

Summary of Day 1

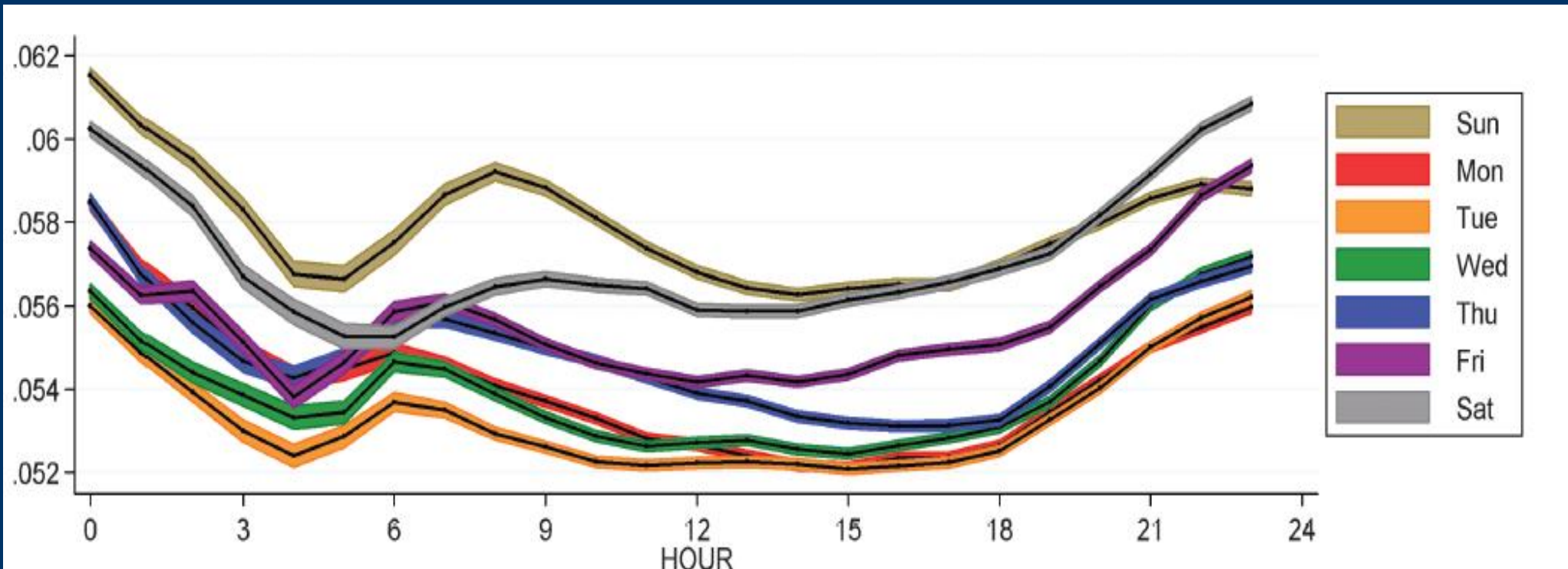
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Diurnal and Seasonal Mood Vary with Work, Sleep, and Daylength Across Diverse Cultures

Scott A. Golder* and Michael W. Macy



- 508 million tweets
- Across the globe
- 2008 to 2010

Selected Points

- Large simple trials are not so simple, and can also be called large streamlined trials
- Reasons for not streamlining trials are complex and each group involved bears some responsibility: industry sponsors, NIH, FDA, ARO's, CRO's
- Streamlining involves smart design, agreement with FDA/EMA, focus on site's productivity
- Lack of following FDA draft guidance on monitoring and AE reporting is an opportunity
 - Concern over missing details for OSI audits/ FDA reviews
- Novel approaches using elements of EMR, existing follow-up mechanisms, registries have shown promise

Models of Trials

	Large Simple Trials		
	Traditional Industry	Streamlined Industry/NIH	Novel Streamlined
Sites	Unselected	Selected	Very selected
CRF	Extensive	Focused	EHR based
AE collecting	All AEs	Selected AEs	Selected AEs
AE reporting	Expedite SAEs	Expedite SUSARs	Expedite SUSARs
Monitoring	100% SDV	10-15% SDV	Central and selected
Follow-up	Visits	Visits, phone	EHR sources
Costs per pt		2/3	<25%



Answers to “3” Questions
13 May 2013
27 yellow sheets completed
75 barriers identified

Barriers

Category	Responses (n)
Perception of regulatory burden	15
Safety reporting	7
Data “exuberance”	7
Culture barriers and stakeholder desire	7
Excessive monitoring	5
Cost of large trials	5

Barriers

Category	Responses (n)
Patient recruitment and compliance	5
SOPs	4
Harmonization of regulators	4
Academic incentives	4
Informatics and technology	2

Barriers

Category	Responses (n)
NIH basic science	2
Lack of consistency with clinical practice	2
Other	6

Solutions - Perception of regulators

- * Communication from FDA on why LSTs are important and streamlining is desirable and acceptable
- * Guidance written on LSTs with real life examples
- * Greater cross table discussions with all stakeholders
- * Formalize and enhance talking with FDA agency early, obtain upfront commitment and agreement from FDA and sponsors on protocol plan (simple); eliminate multiple rounds of discussion
- * Pilot trials using LSTs share lessons learned

Solutions - Perception of regulators

- * Education and training (including publication of examples and more broadly publish FDA viewpoint)
- * CTTI emphasize linkage between Quality by Design and LST
- * Track and be transparent on what “is” and what “is not” being done in LSTs
- * Develop mechanisms to incorporate patient perspective
- * Design effective data collection tools

Solutions - Need for safety reporting

- * Guidance of general numbers in Phase I and II that permit decreased AE collection in phase III
- * Upfront agreement with regulators on what is going to be collected for AE's (reduce unnecessary AE collection)
- * Greater education on IND safety rule and “AE lite” amongst all stakeholders
- * Enhanced collaboration of FDA and EMA – invite EMA to meetings like this

Solutions - Data exuberance

- * Define relevant AE's to collect, when, and how
- * Published documentation that details acceptable approach to collect what is needed (and not fear needing additional data later)
- * Focus on trial question and data needed to answer and not prepare for “what if” scenarios
- * Agreement by all stakeholders to adopt a “collect as needed” mentality

Solutions - Culture barriers and stakeholder desire



- * Publish/share examples of success of streamlined/simple approach
- * Need more case studies and public access to examples of monitoring plans, AE plans, and data plans that are accepted by FDA and EMEA (? Post on ct.gov)
- * Campaign to promote simplified pragmatic trials; communicate and educate to all stakeholders

Solutions - Need for excessive monitoring



- * Educate and promote Risk-based monitoring approach
- * Promote Quality by Design decision making
- * Align workplace tenets
- * Promote and refine FDA guidance on monitoring
- * Promote international harmonization

Solutions - Patient recruitment and compliance



- * Build trust with patients
- * Public education on what participation entails and commitment to long term participation (minimize loss to follow up)
- * Use of informed consent forms that is standard and that clarifies what withdrawal from treatment means and state that there is no withdrawal from follow up.
- * Randomly sample from the whole randomized cohort longitudinally for a surrogate for the interventions

Solutions - Cost of large trials

- * Use of registry data
- * Minimize unnecessary procedures and data collection
- * Use of Electronic Health Records

Broad Themes

1. Need to identify methods to increase stakeholder knowledge on current Monitoring and SAE guidance's
2. Need transparent and documented examples of what has been successful and not successful.
3. Need documented guidance on LSTs and the regulatory position that it is acceptable.
4. Need international harmonization.