Diagnosis: an impossible but essential task?

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What is this?
What is this?
Diagnosis by visual pattern matching
quick – but requires experience of pattern
Diagnosis by visual pattern matching quick – but requires experience of pattern

1. Fracture radius & ulna

2. Thenar wasting in carpal tunnel syndrome

3. Lichtenberg figures from lightening strike

4. Retinal detachment
Patterns change with time

Diagnosis not essential for spontaneously remitting diseases

Del Mar, Doust, Glasziou
Clinical Thinking: Evidence, Communication and Decision-Making
Types of Diagnostic Thinking processes

- Fast thinking:
  Intuitive, heuristic

- Slow thinking:
  analytical, deliberate
Diagnosis: 3 Stages and 14 Skills

Stage

- Initiation of the diagnosis
- Refinement of the diagnostic causes
- Defining the final diagnosis

Strategy

- Spot diagnoses
- Self-labelling
- Presenting complaint
- Pattern recognition

Heneghan, Glasziou, Thompson et al. Diagnostic strategies used in primary care BMJ 2009
Lately I feel **tired** all the time …

Patient 1: Few specific features,
- But Beck DI suggested depression
- Inquiry -> **Depressed**

Patient 2: Few specific features,
- But on taking BP, noted pulse of 30
- **Complete Heart Block**
Diagnosis: 3 Stages and 14 Skills

**Stage**

- Initiation of the diagnosis
- Refinement of the diagnostic causes
- Defining the final diagnosis

**Strategy**

- Spot diagnoses
- Self-labelling
- Presenting complaint
- Pattern recognition
- Restricted Rule Outs
- Stepwise refinement
- Probabilistic reasoning
- Pattern recognition fit
- Clinical Prediction Rule
- Known Diagnosis
- Further tests ordered
- Test of treatment
- Test of time
- No label

Heneghan, BMJ 2008
Tired: Is the patient anaemic?

302 patients scored by 3 clinicians vs Hemoglobin
Scores for agreement between paired observers were
κappa = 0.75 between observers A and B and
κappa = 0.54 between observers A and C.
Conjunctival pallor for anaemia

- Sensitivity = 55%; Specificity = 75%

Sensitivity = 50%; Specificity = 50%

Positive test  |  Negative test

Table 3. Likelihood Ratios for Conjunctival Pallor with Anemia Defined as Hemoglobin ≤ 90 g/L

<table>
<thead>
<tr>
<th>Pallor</th>
<th>Hemoglobin ≤ 90 g/L (n)</th>
<th>Hemoglobin ≥ 91 g/L (n)</th>
<th>Likelihood Ratios (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>8</td>
<td>8</td>
<td>4.49 (1.80, 10.99)</td>
</tr>
<tr>
<td>Borderline</td>
<td>22</td>
<td>55</td>
<td>1.80 (1.18, 2.62)</td>
</tr>
<tr>
<td>Absent</td>
<td>25</td>
<td>184</td>
<td>0.61 (0.44, 0.80)</td>
</tr>
</tbody>
</table>
Clinical Rules: combine several weakly predictive symptoms, signs, and tests

- Charchot’s triad – 1880’s
  - jaundice; fever; RUQ pain

- Apgar score – 1953
  - 0–10 Scale

- Ottawa Rules
  - Ankle
  - Knee
  - Cervical spine

- Well’s DVT & PE rules
Clinical Prediction Rules as ‘instant’ experience

MDCalc – free App, 170 prediction rules; 53 for GPs
Half GP consultations are for 30 conditions
Other half are for over 800 conditions

Core topics: Must know (almost) everything
“Just in case” learning

Must know some basics
“Just in time” learning

The number of diseases/diagnoses

NLM MetaThesaurus - 875,255 concepts

Diagnosis Pro (www.diagnosispro.com)
- 13,000 diseases;
- 30,000 abnormalities (symptoms, signs, tests)

1 disease per day for 40 years

How many rare diseases are there?

There are thousands of rare diseases. To date, six to seven thousand rare diseases have been found and approximately five new diseases are described every week in the medical literature. This number also depends upon the accuracy of the...
- 6-8,000 rare* diseases
- 7% of population
- 68% saw 3+ doctors before diagnosed

*Rare = less than 5/10,000
S yndrome W ithout A Name

We support families and those affected by a syndrome without a name

Hysteria or syringomyelia? (From: Toscanini's Fumble)
Summary so far

- Diagnosis uses both fast & slow processes
- Fast ("intuition") requires experience
- CPG’s provide “experience”
- Over 10,000 diseases
- $\frac{1}{2}$ consults involve 30 conditions

www.bmj.com/specialties/diagnosis-general-practice
Overdiagnosis

oh darling... what a pity...
I think your interesting personality
has just been classified as
a personality disorder.

