Overdiagnosis: Our Compulsion for Diagnosis May be Harming Children

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Outline

• Definition
• Measurement
• Pediatric Examples
• Drivers
• Harms
• The Way Forward
• Discussion

What is OD?

• The accurate detection of an abnormality from which a patient does not receive net benefit


Which of the following vignettes are examples of OD?
**Misdiagnosis**

A 5 year old girl with a history of asthma is following up in your office after being seen the day before by a colleague. She was treated with steroids, bronchodilators, and amoxicillin. You believe her CXR is more consistent with atelectasis, discontinue antibiotic therapy, and she does well with treatment of her asthma.

**Overtreatment**

A previously healthy 4 year old boy with uncomplicated MSSA osteomyelitis of his R femur is discharged from the hospital with a PICC and an anticipated 4+ weeks of intravenous antibiotic therapy.

**Overdiagnosis (hypoxemia)**

A convalescing 5 month old girl with bronchiolitis on continuous pulse oximetry desaturates for a brief period overnight to 88% and is placed on supplemental O2 by nasal cannula.

**Overdiagnosis (GER)**

A 3 month old, well appearing girl has been gaining weight appropriately but her parents are distressed by her frequent spitting up. She is diagnosed with gastroesophageal reflux and prescribed an H2 blocker.

**Misdiagnosis**

A 2 yr old boy has been tugging at his right ear for the last week. Review of systems is otherwise negative. On exam, the boy’s right ear is red, but there is no evidence of a middle ear effusion. He is prescribed a course of amoxicillin.

**Measuring OD**

1. Randomized Trial
2. Missed diagnosis but No Harm
3. Increasing Incidence but Unchanged Outcomes
1. RCT (Breast Cancer)

90k women age 40-59 yo

\[ \text{mortality} = \text{mortality} \]

2. Missed Diagnosis, No Harm (Prostate Cancer)

3. ↑ Incidence, Unchanged Outcome (Pulmonary Emboli)
Weiner et al. BMJ. 2013.

Drivers
- Physician: unawareness of OD, discomfort with uncertainty
- System Incentives: fee for service, supply sensitive care, quality measures
- Industry
- Psychological Factors: technological imperative, belief in screening
Neuroblastoma

Table 3: Distribution of Cases of Neuroblastoma According to Stage in the Screening Group as Compared with the Children in the Control Area.*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Screening Group</th>
<th>Control Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence per 100,000 (95% CI)</td>
<td>Incidence per 100,000 (95% CI)</td>
</tr>
<tr>
<td>Stage 1</td>
<td>66 (4.4-5.3)</td>
<td>5.1 (3.9-6.2)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>40 (6.5-3.3)</td>
<td>23 (2.1-3.9)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>25 (3.9-3.2)</td>
<td>0.9 (0.7-1.1)</td>
</tr>
<tr>
<td>Stage 4</td>
<td>1.7 (1.0-2.2)</td>
<td>0.9 (0.7-1.1)</td>
</tr>
<tr>
<td>Fat stage</td>
<td>1.3 (0.7-1.9)</td>
<td>2.3 (2.0-3.7)</td>
</tr>
<tr>
<td>No.</td>
<td>25</td>
<td>15</td>
</tr>
</tbody>
</table>


Hypothesized Examples

- Aspiration
- Hypercholesterolemia
- ADHD
- Hypoxemia
- Bacteremia
- MCAD Deficiency
- Cholelithiasis
- OSA
- Food Allergy
- Skull Fracture
- GER
- UTI
- Hyperbilirubinemia
- VUR


Swallowing Abnormalities

- Potential benefit: Reduced pneumonia
- Potential harm: Altered feeding, radiation

Net Benefit?

