Sobrediagnóstico: Un mal que daña a nuestros niños

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Overdiagnosis: a new concept in Pediatrics

- Articles indexed in Medline with the word "overdiagnosis" in the title:
  - All articles: 679
  - Articles indexed under "child": 40
    - And some of these are about prostate cancer…
    - Only a few related to the current concept of overdiagnosis

Evolving Definition of “Overdiagnosis”

- 1977 – misattribution (true-true, unrelated): diagnosis of linea alba hernia as cause of otherwise unexplained abdominal pain; status thymicolymphaticus (1930’s and 40’s)
- 1987 – misdiagnosis: “sinusitis” based on sinus opacity on x-ray; “asthma” based on single episode of wheezing, Lyme disease diagnosed by misinterpretation of Western blot
- 1991 – true diagnosis, but without net clinical benefit: neuroblastoma screening
- 1998 – medicalization of normal variations: ADHD, pre-hypertension

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Definitions

- Overdiagnosis: a true abnormality is discovered, but detection does not benefit the patient
- Misdiagnosis: the diagnosis is not accurate
- Overtreatment: excess medication or procedures regardless of correctness of diagnosis
- Overuse: use of unnecessary screening, diagnostic, and therapeutic interventions

Focus in pediatric literature

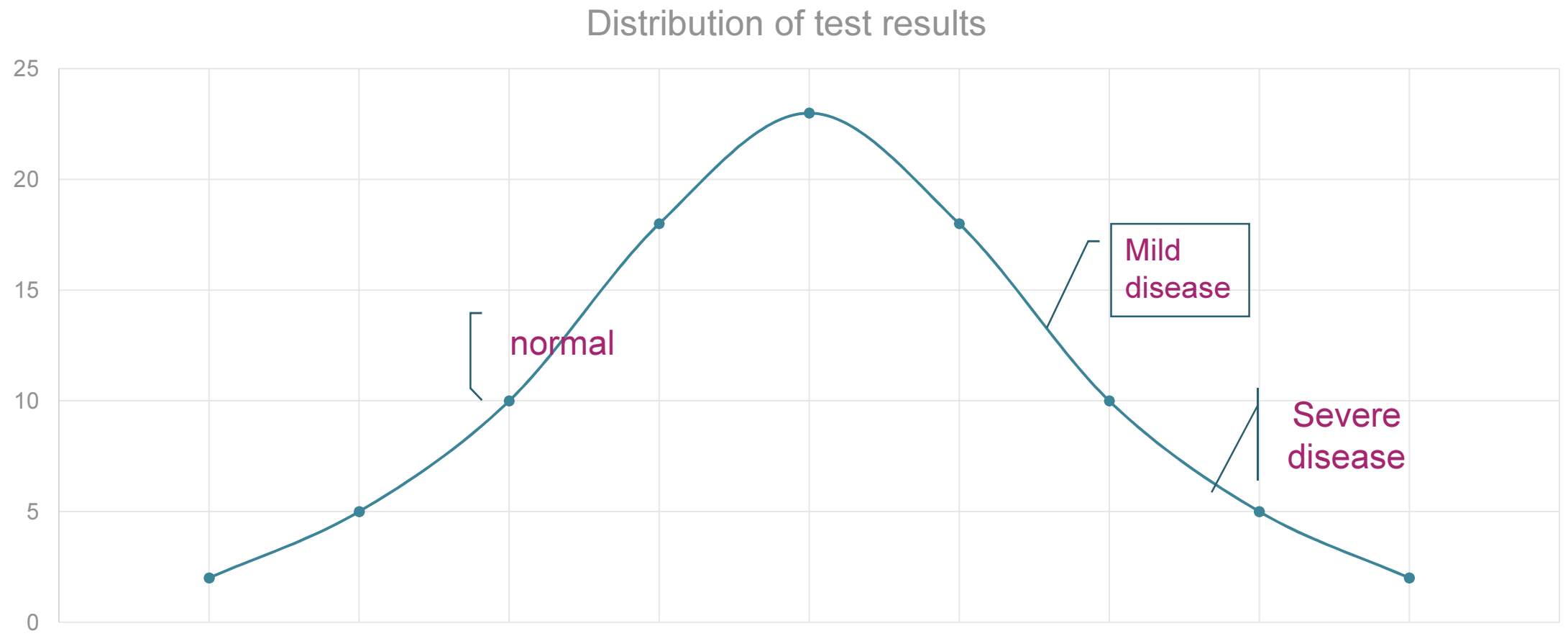
- Misdiagnosis and resultant overtreatment:
  - Otitis media, sinusitis, malaria, head lice, Lyme disease
- Medicalizing variants of normal:
  - ADHD, GER(D), mild hypoxia in bronchilolitis, mild hyperbilirubinemia, pre-disease
- True diagnosis but no net benefit of treatment
  - Neuroblastoma, food allergy, OSA, bacteruria, VUR, MCAD, skull fracture