Allen Frances
Chair DSM IV

normal (nərˈməl) 1. an insider’s revolt against out-of-control psychiatric diagnosis, DSM-5, big pharma, and the medicalization of ordinary life

Allen Frances, M.D.
*Chair of the DSM-IV Task Force
Three types of Overdiagnosis

1. Overdetection

2. Overdefinition

3. Medicalization
A. Overdetection: a thyroid cancer ‘epidemic’?

Thyroid cancer tripled in 25 years; no more deaths

Screening for Thyroid Cancer

Since South Korea adopted widespread cancer screening in 1999, thyroid cancer has become the most diagnosed cancer in the country. But if this early detection were saving lives, the already-low death rate from thyroid cancer should have fallen, not remained steady.

NEW CASES AND DEATHS FROM THYROID CANCER
Per 100,000 people

South Korea begins a national screening program

New cases in South Korea

New cases in the U.S.

Deaths in both countries

Sources: New England Journal of Medicine; National Cancer Institute
By The New York Times

Notes:
1. Incidence and mortality rates are age standardised to the Australian population as at 30 June 2001 and are expressed per 100,000 population.
2. Survival data for this figure are presented in online Table S26.3.
Source: AIHW Australian Cancer Database (2007); AIHW 2010b.

Figure 4.73: Yearly trends in incidence, mortality and 5-year relative survival of thyroid cancer, 1982 to 2007
Overdetection

**CANCER**
Increase in adult cancer incidence: 1980 to 2010

- **Breast Cancer**: 1.4-fold increase
- **Thyroid Cancer**: 3-fold increase
- **Prostate Cancer**: 2-fold increase
- **Renal Cancer**: 2-fold increase
**MUSCULOSKELETAL**
Imaging findings in 50-60 yr old **asymptomatic** adults

- Ultrasound shoulder
  - Rotator cuff tear – 13%
- MRI Spine
  - Disc bulge – 78%
  - Disc protrusion – 28%
- MRI Knee
  - Meniscal damage – 20%
  - Any abnormality – 84%

**CANCER**
Increase in adult cancer incidence: 1980 to 2010

- Thyroid Cancer
  - 3-fold increase
- Breast Cancer
  - 1.4-fold increase
- Renal Cancer
  - 2-fold increase
- Prostate Cancer
  - 2-fold increase
B. Expanding definitions of Diabetes

US Prevalence by age

- 20-44: 3.7%
- 45-64: 13.7%
- ≥65: 26.9%

Change of Definition

“Under the new guidelines, at least 1 million Americans (and possibly more) with fasting plasma glucose levels of 126 to 140 mg/dL... will now be informed that they harbor a disease.”

2003 ADA update
A Tale of Two GDM Definitions

- **2008**: New criteria for Gestational Diabetes (GDM) by International Association of Diabetes in Pregnancy Study Group (IADPSG)
  - Increase GDM diagnoses from 6% (WHO) to 18% (IADPSG)
  - **Cost** extra $US2.5 billion/year

- **2013**: NIH NO evidence treatment of new cases improve outcomes
Of 16 publications on 14 common conditions, 10 widened and 1 narrowed definitions.

Widen by 3 methods: (i) “pre-disease”; (ii) lowering thresholds; (iii) earlier or new diagnostic methods.

CONCLUSION:
“research and policy attention might be directed at designing new processes for reviewing disease definitions, free of financial conflicts of interest and informed by rigorous analysis of benefits and harms.”
Then you might have
“Body Dysmorphic Disorder by Proxy”
Medicalization of normal aging
Overdiagnosis is hidden in the garden of diagnosis

http://natassatriviza.com/pepperdine/weekfive.html
Diagnosis: impossible but essential task

Diagnosis:

- Requires fast and slow thinking
- An essential skill; but not essential for every presentation
- Half consultations involve 30 conditions; but other half involves 1,000s
- Overdiagnosis is a growing problem

www.bmj.com/specialties/diagnosis-general-practice
www.preventingoverdiagnosis.net
A. Overdetection: 4 cancers

An epidemic of diagnosis, not an epidemic of cancer!

