METHODS

- Using Web of Science, searching for *"ped*" OR child* and limiting the results to the Web of Science category "pediatrics."
- Limited by year.
- "Hot papers" : http://esi.webofknowledge.com/help/h_dathot.htm. Have been cited three times since published.
- "Highly cited": received enough citations to "place it in the top 1% of the academic field of Clinical Medicine based on a highly cited threshold for the field and publication year".

Paper #1

Benefits of Strict Rest After Acute Concussion: A Randomized Controlled Trial

Thomas DG, et al. Pediatrics 2015: 135: 239-245

Background

- Concussion rates up significantly in past 15 years
- >4,000,000/year
- Most happen in practice
- Cumulative concussions are bad!
- Football>Ice Hockey>Soccer>Lacrosse>Wrestling
- http://www.cdc.gov/headsup/index.html
- Return to competition guidelines
  - 1-2 days* of rest prior to staged activity

Design

- Prospective
- mTBI/concussion diagnoses (ACE form http://www.cdc.gov/headsup/pdfs/providers/ace-a.pdf) from CHW ED 5/2010-12/2012
- 11-22 yo; ED within 24 hrs, injury to head with associated mechanism
- Excluded non-English speaking; IQ<70; behavioral dx (ADHD; LD); intracranial injury; no adult; admitted; lived at a distance

Procedures

- Screening—demographics, injury details, symptoms
- Neurocognitive testing & Balance assessment
- Randomized
  - Group 1: Strict rest—5 days of rest at home (no work/activity)
  - Group 2: Usual care
- 3 and 10 day followup with repeat testing (home)
- Compliance: 7-Day Activity Diary w/PCSS
- ImPACT test (verbal memory; visual memory; reaction time; processing speed; impulse control)
- Balance Error Scoring System

Results

- 99 included (adequately powered for mod effect size)
- Both groups reduced activity (SR more so)
- SR with longer to symptom resolution
- No difference in neurocog or balance (D3 or D10)
- SR with higher physical and emotional symptoms

Take-Aways

- Strict Rest did not improve symptoms, neurocognitive testing or balance scores—rather this group reported more symptoms
- Strict rest may complicate emotional distress (absence from school; activity restriction)?
- Strict rest after mTBI offers no benefit over usual care in the acute care setting.
- Symptom reporting may be influenced by restricting activity

Paper 2

Cesarean Section and Chronic Immune Disorders

Sevelsted A, et al. 2015. Pediatrics 135: e92-e98

Background

- In Western nations, asthma, allergy, inflammatory bowel and T1DM rates have increased over the past several decades
- A parallel rise in Cesaerean delivery rates has been noted
- What do you think?

Design

- Cohort
- Danish children born from Jan 1, 1973-Jan 1, 2012
- Health registries
- Excluded premature births
- ICD-8 and ICD-10 diagnoses
- Statistical analysis
  - Log-linear Poisson regression models
  - Incidence Rate Ratios (IRR)
  - Population Attributable Risk Fraction (PARF)

Results

- 2.5 million births; 1.9 million included in cohort
- 14% c-section rate (increased from 1973-2012)
- C-section associated with increased aIRR for:
  - Asthma
  - Connective tissue disorders
  - Juvenile arthritis
  - Inflammatory bowel diseases
  - Immune deficiencies
  - Leukemia
  - T1DM; psoriasis and celiac disease NOT assoc with c-section

Conclusion

- Cesarean delivery appears to be a shared risk factor for several immune-related conditions
- Why?? Cytokines? Anesthetics? Antibiotics? Microbiome? Stress hormones?
- Observational NOT causal

Paper 3

Prevalence of Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis

Thomas R, et al Pediatrics 2015; 135(4): e994-e1001

Background

- Controversy surrounds diagnosis of ADHD—too much? Too little
- Diagnostic criteria have 'changed' DSM III; DSM III-R; DSM IV; DSM V

1. What is pooled prevalence rate of ADHD?
2. Have rates changed with different DSM?
3. What influence do informants, instruments and geography have on estimates?

Design

- Databases: Medline: PsychINOF, CINAHL, Embase, Web of Science
- Attention-deficit; ADHD, hyperactivity, disorder, epidemiology, point estimate, child, adolescent
- Any language; < 18 years
- DSM III; DSM III-R; DSM IV

Results

- 5,134 studies screened
- 175 unique studies included (>1 million subjects over 36 years)
- European > North American geography
- Parents increasingly primary informants—fewer interviews over time; increase reliance on symptoms
- Most studies at risk for bias
- Overall prevalence ~7% (C.I. 6.7-7.8%)
- Dx increase 2-3% with DSM IV; Sx reliance

Conclusions

- Estimates not statistically significantly different with different DSM (over time)
- Increase with parent report (vs clinical interview)
- Geographic variations exist (Europe; North America; Middle East)

Paper #4

Antibiotic Exposure in Infancy and Risk of Being Overweight in the First 24 Months of Life