Medicalizing variants of normal

- ADHD
  - The youngest children in a grade level are diagnosed with ADHD more often
- GER(D)
  - If spitting up in an otherwise well child (>50% do it) is labeled as having GER *disease,* parents are more likely to ask for medication
- Pre-disease
  - pre-hypertension, overweight, hyperlipidemia
- Hyperbilirubinemia
  - Bilirubin is an anti-oxidant, and nearly all infants have some elevation in bilirubin

Some new tests are too good

As test sensitivity increases, usefulness may decrease



True finding but no net benefit of treatment

- Urinary Tract Infection
  - In one study of febrile infants, 61 were expected to have UTI. None were tested, all were followed up.
  - Only 2 infants were later diagnosed with UTI, neither had adverse outcome
- Vesicoureteral Reflux
  - Most VUR resolves spontaneously, no known interventions to reduce renal scarring or insufficiency
- Developmental Hip Displasia in first weeks of life
  - >90% of sonographically abnormal hips resolve to normal within weeks to months.
- Linear skull fracture in minor head injury
  - Uniformly good outcome, but frequently subjected to hospitalization and repeat CT scanning
  - Head CT increases risk of brain cancer

Evidence for Overdiagnosis in pediatrics Example: hypoxemia in bronchiolitis

- Delayed or missed diagnosis but no evidence of harm
- Increased detection but no change in outcome
- Randomized trials

Natural Experiment: Delayed or missed diagnosis without evidence of harm

- Transient desaturations occur commonly during sleep in healthy infants
- Prospective study of desaturations in mild bronchiolitis not requiring hospitalization (N=118)
- Infants discharged from ED with O2 saturation monitor/recorder; no alarm, no display
- Follow up to determine clinical status, including return to ED and hospital admission
- 64% of infants had O2 sat<90% for at least one minute; 25% had O2 sat to 70%.
- No increase in unscheduled ED or admissions in these infants

Increased detection of “disease” but no change in outcome

- As use of pulse oximetry has increased, admissions for bronchiolitis have tripled in the US
- No change in mortality rates
- Suggests that children with very mild bronchiolitis are being diagnosed with hypoxia, and treated as if they were more severe cases of bronchiolitis

Randomized trials of screening tests

- 2 trials randomizing children with bronchiolitis to different displays of levels of hypoxia, 1 trial used intermittent vs continuous display
  - Infants with the same actual O2 Sat had different displays
- The higher the displayed O2 saturation, the lower the rate of hospitalization/ shorter the hospital stay
- The fewer children who were diagnosed with hypoxia, the less medical intervention with no change in outcomes.

