### Discussion

- The Parent Panel has participated in diverse aspects of study conduct including planning, enrollment, retention, data analysis and manuscript development.
- High retention rates may be attributable to Parent Panel recommendations for follow-up and retention methods.
- Stakeholder involvement has lead to more purposeful use of scarce resources and funds to specifically target the needs of our children and families.
- Parent-proxied studies are taken to the next level with parent stakeholder involvement during the entire process bringing a new level of innovation to pediatric research.
- Results from this study will be used to inform duration of anti-seizure medications following acute symptomatic neonatal seizures. Parent involvement in study design and dissemination of data will help ensure that study results are widely adopted by clinicians and accessed by parents.
- Planned future involvement of the Parent Panel includes planning and conduct of dissemination study, school age follow-up.


### Acknowledgments

This work was supported by the Patient-Centered Outcomes Research Institute (PCORI), 15CC12187, AC120790375.



Co-production with parents and stakeholders is valuable.

# Parent experience of caring for neonates with seizures

Monica Lemmon,<sup>1</sup> Hannah Glass,<sup>2,3</sup> Renee A Shellhaas,<sup>4</sup> Mary Carol Barks,<sup>5</sup> Bria Bailey,<sup>2</sup> Katie Grant,<sup>6</sup> Lisa Grossbauer,<sup>7</sup> Kamil Pawlowski,<sup>8</sup> Courtney J Wusthoff,<sup>9</sup> Taeun Chang,<sup>10</sup> Janet Soul ,<sup>11</sup> Catherine J Chu,<sup>12</sup> Cameron Thomas,<sup>13</sup> Shavonne L Massey,<sup>14</sup> Nicholas S Abend,<sup>15</sup> Elizabeth E Rogers,<sup>16</sup> Linda S Franck,<sup>17</sup> on behalf of the Neonatal Seizure Registry

## ORIGINAL ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS



### Associations between Infant and Parent Characteristics and Measures of Family Well-Being in Neonates with Seizures: A Cohort Study

Linda S. Franck, RN, PhD<sup>1</sup>, Renée A. Shellhaas, MD, MS<sup>2</sup>, Monica Lemmon, MD<sup>3</sup>, Julie Sturza, MPH<sup>2</sup>, Janet S. Soul, MDCM<sup>4</sup>, Taeun Chang, MD<sup>5</sup>, Courtney J. Wusthoff, MD, MS<sup>6</sup>, Catherine J. Chu, MD<sup>7</sup>, Shavonne L. Massey, MD<sup>8</sup>, Nicholas S. Abend, MD, MSCE<sup>8,9</sup>, Cameron Thomas, MD, MS<sup>10,11</sup>, Elizabeth E. Rogers, MD<sup>12</sup>, Charles E. McCulloch, PhD<sup>13</sup>, Katie Grant<sup>14</sup>, Lisa Grossbauer, MS<sup>15</sup>, Kamil Pawlowski, MS<sup>16</sup>, and Hannah C. Glass, MDCM, MAS<sup>17</sup>, on behalf of the Neonatal Seizure Registry study group\*



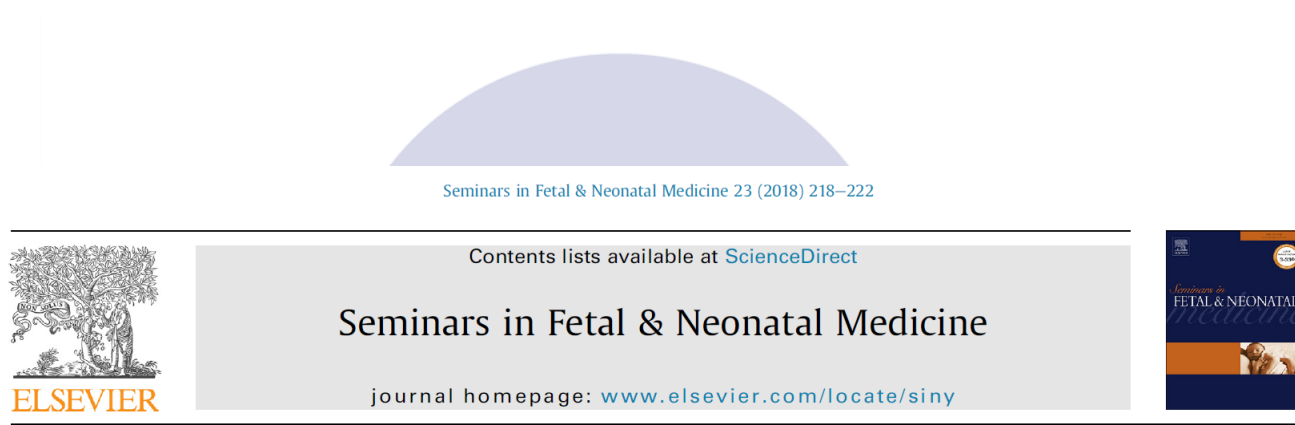
JAMA Neurology | **Original Investigation**

