NIH Collaboratory Rethinking Clinical Trials®
Health Care Systems Research Collaboratory

Blood Pressure Medication Timing Study (BPMedTime)

Gary Rosenthal, MD

Meeting Participants (May 31, 2013):

☒	Jeremy Sugarman (Johns Hopkins)	☒	Brian Gryzlak (Univ Iowa)	☒	Barbara Wells (NIH)	☒	Josephine Briggs (NIH)
☒	Rob Califf (Duke)	☒	John Bertolatus (Univ Iowa, IRB)	☒	Denise Bonds (NIH)	☒	Tammy Reece/Cheri Janning (Coord Center)
☒	Gary Rosenthal (Univ Iowa)	☒	Julie Kaneshiro (OHRP)	☒	Catherine Meyers (NIH)	☒	Monique Anderson (DCRI)
☒	Christian Simon (Univ Iowa)	☒	Jerry Menikoff (OHRP)	☒	Wendy Weber (NIH)	☒	Jonathan McCall (Coord Center)
☒	Michelle Countryman (Univ Iowa, IRB)	☒	Irene Stith-Coleman (OHRP)	☒	Valery Gordon (NIH)	☒	Swati Chakraborty (DCRI)
☒	Elizabeth Chrischilles (Univ Iowa)	☒	Ivor Pritchard (OHRP)	☒	Dave Wendler (NIH)	☒	Eric Eisenstein (DCRI)

The minutes from the May 31, 2013 meeting were circulated to all participants on the call for two rounds of review and they reflect all corrections that were received.

AGENDA ITEMS	DISCUSSION May 31, 2013	ACTION ITEM May 31, 2013	CURRENT STATUS as of June 1, 2015
	• Dr. Rosenthal gave an overview of the BPMedTime trial (Blood Pressure Medication Timing Study). The study will compare the risk of adverse cardiovascular events in patients who		The Blood Pressure Medication Timing Study (BPMedTime)

	are randomized to receive instructions to take their currently prescribed once daily antihypertensive medications at bedtime vs. patients who continue to take their once daily antihypertensive medications in the morning or afternoon. • Primary endpoint: o Cardiovascular events (CV death or hospital admission for acute MI, ischemic heart disease, cerebrovascular accident, heart failure, or coronary, cerebral, or peripheral revascularization) • Secondary endpoints: o Blood pressure recorded in clinic during outpatient visits o Self-reported medication adherence o Health-related quality of life o Resource utilization (counts of admissions, ED visits, and clinic visits) • Centers involved: University of Iowa and Duke University. • Eligible participants will be identified through the electronic health record (EHR) at both sites and will include adults 50–85 years of age. Potential study participants will be sent an initial packet including a letter describing the trial and informing them of their eligibility. Study endpoints will be collected from: 1) the EHR; 2) a secure, password-protected, web-		project did not transition to the UH3 Implementation Phase.

	based personal health record or mailed questionnaires; 3) Medicare claims data for Medicare beneficiaries; 4) hospital discharge summaries for patients who are not Medicare beneficiaries; 5) state death certificate files; and 6) the National Death Index. • No questions regarding protocol design were voiced.		
Minimal risk	• The investigators proposed that the study poses no more risk to participants for than they would experience from routine clinical care for hypertension. • Participants randomized to the intervention arm of the study will be asked to take their blood pressure medications at nighttime; there is no change to the kind of medication or dose. Participants are not exposed to any other additional risk. • In their 2013 clinical practice guidelines, the American Diabetes Association recommended that at least one hypertension medication be given at bedtime, based on reported results from recent randomized controlled trials conducted by a single Spanish team of investigators. The International Society of Nephrology did not feel that the evidence warranted this recommendation. • A review of pharmacy prescribing data at the University of Iowa found that 92% of instructions for once-daily hypertension medications lacked specific instructions	• Dr. Rosenthal will send background reference materials to OHRP representatives participating in this teleconference so that the discussion about a risk determination can continue.	

	regarding what time of day to take them, leaving patients free to take medications at times they felt most convenient. • Observational studies have suggested that nighttime hypotension may be associated with ischemic optic neuropathy (a rare condition), although not specifically with nighttime dosing of antihypertensive medications. One small (n=88) Polish observational study found an association between nighttime dosing of antihypertensive medications and visual field loss in subjects with open-angle glaucoma. Because of these studies, patients with histories of ischemic optic neuropathy and/or glaucoma will be excluded. • Discussion ensued about whether the study would meet criteria for a determination of minimal risk, but no consensus was reached about this during the call.		
Consent (patient and physician)	• Informed consent will be obtained using an online interactive platform (preferred) or a mailed a consent letter that will provide identical information. • A waiver of documentation of consent (i.e., waiver of the requirement for a witnessed signing of the consent form) is requested because: 1) the study involves only minimal risk and 2) the study involves no procedures for which consent is normally required outside of a research context.	• Further discussion with OHRP regarding the consent process, especially issues regarding documentation of consent, is needed.	

	• Mention was made that there is no requirement for witnessed signing of consent under 45 CFR 46; however, witnessing can be required under other guidances if they are applicable.		
HIPAA	• Post-consent, a full waiver of HIPAA authorization is planned. It is not practicable to obtain this authorization without losing the pragmatic nature of the trial (i.e., obtaining such authorization would substantially reduce enrollment efficiency). • No concerns about this were raised on the call.		
Monitoring and oversight	• Information will be reviewed by a data safety monitoring board that will be constituted according to NIH policies.	The study will require a Data and Safety Monitoring Plan, which will be developed by the study team, and approved by NHLBI prior to study implementation.	
Issues beyond the BP MedTime Trial	• None voiced.		
Conclusion of meeting	• Follow-up needed as noted in action items.	• A case study will be drafted to provide guidance for others planning similar trials to facilitate navigation of the ethical and regulatory issues.	
Additional regulatory or ethics issue(s) that arose after the meeting			

Additional follow-up information			