True diagnosis but no net benefit from treatment

- Neuroblastoma
  - Widespread screening in Japan
- MCAD (medium chain acyl-coenzyme A dehydrogenase deficiency)
  - Some infants never become symptomatic; treatment is burdensome
- VUR (vesico-ureteral reflux)
  - Mostly resolves over time, interventions do not appear to change outcome
- Incidental finding of cholelithiasis in asymptomatic children
  - 95% have no long term symptoms or complications

Neuroblastoma

- Screening test is easy and cheap.
- Sharp increase in early stage tumors diagnosed, without change in end-stage disease or tumor mortality.
- Neuroblastoma in the <1 y.o. is biologically different, tumor usually regresses.

Neuroblastoma

TABLE 3. DISTRIBUTION OF CASES OF NEUROBLASTOMA ACCORDING TO STAGE IN THE SCREENED GROUP AS COMPARED WITH THE CHILDREN IN THE CONTROL AREA.*

STAGE	SCREENED GROUP		CONTROL AREA	
	DETECTED BY SCREENING	DIAGNOSED 12–60 MO	DIAGNOSED 12–24 MO	DIAGNOSED 12–60 MO
Stage 1				
No.	66	75	13	28
Incidence per 100,000 (95% CI)	4.5 (3.4–5.5)	5.1 (3.9–6.2)	0.6 (0.3–0.9)	1.5 (0.9–2.0)
Stage 2				
No.	39	44	9	14
Incidence per 100,000 (95% CI)	2.6 (1.8–3.5)	3.0 (2.1–3.9)	0.4 (0.1–0.7)	0.7 (0.3–1.1)
Stage 3				
No.	25	35	18	27
Incidence per 100,000 (95% CI)	1.7 (1.0–2.4)	2.4 (1.6–3.2)	0.9 (0.5–1.2)	1.3 (0.8–1.8)
Stage 4				
No.	19	50	28	74
Incidence per 100,000 (95% CI)	1.3 (0.7–1.9)	3.7 (2.7–4.7)	1.3 (0.8–1.8)	3.8 (2.9–4.6)
Any stage				
No.	149	204	68	143
Incidence per 100,000 (95% CI)	10.1 (8.5–11.7)	14.2 (12.2–16.1)	3.2 (2.4–3.9)	7.3 (6.1–8.5)

Schilling et al. *N Engl J Med*. 2002 Apr 4.

TABLE 4. INCIDENCE OF STAGE 4 NEUROBLASTOMA AND MORTALITY AMONG CHILDREN WITH NEUROBLASTOMA DIAGNOSED BETWEEN 12 AND 60 MONTHS OF AGE.*

END POINT	CONTROL AREA	SCREENING AREA		
		ALL CHILDREN	PARTICIPANTS (SCREENED GROUP)	NONPARTICIPANTS
Stage 4 neuroblastoma				
No.	74	105	50	55
Incidence per 100,000 births (95% CI)	3.8 (2.9–4.6)	4.4 (3.6–5.3)	3.7 (2.7–4.7)	5.4 (4.0–6.8)
Death among children with neuroblastoma				
No.	24	33	17	16
Rate per 100,000 births (95% CI)	1.2 (0.7–1.7)	1.4 (0.9–1.9)	1.3 (0.7–1.8)	1.5 (0.8–2.3)

*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 either 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.

Adverse effects of overdiagnosis

- Direct risk from testing:
  - Radiation risk (CT and CXR) - Increase in lifetime cancer risk
  - 2-3 head CTs triples brain cancer risk
- “Pediatric Pathogenesis”
  - “Vulnerable child syndrome”, first described in 1964 related to innocent heart murmurs
  - A disease label increased belief in medication, even knowing medication is likely not effective
  - 1/3 of kids diagnosed with food allergies are bullied, with poorer QOL

Adverse effects of overdiagnosis

- Harm due to resultant overtreatment
  - Increase in hospitalization and length of stay for bronchiolitis
  - Surgery for neuroblastoma, GERD, VUR
  - Phototherapy may be related to leukemia risk; increased mortality in one neonatal RCT
  - Antibiotic resistance (prophylaxis for VUR)
- Cost – financial and opportunity
  - Contributes to waste in the system
  - Low value care

Why do we overdiagnose?