Potential benefit: Reduced pneumonia
Potential harm: Altered feeding, radiation

Increasing VFSS Testing Among Infants

Table 4: Incidence of Stage 4 Neuroblastoma and Mortality Among Children with Neuroblastoma Diagnosed Between 12 and 60 Months of Age.*

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Control Area</th>
<th>Screening Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children (screened group)</td>
<td>Nonparticipants</td>
<td></td>
</tr>
<tr>
<td>Stage 4 neuroblastoma</td>
<td>74</td>
<td>105</td>
</tr>
<tr>
<td>Incidence per 100,000 births</td>
<td>3.8 (2.9-4.6)</td>
<td>4.4 (3.6-5.3)</td>
</tr>
<tr>
<td>Death among children with neuroblastoma</td>
<td>74</td>
<td>22</td>
</tr>
<tr>
<td>Rate per 100,000 births</td>
<td>1.3 (0.7-1.7)</td>
<td>1.4 (0.9-1.8)</td>
</tr>
</tbody>
</table>

*All children were born between 1994 and 1999, and all cases of neuroblastoma were registered by June 30, 2001. There was no significant difference in the rate of earlier end point between the entire group offered screening and the control group or between the participants in the screening program and the control group. CI denotes confidence interval.

### Swallowing Abnormalities

<table>
<thead>
<tr>
<th>VFSS Result</th>
<th>Person Months</th>
<th>HR + (95% CI)</th>
<th>Person Months</th>
<th>HR + (95% CI)</th>
<th>Person Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1 (ref) 6,335 2.18 (1.69-2.81)*</td>
<td>1 (ref) 2,070 1.56 (1.18-2.07)*</td>
<td>1 (ref) 1,935</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>1 (ref) 1,001 1.30 (0.73-2.29)</td>
<td>1 (ref) 1,003 1.21 (0.57-2.56)</td>
<td>1 (ref) 413</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPA</td>
<td>1 (ref) 175 0.59 (0.35-1.02)</td>
<td>1 (ref) 2,131 1.07 (0.45-1.43)</td>
<td>1 (ref) 1,099</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any OPA</td>
<td>1 (ref) 155 0.40 (0.15-1.07)</td>
<td>1 (ref) 534 0.53 (0.28-1.12)</td>
<td>1 (ref) 429</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thin OPA</td>
<td>1 (ref) 26 1.31 (0.26-6.76)</td>
<td>1 (ref) 1,001 2.64 (0.53-13.18)</td>
<td>1 (ref) 463</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silent OPA</td>
<td>1 (ref) 149 0.49 (0.30-0.90)</td>
<td>1 (ref) 799 0.73 (0.35-1.58)</td>
<td>1 (ref) 636</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* a Analyzed with shared frailty cox regression, adjusting for age at time of first VFSS and CCCs.

* p < 0.05

Accepted for publication at Hospital Pediatrics.

### Parent Perspective

“... It is really difficult, you are feeding all the time. He is attached and you cannot pick him up whenever you want to go.”

“... You get sarcastic looks, they see you, you are walking with this tube hanging around [your child] all the time...”

“... I'm constantly giving her medication, changing the feed, like it's a lot of work during the night, so it's really difficult for her sometimes, and us, you can't sleep because of that. We constantly have to watch the tube [to see] if it is blocked, broken, leaked, and constantly going to [the hospital].”


### Hyperbilirubinemia

**Potential benefit=**

-kernicterus prevention

**Potential harm=**

-disrupted breast feeding and bonding,

-malignancy

### Hyperbilirubinemia

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths</th>
<th>Death Rate (per million live births)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>2</td>
<td>0.37</td>
</tr>
<tr>
<td>1980</td>
<td>2</td>
<td>0.55</td>
</tr>
<tr>
<td>1981</td>
<td>1</td>
<td>0.28</td>
</tr>
<tr>
<td>1982</td>
<td>1</td>
<td>0.54</td>
</tr>
<tr>
<td>1983</td>
<td>1</td>
<td>0.27</td>
</tr>
<tr>
<td>1984</td>
<td>1</td>
<td>0.27</td>
</tr>
<tr>
<td>1985</td>
<td>1</td>
<td>0.27</td>
</tr>
<tr>
<td>1986</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1987</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1988</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1989</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1990</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1991</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1992</td>
<td>1</td>
<td>0.25</td>
</tr>
</tbody>
</table>


“The US Preventive Services Task Force (USPSTF) found inadequate evidence that treating elevated bilirubin levels in term or near-term infants to prevent severe hyperbilirubinemia resulted in the prevention of chronic bilirubin encephalopathy.”

