Pediatric Eye Disease Investigator Group (PEDIG)

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Pediatric Eye Disease Investigator Group

- Network of community- and university-based providers
- National Eye Institute
- Central Data Coordinating Center
  - Jaeb Center for Health Research
- Data and Safety Monitoring Board
Pediatric Eye Research – circa 1996

- Randomized trials have been performed in Ophthalmology for 25 years
- Much research in pediatric ophthalmology consisted of anecdotal or retrospective case series
  - Inadequate power
  - Substantial investigator bias
- Dogma was passed on from one generation to the next
- Schools of thought based on site of training
Pediatric Ophthalmology RCT’s

- Pleoptics for amblyopia (NIH sponsored 1960’s)
- Era of the large Multicenter Trials (1980’s)
  - Expensive
  - Long lead times
  - Usually designed as efficacy
    - Made generalizability suspect
  - Paid full-time coordinators at each site
  - Coordinating center
  - Study chairman’s office
  - Answered some important questions (DRS, ETDRS, etc)
Conventional RCTs in Pediatric Ophthalmology

• Prism Adaptation Study (1980s)
  – Recruitment took twice as long as expected
  – Clinical question was not burning
    • How much surgery for acquired non accommodative ET
  – Little excitement with results
  – No apparent change in clinical practice

• CRYO-ROP (1986-2005)
  – Cryotherapy is better than no therapy for ROP
  – Major change in clinical practice
Transitional RCT

- STOP-ROP
  - Supplemental Therapy with Oxygen to Prevent ROP
  - Some centers funded, some not
  - Recruitment took twice the expected time
  - Primary outcome
    - No effect
    - Post-hoc analyses
      - maybe a benefit in a subgroup
Consequences of Few RCTs

• Variability in treatment guidelines
• Evidence basis of clinical practice was primarily your schools of thought
  – Based on training
  – Preferred practice patterns were developed with this level of information
• Certainty of opinion
  – Something never or always works
Mid 1990’s

• National Eye Institute Director and NIH Road Map
  – Move to large simple trials
• Community based
• Incorporate research into clinical practice
• Carefully spend research dollars
• “effectiveness” type trials
  – Answer relevant clinical questions
  – Reduce costs
PEDIG - Beginning

• Application to NEI for single study – 1996
  – Study timing of surgical treatment of congenital esotropia
    • Would become CEOS (Congenital Esotropia Observational Study)
  – Fund creation of a network to undertake the trial
    • Coordinating Center
      – Data
      – Patient retention
    • Large group of investigators
      – Community
      – University
    • Email access required!

• Collaborative project with National Eye Institute
PEDIG

• 1997- NIH Application for a new study and extend the network
  – Amblyopia Treatment Study 1 (ATS1)
    • Atropine versus patching for moderate amblyopia
  – PEDIG Network
    • Bylaws and policies
      – Corporate authorship
    • Officers

• Common clinical problems
  – Investigator interest high

• Investigator concern about research monopoly
ATS1 Issues prior to submission

- **Outcome measure**
  - ATS Visual Acuity Protocol
    - Developed and pilot tested

- **Draft Protocol and Procedures Manual**

- **Certification planning**
  - Phone calls and written examples
  - Later web based simulations

- **Quality of life measure had to be developed**
Network Issues following review

- Role for optometry
- Appointment of a DSMC
Initial Structure

• Steering committee
  – Meetings
  – Teleconference
  – Study documents and protocol review

• IRB
  – Provide IRB review/coverage for community practices
  – Do as much as possible for university applications – develop templates
Role of the National Eye Institute

• Collaboration
  – Program manager involved

• Appointment of the DSMC
  – Same body continued for the additional trial

• Appoint external review committees when needed
ATS1 Enrollment and Participation

- 419 patients
- 72 investigators enrolled at least one patient
- Equivalence Trial
ATS1 - Amblyopic Eye
Mean Acuity at Each Visit

- **Patching**
- **Atropine**

Mean Acuity at Each Visit:
- 20/20
- 20/25
- 20/30
- 20/40
- 20/50
- 20/60
- 20/80

- 20/60- at 5 wks
- 20/50 at 5 wks
- 20/40 at 16 wks
- 20/30 at 16 wks
- 20/30- at 6 mos
- 20/30 at 6 mos
Beyond ATS1