Saari A, et al. Pediatrics 2015 135(4): 617-626

Background

- The extended use of antibiotics has presented unanticipated and unintended public health challenges
- Antibiotic alter the gut microbiome
- Infants may be particularly vulnerable
- ? Lessons from the farm: in 1950's antibiotics noticed to promote weight gain in livestock
- ?type ?dose ?exposure window

Design

- Finnish population-based study (Espoo, Finland)
- Jan 1, 2003-April 30, 2007
- Prenatal/postnatal growth disorders excluded (registry data)
- Antibiotic prescriptions (registry data)—4 exposures Birth-5mo; 6-11mo; 12-17mo; 18-23mo
- Logistic regression; Odds Ratio

Results

- Children receiving antibiotics were heavier (zBMI)
  - Both boys and girls
- In boys, any exposure increases risk; with younger exposure having greater risk. In girls only significant exposure window was 12-17 months
- Macrolide exposure with greatest risk
- Multiple exposures increased risk (boys)
- aOR boys: 1.3 (1.1-.1.7); girls 1.16 (0.9-1.6)
- Height also affected

Conclusions

- Antibiotics with growth-promoting effects—particularly for boys.
  - Increased with early exposure and multipe exposure
- Macrolides showed most pronounced effects
- Impact on weight AND height (>> on weight)

- Narrow spectrum; Avoid repeat exposure

Paper #5

Age at Gluten Introduction and Risk of Celiac Disease

Aronsson CA, et al. Pediatrics 2015; 135(2): 239-245

Background

- Gluten is common – wheat; rye; barley; oat
- Gluten proteins (prolamines) trigger celiac disease
- Optimal age for introduction of gluten is controversial.

- Designed to investigate if timing of gluten introduction is an independent risk factor for CD

Design

- TEDDY (The Environmental Determinants of Diabetes in the Young). 6,436 kids in Finland, Germany, US and Sweden
- Tissue transglutaminase (tTGA) antibodies x 2
- N = 307 with CD (bx at provider discretion)
- Feeding questionnaires
- Cox proportional hazards model

Results

- Median introduction of gluten was 6 months (Sweden 5 months; US 7 months)
- 8 months was median breastfeeding duration

- Swedish; female; family history; HLA as biggest risk
- Timing of gluten introduction NOT a risk for developing CD by age 5

Paper 6

Geographic Clusters in Underimmunization and Vaccine Refusal

Lieu T, et al. Pediatrics 2015; 135(2): 280-289

Background

- Refusal of immunizations has increased in recent years
- Reasons are multifactorial—misinformation; mistrust

- Are there 'clusters' of refusal that are predictable?

Design

- Kaiser Permanente—Northern CA (KPNC)
  - 3 million members; 30,000 annual births; under-representation of low income/education
- Infants born Jan 1, 2000-Dec 21, 2009
- "Underimmunized": missed 1+ recommended vax; HEDIS 'Combination 3' measure (4DtaP; 3 IPV; 1 MMR; 2 Hib; 3 HBV; 1 VZV and 4 PCV by age 2)
- "Shot limiting": No more than 2 vax at any visit
- Spatial scan statistics

Results

- 154,424 children in analysis: 38% white; 25% Hispanic; 22% Asian; 6% black; 9% other
- Median income $88,200; 9% below poverty
- Underimmunized: 8% ('02-'05)-12% ('10-'12)
  - 6% annual rate of increase
- Asian/Hispanic more likely to be fully immunized
- Clear geographic clusters of underimmunized
  - Sonoma; Napa; East Bay
- Similar phenomenon in clustering shot refusal

Conclusions

- Interesting application of spatial/public health software
- Policy implications
  - Benchmarks
- Practice implications
  - Measles
  - Pertussis

Paper #7

Association of Child Poverty, Brain Development and Academic Achievement

Hair N, et al JAMA Pediatr 169(9): 822-829

Background

- Children living in poverty tend to do poorly in school
- The relation strengthens across time
- Reduced academic achievement = occupational disadvantage

- Is there a difference in structural brain development mediating the relationship between poverty and academic performance?

Design

- NIH MRI Study of Normal Brain Development
- 433 children ages 6 to 17; 6 centers across US
- Strict eligibility criteria (family; medical; prenatal; medication histories)
- 823 observations of 389 children with complete sociodemographic and neuroimaging data
- MRI; Wechsler Abbreviated Scale of Intelligence; Woodcock-Johnson III Test of Achievement
- Amygdala as control—relative regional gray matter

Result

- Low SES associated with atypical gray matter development.
- Structural differences in frontal lobe; temporal lobe and hippocampus
- 1.5x below FPL = 3-4 % below developmental norms and 4-8 points lower on testing
- Children from poorest households most impacted

Conclusion

- Specific brain structures (temporal lobe; frontal lobe; hippocampus) appear vulnerable to environmental circumstances of poverty.
  - Executive functions
  - Attention
  - Planning
  - Cognitive flexibility
- Long-term deleterious effects