- Uncertainty is uncomfortable
- We are afraid of missing something and looking foolish
- Pressure from colleagues
- Medico-legal fears
- Ordering fewer tests can be more difficult
  - May result in added effort in clinical follow up
  - Possibly more time on discussion with family
- Publication bias, which may limit knowledge of “negative” tests
- Economic pressure of “fee for service” payment

Physicians and patients together are ”co-conspirators in a behavioral system that often sacrifices safety for action”

Ironically, the maxim of doing something “just to be safe” may be undermining our efforts in patient safety.

Schroeder AR et al, Pediatrics, 2011

The way forward

- Education
- Better Quality Measures
- Research
- Public Campaigns

Education

- “The identification and correction of physiologic abnormalities is ingrained in medical culture” *(Quińonez and Schroeder, 2015)*
- *Primum non nocere*
  - First, do no harm
- Promote comfort with uncertainty
- Promote Value Based Care

Quality Measures

- Most measures related to diagnosis currently focus on underuse of diagnostic or screening tests
- Measures based on guideline implementation
- Develop measures based on value – what does each test or diagnosis add to the health of the patient?
- Include errors of commission in adverse event reviews
  - was the test or intervention warranted in the first place?

Research

- Identify and study potentially overdiagnosed conditions
- Critically evaluate accepted practices
  - Routine treatment of PDA
  - Long courses of IV antibiotics for osteomyelitis
  - Routine VCUG after febrile UTI
- Focus on test value, not accuracy
  - Will the patient be better off for having the test?

Public Campaigns

- Choosing Wisely
- Safely Doing Less
- Too Much Medicine

Choosing Wisely
American Academy of Pediatrics

1. Use clinical observation instead of CT for minor head injury
2. Do not use CT or MRI for simple febrile seizures
3. Do not use CT for routine evaluation of abdominal pain
4. Do not use antibiotics for apparently viral respiratory illness (sinusitis, pharyngitis, bronchitis)
5. Do not use cough and cold medications in children under 4 years old

Choosing Wisely: Pediatrics
Five more things to question:

6. Do not use high dose steroids for BPD
7. Do not use screening IgE for food allergies
   - Clinical history should guide specific testing
8. Do not treat physiologic GER (“the happy spitter”)
   - This is not a disease
9. Do not screen for asymptomatic bacteruria
   - This is also not a disease
10. Do not use home apnea monitors to prevent SIDS (SUID)

Choosing Wisely: Newborns
Five MORE things to question:

11. Do not obtain predischarge pneumograms in preterm infants
12. Avoid daily CXR for intubated infants
13. Do not obtain screening brain MRIs in preterm infants
14. Do not use anti-reflux medications for GERD or apnea/desats in preterm infants
15. Stop presumptive antibiotics after 48 hours in asymptomatic infants

Wise people saw this coming 20 years ago

Misperceptions of disease prevalence and therapeutic effectiveness can promote a cycle of increasing medical intervention, despite the best intentions of all parties. The cycle usually begins with some form of increased testing that lowers the threshold for detecting disease-such as technical improvement in imaging, more frequent testing, or closer scrutiny of the images-which immediately leads to a higher diagnostic yield of the disease and a spectrum of milder disease, which then may be unnecessarily treated with pseudosuccess.

Richard Behrman, 1996

Reading and Resources

- ***Overdiagnosed: Making People Sick in the Pursuit of Health***
  - 2011 Gilbert Welch, Lisa Schwartz, Steven Woloshin
- ***Selling Sickness***
  - 2009 Ray Moynihan and Alan Cassels
- Preventing Overdiagnosis
  - Annual Conference (Copenhagen in 2018)
  - www.preventingoverdiagnosis.net

Don’t just do something, Stand there!