Source: AIHW
Incidentalomas in MRI of spine

% of asymptomatic patients with MRI

Disc Bulge
Disc Protrusion

20-29 30-39 40-49 50-59 >60

Jensen MC, NEJM, 1994

Disc protrusion in 24 year old with no back pain
Incidental findings with MRI of head

Frequency of incidental findings with MRI of head: a meta-analysis

<table>
<thead>
<tr>
<th></th>
<th>Prevalence (%)</th>
<th>NNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arachnoid cyst</td>
<td>0.5</td>
<td>200</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>0.35</td>
<td>286</td>
</tr>
<tr>
<td>Meningioma</td>
<td>0.3</td>
<td>345</td>
</tr>
<tr>
<td>CCM</td>
<td>0.16</td>
<td>625</td>
</tr>
<tr>
<td>AVM</td>
<td>0.05</td>
<td>2,000</td>
</tr>
<tr>
<td>Low grade glioma</td>
<td>0.05</td>
<td>2,000</td>
</tr>
</tbody>
</table>

*Victims of Modern Imaging Technology*  *BMJ 2009;339:b3016*

For most, treatment is *not needed* or is *harmful*. SIGN Guidelines suggest: “DO NOT do MRI unless ...”
"A well person is someone who has not been completely worked up."

- Clifton Meador
Declining thresholds; increasing prevalence

LOWERING OF THE CVD RISK THRESHOLD

5-year CVD risk threshold
1990’s New Zealand 15%

CVD Risk Groups: Cumulative % of 30-79yr olds

Proportion of CVD events covered
Declining thresholds; increasing prevalence

**LOWERING OF THE CVD RISK THRESHOLD**

5-year CVD risk threshold

- 1990’s New Zealand: 15%
- 2001 - Australia: 10–15%
- 2006 - NICE (UK): 10%
- 2014 - NICE (UK): 5%
- 2014 - CC-AHA (USA): 3.75%
  (* CC-AHA is 7.5% in 10-yrs)

CVD Risk Groups: Cumulative % of 30-79yr olds
Saving Normal

**DSM 5 Is Guide Not Bible—Ignore Its Ten Worst Changes**

APA approval of DSM-5 is a sad day for psychiatry

Post published by Allen J. Frances, M.D. on Dec 02, 2012 in DSM5 in Distress

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**Sackett’s “Normal”s**

<table>
<thead>
<tr>
<th>Number</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Gaussian: the mean ± 2 standard deviations (SD) – this one assumes a normal distribution for all tests and results in all “abnormalities” having the same frequency.</td>
</tr>
<tr>
<td>2.</td>
<td>Percentile: within the range, say of 5–95% – has the same basic defect as the Gaussian definition. Implies a specificity of 95% but with unknown sensitivity.</td>
</tr>
<tr>
<td>3.</td>
<td>Culturally desirable: when “normal” is that which is preferred by society, the role of medicine gets confused.</td>
</tr>
<tr>
<td>4.</td>
<td>Risk factor: carrying no additional risk of disease; nicely labels the outliers, but does changing a risk factor necessarily change risk?</td>
</tr>
<tr>
<td>5.</td>
<td>Diagnostic: range of results beyond which target disorders become highly probable; the focus of this discussion.</td>
</tr>
<tr>
<td>6.</td>
<td>Therapeutic: range of results beyond which treatment does more good than harm; means we have to keep up with advances in therapy!</td>
</tr>
</tbody>
</table>

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Allen Frances, Chair DSM IV

**saving**

1. an insider’s revolt against out-of-control psychiatric diagnosis, DSM-5, big pharma, and the medicalization of ordinary life

**Allen Frances, M.D.**

Chair of the DSM-IV Task Force
What can we do?