# Safety of Early Discontinuation of Antiseizure Medication After Acute Symptomatic Neonatal Seizures

Hannah C. Glass, MDCM, MAS; Janet S. Soul, MDCM; Taeun Chang, MD; Courtney J. Wusthoff, MD, MS; Catherine J. Chu, MD; Shavonne L. Massey, MD; Nicholas S. Abend, MD, MSCE; Monica Lemmon, MD; Cameron Thomas, MD, MS; Adam L. Numis, MD; Ronnie Guillet, MD, PhD; Julie Sturza, MPH; Nancy A. McNamara, MD; Elizabeth E. Rogers, MD; Linda S. Franck, RN, PhD; Charles E. McCulloch, PhD; Renée A. Shellhaas, MD, MS



# Lesson #5: leverage related experience



## Outcomes after acute symptomatic seizures in neonates

Hannah C. Glass<sup>a, b, \*</sup>, Zachary M. Grinspan<sup>c</sup>, Renée A. Shellhaas<sup>d</sup>

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<sup>b</sup> Department of Epidemiology and Biostatistics, University of California, San Francisco, CA, USA

<sup>c</sup> Department of Healthcare Policy, Department of Research and Pediatrics, Weill Cornell Medicine, New York, NY, USA

<sup>d</sup> Department of Pediatrics, Department of Communicable Diseases, University of Michigan, Ann Arbor, MI, USA



Recall Lesson 1C: Test projects can be helpful!



# Lesson #5: leverage related experience

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**FULL LENGTH ORIGINAL RESEARCH**

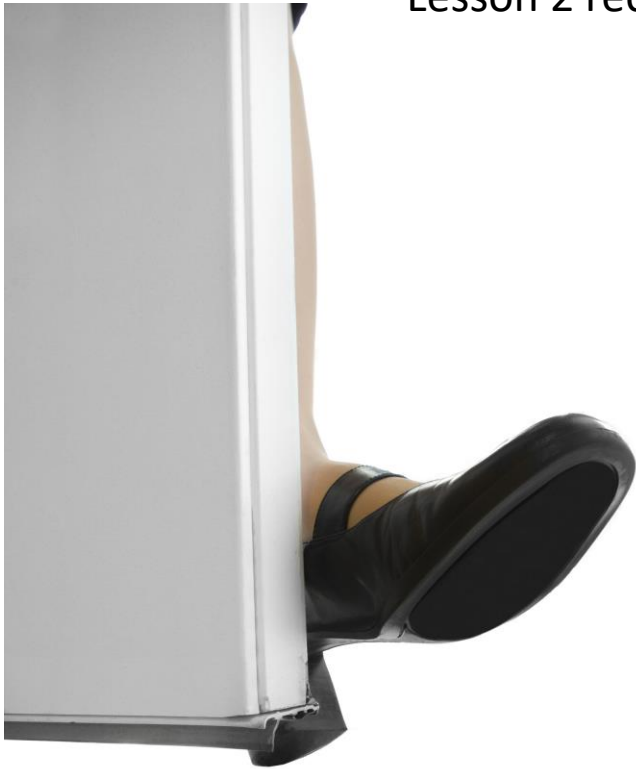
**Epilepsia**<sup>®</sup>

## **Risk for infantile spasms after acute symptomatic neonatal seizures**

**Hannah C. Glass**<sup>1,2,3</sup>  | **Zachary M. Grinspan**<sup>4</sup>  | **Yi Li**<sup>5</sup> | **Nancy A. McNamara**<sup>6</sup>  |  
**Taeun Chang**<sup>7</sup> | **Catherine J. Chu**<sup>8</sup>  | **Shavonne L. Massey**<sup>9</sup> | **Nicholas S. Abend**<sup>9,10</sup>  |  
**Monica E. Lemmon**<sup>11</sup> | **Cameron Thomas**<sup>12</sup> | **Charles E. McCulloch**<sup>3</sup> |  
**Renée A. Shellhaas**<sup>6</sup>  | **the Neonatal Seizure Registry Study Group**



# Lessons 6 – 11 – getting your foot in the door



Lesson 2 recap: Start small. The simplest questions are often the best.

Lesson 1 recap: Find your people.

Answer your email!

SHOW UP TO PERC SIG MEETINGS!

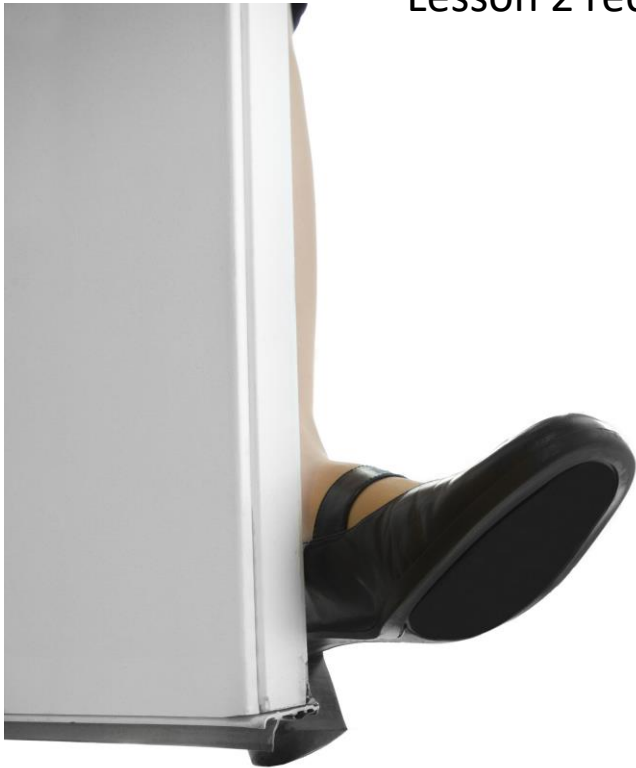
Do a great job - every time.