• Results led to other questions that could be answered with this model
  – Role of patching, role of glasses, role of near activities
  – Impact of age
    • No age effect from 3 to 7, unlike clinical opinion
New Studies Development

• Questions solicited from investigators
  – At national meetings
  – Teleconferences
  – Email discussion
• Ideas from steering committee
Completed Studies

- ATS1 – 2 year outcome
  - Examine recidivism
- ATS 2A, 2B, 2C
  - Look at patching dosage and recurrence risk
- ATS3 pilot study
  - Can we treat older patients
- ATS 3 treatment phase
  - Amblyopia treatment of children 7-18
    - 507 pts, 49 sites (median = 7)
- ATS4
  - Atropine dosage
    - 168 patients, 30 sites (median = 3, range 1-28)
- ATI pilot study
- NLD Questionnaire pilot study
Studies Underway

- ATS1 long term follow-up
- ATS3 observation phase
- ATS5
  - Patching versus a spectacle control
- ATS7
  - Bilateral amblyopia
- ETS1
  - Observational study of preoperative alignment
- ATS6
  - Does near activities really matter
- ATS8
  - Atropine compared to atropine plus a plano lens
- NLD1
  - Observational study of primary surgery
  - Feasible because procedures and framework in place for NLD2
- NLD2
  - RCT for children who failed probing
Studies launching spring 2005

• COMET 2
  – Bifocals for myopia
• COMET 3
• ATS 9
  – Atropine versus patching for older children
PEDIG Organization

- Executive committee
- Study Steering Committees
- Coordinating Center
- Jaeb IRB
- Data Safety Monitoring Committee
  - Twice yearly plus as needed
Executive Committee

- Allocates resources
- Prioritizes projects
- Does grant applications
  - PEDIG is funded, not the particular project
- Approves new sites, sanctions poorly performing sites
- NEI representatives
- Weekly phone calls
- Face to face about once per month
Steering Committees

- Protocol chairmen
- Statistician
- Protocol development person
- Study group clinicians (~2)
- Vision scientist
- PEDIG exec committee represent
Steering committees

• At least monthly conference calls
  – May be weekly during development
• Face to face meetings as needed
• Writing committee or editorial committee
Coordinating Center

- Study operations
  - Statistical, epidemiological, site support, site visits, certification
- IT and Web Department
- Development committee
- Contracts office
IRB – Coordinating Center

• JAEB IRB is separate, private IRB for all our community sites

• Institutional IRBs
  – Templates provided based on local, ever-changing needs

• Review and coordinate content of all university and JAEB IRBs
IRB Issues

- Many novice investigators
- Teaching about equipoise
- Assuring time for consent process in busy practice
Investigator contact

- Web
- Monthly phone calls (3 chances)
- Annual winter meeting (2 days)
  - New studies
  - Protocol certification
  - New data review
  - Unmasking
- Summer 1 day meeting
  - Manuscript unmasking
- Meetings at all relevant national meetings
Coordinator Contacts

- Monthly phone calls
- Weekly patients needing visit logs
- Email
- Same meetings as investigators
Funding

• Per patient capitation for investigator
  – For work beyond standard clinical care
  – Pays for extra study visits, time to do consent and other study procedures including forms
  – IRB capitation for University sites
  – IDC’s are added on

• Coordinator payments
  – For each patient completing in-window visits

• Patients/parents
  – Some expense reimbursement funded directly
PEDIG

L I V E - Site

This is the LOG IN for all PEDIG Studies

Enter your Study ID and password

Study ID       
Password       
Confirm Password

(Passwords are case-sensitive. Sessions will last approximately 1 hour.)

LOGIN

Please note: Regular maintenance is performed on this site every Wednesday from 7:00 - 8:00 AM EST. Access to the site may not be available during that time.

Password Help

Supported by The National Eye Institute

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National Institutes of Health
Web-based studies

- All forms and study documents on the web
- All data entry
- Much of certification
  - Some one-on-one contact
- Paper
  - Only study consents
  - Patient information
New Study

• Idea is floated.
• Exec committee approves presentation of a one page abstract at group meeting
• Development committee formed
  – Protocol and MOP created
    • Reviewed by exec committee, investigators, DSMC for interest, science, and feasibility
• Steering Committee formed
  – Contracts and IRB applications
Caution

• Not every project is suitable
  – Complicated protocol
  – Time consuming
  – Large per patient cost