1. Raise awareness
2. Inform patients of pros & cons
3. Guidelines for disease definitions
4. Invest in research & policy initiatives
5. …
1 Raise Awareness: #Overdiagnosis

Launch in April, 6 Colleges
2 Inform patients of pros and cons

- Patients overestimate benefits and underestimate harms (of screening, treatments, etc)
- Informing patients often dampens enthusiasm
- Two processes
  - For individuals: shared decision making
  - For policy: community juries
3 Guidelines for disease definitions

Expanding Disease Definitions in Guidelines and Expert Panel Ties to Industry: A Cross-sectional Study of Common Conditions in the United States

Raymond N. Moynihan¹, Georgia P. E. Cooke¹, Jenny A. Doust¹, Lisa Bero², Suzanne Hill³, Paul P. Glasziou¹

¹Bond University, Robina, Australia; ²University of California, San Francisco, San Francisco, California, United States of America; ³Australian National University, Acton, Australia

- Guidelines being developed by GIN, GRADE, WHO collaboration
- 1-day Meeting: August 2014
- Position paper: 2015
“Our combined resources are a few $million, but for those promoting overdiagnosis it is $billions. It is a David and Goliath struggle.”

Allen Frances
Chair DSM IV
What can we do?

1. Raise awareness
2. Inform patients of pros & cons
3. Guidelines for disease definitions
4. Invest in research & policy initiatives
5. …

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Meniscal tears: MRI vs pain

Before You Go for Surgery...
A study showed that frequent knee pain and stiffness may have nothing to do with the knee injury called a meniscal tear but may be related to arthritis.

Patients with evidence of Osteoarthritis

<table>
<thead>
<tr>
<th>Had pain</th>
<th>Patient had one or more meniscal tears</th>
<th>No meniscal tear</th>
</tr>
</thead>
<tbody>
<tr>
<td>63%</td>
<td></td>
<td>37%</td>
</tr>
<tr>
<td>No pain</td>
<td></td>
<td>40%</td>
</tr>
</tbody>
</table>

Source: Dr. David T. Felson, Boston University School of Medicine

THE NEW YORK TIMES
Beware pseudo-diseases

- **1800’s – diseases**
  - Germ theory; endocrine; etc

- **1900’s – risk factors**
  - Hypertension; hypercholesterolemia; etc

- **2000’s – risk factors for risk factors**
  - Pre-hypertension; pre-diabetes; etc

100% fatality rate!
Alicia decided the doctor was over-zealous when he recommended Alzheimer screening on her 25th birthday.
Surgery, drug side effects, even death. Yet, most over-diagnosis sufferers are not even aware they’re part of this epidemic!

Hum—must be Disease De-Awareness Day

MILLIONS SUFFERING FROM DISEASES THEY DON'T HAVE

Proposed Psychiatrists' Disorders:
1. MANIC AGGRESSIVE DIAGNOSIS (M.A.D.)

Knowing they did not need definitive research, an accurate test or effective treatment made developing new conditions for DSM-6 so much easier.
Why does Overdiagnosis matter?

Too much testing of well people and not enough care for the sick worsens health inequalities and drains professionalism, harming both those who need treatment and those who don’t.”

Margaret McCartney, GP Glasgow, Author of “The Patient Paradox”. 

Paul Glasziou professor¹, Ray Moynihan senior research fellow¹, Tessa Richards analysis editor², Fiona Godlee editor in chief²

¹Bond University, Robina, QLD 4226, Australia; ²BMJ, London WC1H 8JR, UK
Osteoporosis: Prevalence for changed definition

EXHIBIT 3
Comparison Of Prevalence Of Osteoporosis At Different Disease Definitions, With Ten-Year Risk Of Hip Fracture, For Women Age Fifty And Older, United States, 2000

<table>
<thead>
<tr>
<th>Percent</th>
<th>Ten-year risk of hip fracture</th>
<th>Osteopenic definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>Black</td>
<td>Orange</td>
</tr>
<tr>
<td>60</td>
<td>Gray</td>
<td>Orange</td>
</tr>
<tr>
<td>45</td>
<td>Gray</td>
<td>Orange</td>
</tr>
<tr>
<td>30</td>
<td>Gray</td>
<td>Orange</td>
</tr>
<tr>
<td>15</td>
<td>Gray</td>
<td>Orange</td>
</tr>
<tr>
<td>0</td>
<td>Gray</td>
<td>Orange</td>
</tr>
</tbody>
</table>

NOTE: For explanation of disease definitions, see text.
M. Brooke Herndon et al. Health Aff 2007;26:1702-1711
The many processes of diagnosis

1. Diagnosis uses several processes
   1. Pattern matching
   2. Hypothesis & deduction
   3. Stepwise refinement

2. “EBM” for diagnosis
   1. Using literature for test accuracy
   2. Sensitivity; specificity

3. … but there are some short cuts
   1. Clinical Prediction Rules
Many diagnosis don’t have clear “pattern”, e.g., fatigue, dyspepsia, shortness of breath, …

Usually no individual feature is 100% sensitivity or specific
Topic 1: Diagnosis by pattern matching

What is the diagnosis?
Topic 1: Diagnosis by pattern matching
What is the diagnosis?