“The USPSTF concludes that the evidence is insufficient to recommend screening infants for hyperbilirubinemia to prevent chronic bilirubin encephalopathy”

Latest Work

- Coronary Artery Abnormalities (CAA) among children with Kawasaki Disease
- Skull fractures and intracranial bleeds among children with isolated head trauma
Incidence Compared to Outcome

Disease

Bad Outcome

Year

Incidence Compared to Outcome

Disease

Bad Outcome

Year

Incidence Compared to Outcome

Disease

Bad Outcome

Year

KD and CAA background

• Retrospective cohort
• Patients ≤18 years old
• Receiving care at PHIS hospitals
• Between Jan 2000-Dec 2014
• Diagnosis of KD and received IVIG

KD and CAA background

AHA Scientific Statement

Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease
An Statement for Health Professionals From the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association

**PHIS Hospitals**

- Seattle
- Oakland
- Palo Alto
- Modesto
- Los Angeles
- Chicago
- St. Louis
- Detroit
- Indianapolis
- Milwaukee
- Chicago
- Cincinnati
- Columbus
- Akron
- Buffalo
- Boston
- Hartford
- New York
- Philadelphia
- DC
- Norfolk
- Pittsburgh
- Salt Lake City
- Denver
- Austin
- Dallas
- Fort Worth
- Corpus Christi
- Houston
- Little Rock
- New Orleans
- Birmingham
- Corpus Christi
- Miami

**CAA Bad Outcome**

- Mortality
- Diagnosis codes: cardiac arrest, heart failure, ischemic heart disease
- Procedure codes: angioplasty, CABG, heart transplant, CPR

**CAA Results**

N= 18,037 KD patients

<table>
<thead>
<tr>
<th>Outcome</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Heart Disease</td>
<td>44</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>32</td>
</tr>
<tr>
<td>Conduction Disorders</td>
<td>15</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>12</td>
</tr>
<tr>
<td>Cardiogenic Shock</td>
<td>12</td>
</tr>
<tr>
<td>Operation Vessels</td>
<td>6</td>
</tr>
<tr>
<td>Mortality</td>
<td>5</td>
</tr>
<tr>
<td>Conversion</td>
<td>4</td>
</tr>
<tr>
<td>Cardiac Arrest</td>
<td>4</td>
</tr>
<tr>
<td>Heart Replacement</td>
<td>2</td>
</tr>
</tbody>
</table>

**Latest Work**

- Coronary Artery Abnormalities (CAA) among children with Kawasaki Disease (KD)
- Skull fractures and intracranial bleeds among children with isolated head trauma
Head injury study: background

- Retrospective cohort
- Children presenting for isolated head injury to PHIS hospitals
- ED, Observation, Inpatient
- Between Jan 2001-Dec 2014
- Excluded; pre-existing neurologic illness, non-accidental trauma

Head injury study: results

<table>
<thead>
<tr>
<th>% change/year (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head CT Imaging</td>
</tr>
<tr>
<td>Skull Fracture</td>
</tr>
<tr>
<td>Intracranial Bleed</td>
</tr>
<tr>
<td>Re-visit</td>
</tr>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>Hospitalization</td>
</tr>
<tr>
<td>Neurosurgery</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, race, insurance type, presence of complex chronic condition, hospital level case mix index, clustering within hospitals
Head injury study: results

- Rate per 1,000 TBI Patients
- Fractures/Bleeds
- Re-visit
- Mortality
- Year

For every 10,000 head imaging studies avoided …
- 149 fewer fractures detected
- 49 fewer bleeds detected
- 24 fewer hospitalizations
- 1 fewer neurosurgery performed
- No apparent change in re-visit or mortality

Variation in Head CT Testing Among Children’s Hospitals, 2014

- Provided.

