Pediatric Eye Disease Investigator Group (PEDIG)

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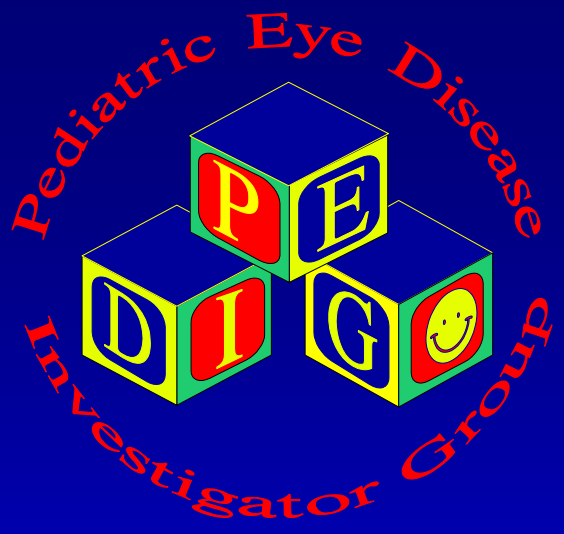
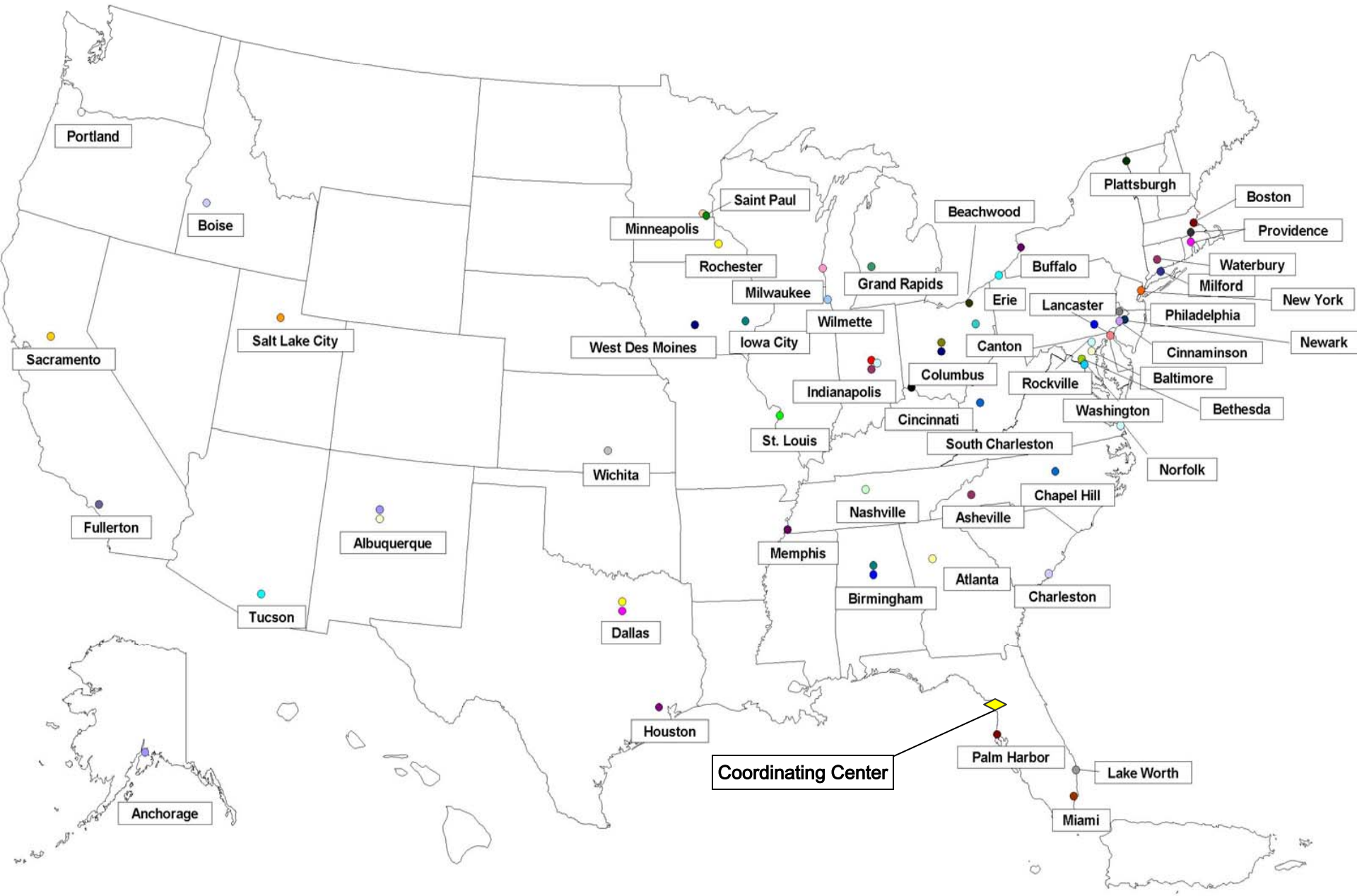