Be the first one done.

Never work hard on a project that can't be published.

Define author order at the time you write the proposal.

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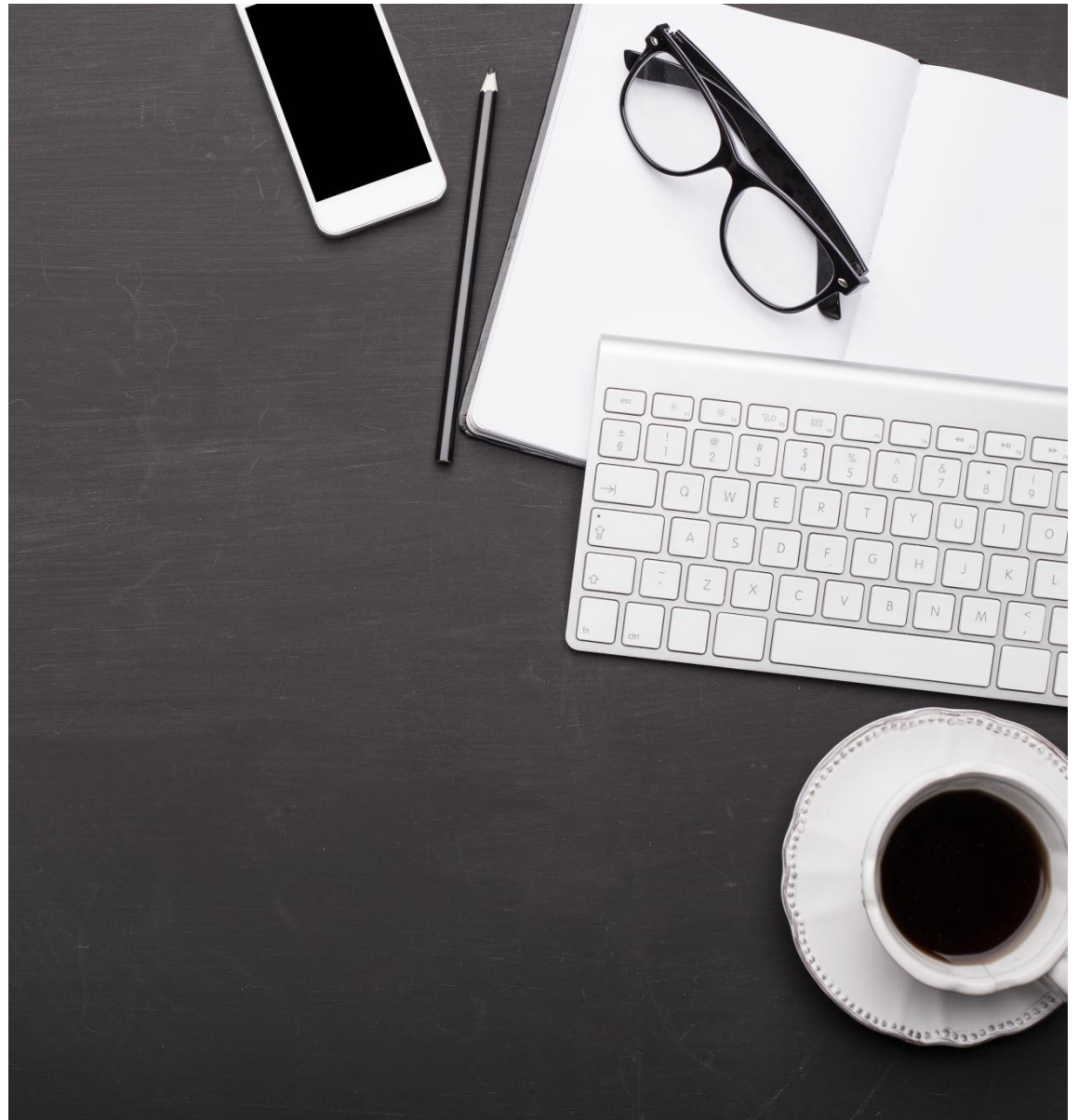
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Side note:  
collaborative  
writing



IF YOU HANG OUT  
WITH ME FOR TOO  
LONG I'LL BRAINWASH  
YOU INTO BELIEVING  
IN YOURSELF AND  
KNOWING YOU CAN  
ACHIEVE ANYTHING.