The Clinical Dilemma:
How to prevent and address the inevitable while addressing important clinical and public health questions.

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Outline

Looking ahead to avoid regret…

• Where to start
  – Document development
  – Trial set up and planning

• Trail conduct

• Ongoing activities
Where to start – Document development

• Protocol generation
  – Minimize participant burden
  – Allow flexibility – visit schedules and visit types
  – Differentiate between stopping study medication and stopping participation in the study
  – Define expectations for participant follow up when study medication is discontinued
  – Define what information will be collected for participants off study medication
  – Include the use of locator agencies as a means of follow up
  – Remove language which encourages discontinuation
Where to start — Document development

• Informed Consent generation
  – Clear expectations for follow up, even after discontinuation of study medication or withdrawal of consent
  – Ensure provisions for contacting other parties for follow up
  – Define alternative contact methods for follow up
  – Include information on the use of locator agencies
  – Provide explanation of what will happen in the event the site closure
Where to start – Trial set up and planning

• CRF design
  – Build in alerts and flags for the study team to receive
  – Consider the addition of intent-to-attend questions

• Training on the importance of missing data
  – All team members
Where to start — Trial set up and planning

• Site feasibility and selection
  – Recent history of enrollment and retention
  – Experience with locator services and utilization of public record data
  – Patient satisfaction scores

• Contracting
  – Site
    • Ensure provision for retention follow up, “Pay-for-performance”
  – Locator agency
  – Retention Committee
Where to start — Trial set up and planning

• Site start up
  – Expectations – if a participant is randomized, they are expected to complete
  – Stress the importance of the informed consent process
  – Training
  – Shift in focus from recruitment to recruitment and retention
    • Retention planning from the start
Trial Conduct — What creates missing data?

• Incomplete follow up
  – Adverse event profile
  – Efficacy – positive or negative
  – Rescue medication
  – Participant time constraints
  – Site issues
Trial Conduct — What creates missing data?

- Participants full withdrawal of consent
- Participants becoming lost to follow up
Trial Conduct — How to impact missing data

• Establishment of a good relationship between participant and site

• Make participation convenient
  – Completion of questionnaires via phone, snail mail or email
  – Be sensitive to wait times
  – Schedule visits times which are convenient – early morning, evenings and weekends

• Ensure multiple contacts for participants
  – Family, friends, other health care providers
Trial Conduct — How to impact missing data

• Maintain contact
  – Send reminders – text, email, mail and messages
  – Encourage good treatment compliance

• Minimize disruptions due to staff turnover
  – Need agreements for a minimum notice before staff leaving
  – Train new personnel prior to old personnel leaving

• Effective trial management
  – Support for sites is critical
  – Create dedicated retention team
Trial Conduct — How to impact missing data

- Incomplete follow up
  - Care and support for adverse events and efficacy impact
  - Participant appreciation
  - Ensure completion of trial related activities prior to participants leaving the office
    - Utilize check lists
  - Ensure site obligations
Trial Conduct — How to impact missing data

• Withdrawal of consent
  – Full withdrawal of consent is rare in well conducted trials
  – Site training necessary to ensure an understanding of levels of withdrawal of participation
  – Ensure provisions for withdrawing from study interventions while remaining in the study
  – Utilize a withdrawal of consent checklist
Trial Conduct — How to impact missing data

• Lost to follow up
  – Ensure multiple contacts
    • Check at each visit contacts are current
  – Utilize all other contact mechanisms – alternative contacts, family, employers, hospital or electronic records
  – Utilize publicly available resources
  – Utilize locator agencies
Ongoing activities

Training.....

Tracking...

Intervening
Ongoing activities

- Training on the importance of missing data
  - Everyone on the team needs trained
    - Site personnel
    - Site monitors and other site support
    - Central monitors
    - Data management
    - Medical monitors
  - Frequent, interesting and up to date
Ongoing activities

• Tracking
  – Real time tracking of participants with special attention to any who may be lost to follow up or withdraw consent
    • Utilize alerts
  – Utilize missing visit reports
  – Create algorithm which utilizes site metrics to determine site risk
  – Know where the ‘hot spots’ are
  – Utilize dedicated retention team
Ongoing activities

• Intervening
  – If you track it, be willing to intervene
  – Set algorithm up front so you know what actions will be taken and follow through
  – Interventions will often require additional training
Ongoing activities

Training...

Tracking…

Intervening

Avoiding regret…