Pediatric Eye Disease Investigator Group

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

PEDIG Clinical Sites



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

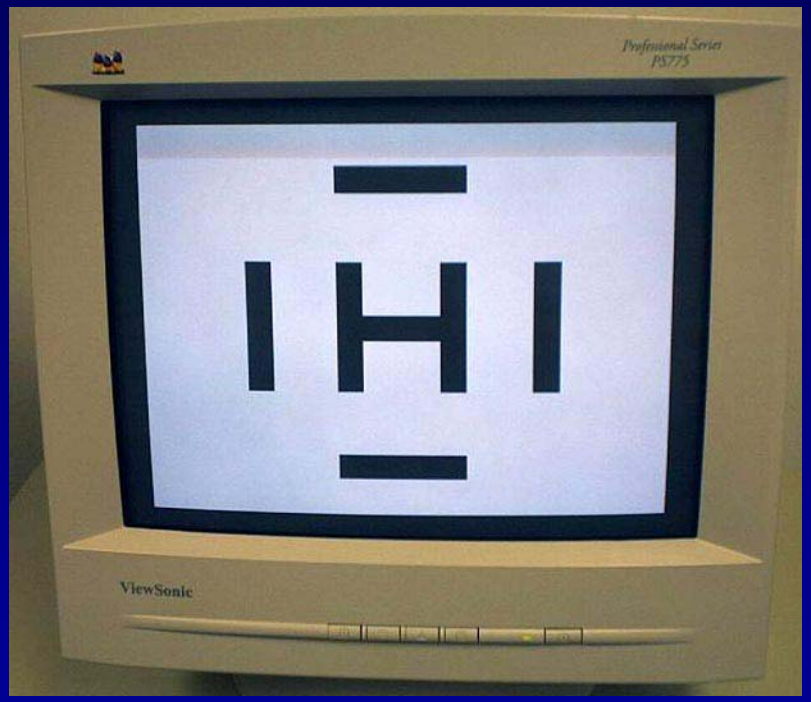
- Application to NEI for single study – 1996
  - Study timing of surgical treatment of congenital esotropia
    - Would become CEOS (Congenital Esotropia Observational Study)
  - Fund creation of a network to undertake the trial
    - Coordinating Center
      - Data
      - Patient retention
    - Large 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