Limitations
- Observational design, relying on administrative data
- No imaging results
- Outcome ascertainment bias
- Mortality is rare
- Possibility that improved treatment matches increased disease

OD is Harmful
- Exposure to treatments and their side effects
- Increased medical utilization
- Opportunity cost
- Decreased quality of life
REACTIIONS TO THE THREATENED LOSS OF A CHILD: A VULNERABLE CHILD SYNDROME
Pediatrics Management of the Dying Child, Part III
Muriel Green, M.D., and Albert J. Solnit, M.D.
Departments of Pediatrics, Indiana University and Education School of Medicine

In our society, the child who loses a parent... (continues)

For some time now, observations of parents of children in our society, 英语原句未完成... (continues)

Children who are expected by their parents to do prematurely often react with a disturbance in psychological development. The repetitive quality of the pathological reactions observed, the number of patients seen, and the relief which both child and parents experience when the prediction becomes refuted through stabilization provide substantial clinical evidence that this hypothesis is a useful and significant one.

Table 1 illustrates some of the clinical data. In 24 of the 30 cases (18 boys and 6 girls) in most instances, the doctor had told the parents that the child was going to die, was likely to die, or would not live very long. In some cases the parents had been... (continues)

The Way Forward

Awareness
- Proximate v long term perspective
Medical Education
- Comfort with Uncertainty
- Stepped Diagnostic Approach
Research
Expert Panel Oversight

Summary

Children can be harmed by accurate diagnoses
Will this test find an abnormality?

Discussion

Children can be harmed by accurate diagnoses
Will this test find an abnormality?
Is the child likely to experience more benefit than harm as a result of this test?


Hypoxemia

213 infants, 1-12 mo, mild/mod bronchiolitis

True

41% hospitalized

True + 3%

26% hospitalized


Hypoxemia

615 infants, age 6 wks-12 mo, hospitalized for bronchiolitis

True

Mean LOS 50 hrs

True + 4%

Mean LOS 40 hrs


Obstructive Sleep Apnea

Potential benefit = Improved attention, behavior

Potential harm = Surgery


Obstructive Sleep Apnea

Outcome | p-value
------- | -------
NEPSY attention and executive-function | 0.16
Connor’s Caregiver Rating | 0.01
Connor’s Teacher Rating | 0.04
BRIEF Caregiver Rating | <0.01
BRIEF Teacher Rating | 0.22


Obstructive Sleep Apnea

Table 4 Maximum grade of vesicoureteral reflux in each patient at entry and at 5 years and 10 years in 102 medically managed patients, followed for up to 10 years

<table>
<thead>
<tr>
<th>Maximum grade of reflux</th>
<th>Number at entry</th>
<th>Number at 5 years</th>
<th>Number at 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV</td>
<td>83</td>
<td>51</td>
<td>22</td>
</tr>
<tr>
<td>BH</td>
<td>19</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Total with dilating reflux</td>
<td>102</td>
<td>57</td>
<td>27</td>
</tr>
</tbody>
</table>


VUR

Renal Scarring | TMP-SMX | Placebo | Absolute difference in risk (95% CI) percentage points
---------------|---------|---------|----------------------------------------
Overall        | 11.9    | 10.2    | -1.7 (-7.4 to 4.0)                    
Severe         | 4.0     | 3.6     | -0.4 (-4.7 to 1.8)                    
New            | 8.2     | 8.4     | 0.2 (4.9 to 5.3)                      
Any Cortical Defect | 12.8 | 10.6 | -2.1 (-6.0 to 1.7)                    

Inclusion Criteria:
- Age 3-36 months
- Rectal temp > 39 C

Excluded:
- Focal infection requiring abx (ie. AOM)
- Toxic appearance
- Specific viral infection
- Immunodeficiency
- Received Abx in last 48 hrs
- DPT immunization in last 48 hrs

Randomization
- Amoxicillin N= 507
- Placebo N= 448

F/U @48 hrs

Randomized N= 955

Non-Randomized N= 228

Amoxicillin N=? Placebo N=?

Total Analyzed N= 1183


Food Allergy

Potential benefit = anaphylaxis prevention

Potential harm = bullying, poor nutrition

Food Allergy


RCT: IVIG/Aspirin vs Aspirin alone