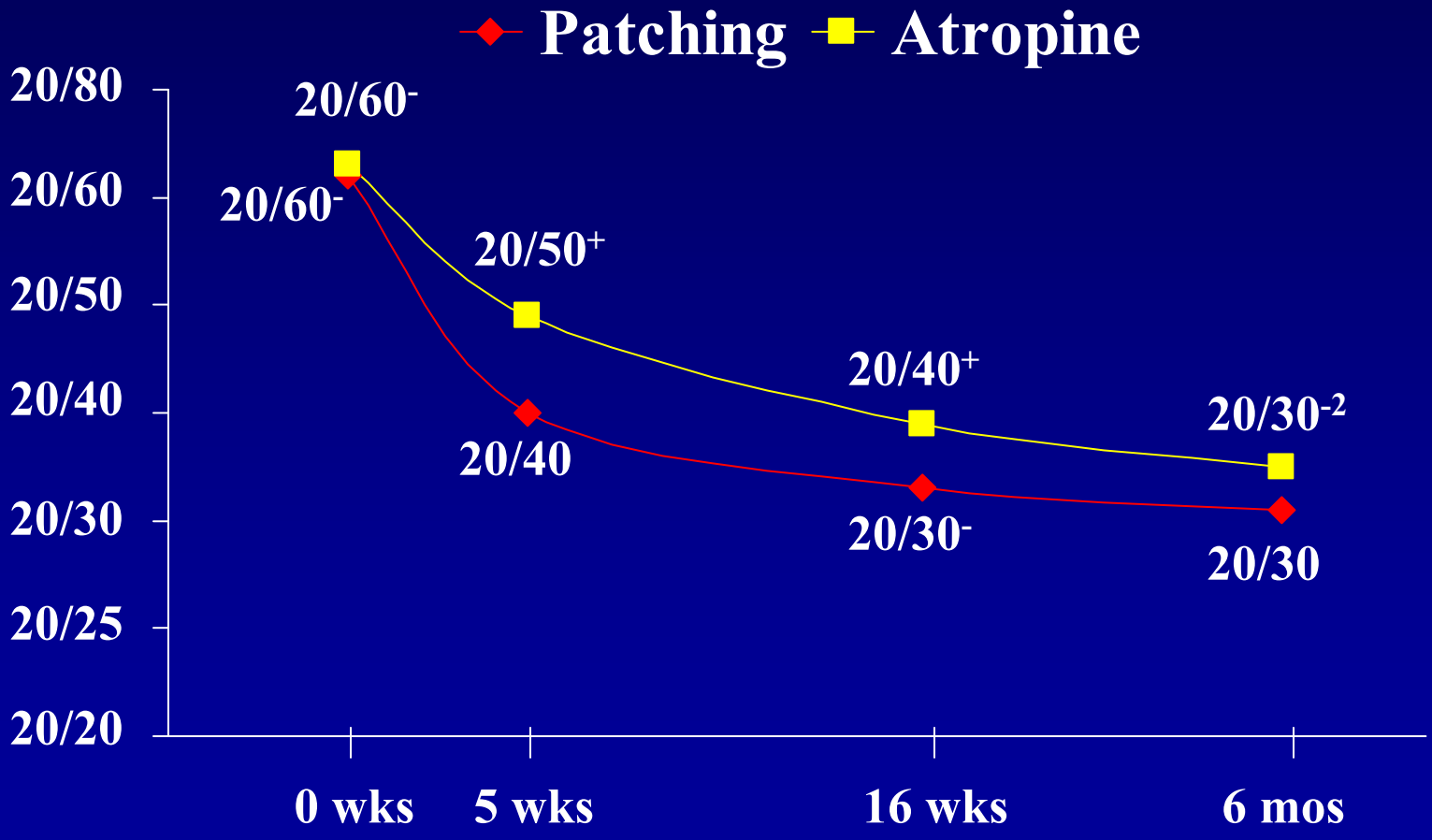
Role of the National Eye Institute

- 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



Beyond ATS1

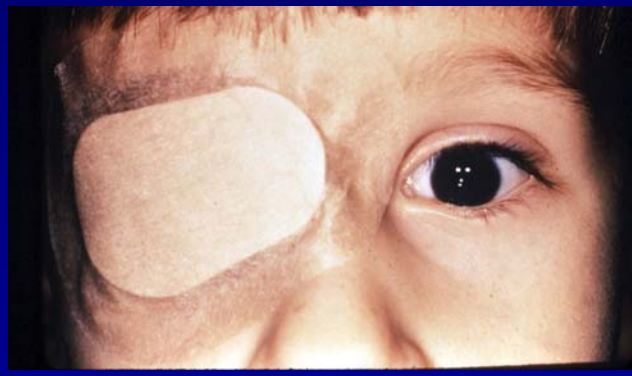
- Results led to other questions that could be answered with this model
  - Role of patching, role of glasses, role of near activities
  - Impact of age
    - No age effect from 3 to 7, unlike clinical opinion

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.)

LOG IN

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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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