1. Fracture radius & ulna
2. Thenar wasting in carpal tunnel syndrome
3. Melanoma
4. Retinal detachment
We learn basic patterns
Then see them in new situations.
Diagnosis and level of experience with a presentation

1. No experience: use first principles / processes
   Vascular, Infection/Inflammatory, Neoplastic, Degenerative, Intoxication/iatrogenic, Congenital, Allergic, Traumatic, ...

2. Some experience: known differential diagnosis
   What is common/important?
   How to rule these in/out?

3. Great Experience: Pattern Matching
   (shortcut? Clinical prediction rule)
Diagnosis: Partly (learned) intuition, partly analysis

**Stage**

1. Initiation of the diagnosis
2. Refinement of the diagnostic causes
3. Defining the final diagnosis

**Strategy**

- Spot diagnoses
- Self-labelling
- Presenting complaint
- Pattern recognition
- Restricted Rule Outs
- Stepwise refinement
- Probabilistic reasoning
- Pattern recognition fit
- Clinical Prediction Rule
- Known Diagnosis
- Further tests ordered
- Test of treatment
- Test of time
- No label

Heneghan, BMJ 2008
3. We can’t know all diseases

Could this be PFAPA?

- Recurrent sore throat, sore mouth, fever (every 4-5 weeks)
Patient -> Paediatrician -> ENT - GP
30 most common consults = 48%


<table>
<thead>
<tr>
<th>Rank</th>
<th>Problem type</th>
<th>Percent of problems (n=305 738)</th>
<th>Rate per 100 encounters (n=194 100)</th>
<th>Rank</th>
<th>Problem type</th>
<th>Percent of problems (n=305 738)</th>
<th>Rate per 100 encounters (n=194 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hypertension</td>
<td>5.7</td>
<td>9.0</td>
<td>16</td>
<td>Test results</td>
<td>1.2</td>
<td>1.8</td>
</tr>
<tr>
<td>2</td>
<td>Immunisation/ vaccination: all</td>
<td>4.2</td>
<td>6.7</td>
<td>17</td>
<td>Urinary tract infection</td>
<td>1.1</td>
<td>1.8</td>
</tr>
<tr>
<td>3</td>
<td>Acute upper respiratory tract infection</td>
<td>3.3</td>
<td>5.1</td>
<td>18</td>
<td>Dermatitis, contact/allergic</td>
<td>1.0</td>
<td>1.6</td>
</tr>
<tr>
<td>4</td>
<td>Depression</td>
<td>2.9</td>
<td>4.6</td>
<td>19</td>
<td>Pregnancy</td>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>5</td>
<td>Diabetes: non-gestational</td>
<td>2.3</td>
<td>3.7</td>
<td>20</td>
<td>Sleep disturbance</td>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>6</td>
<td>Lipid disorders</td>
<td>2.1</td>
<td>3.4</td>
<td>21</td>
<td>Sinusitis acute/chronic</td>
<td>0.9</td>
<td>1.4</td>
</tr>
<tr>
<td>7</td>
<td>General check-up</td>
<td>1.9</td>
<td>3.0</td>
<td>22</td>
<td>Gastroenteritis</td>
<td>0.8</td>
<td>1.3</td>
</tr>
<tr>
<td>8</td>
<td>Osteoarthritis</td>
<td>1.7</td>
<td>2.7</td>
<td>23</td>
<td>Vitamin/nutritional deficiency</td>
<td>0.8</td>
<td>1.3</td>
</tr>
<tr>
<td>9</td>
<td>Back complaint</td>
<td>1.7</td>
<td>2.6</td>
<td>24</td>
<td>Malignant neoplasm of skin</td>
<td>0.8</td>
<td>1.3</td>
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<tr>
<td>10</td>
<td>Prescription</td>
<td>1.6</td>
<td>2.5</td>
<td>25</td>
<td>Abnormal test results</td>
<td>0.8</td>
<td>1.2</td>
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<tr>
<td>11</td>
<td>Oesophagus disease</td>
<td>1.6</td>
<td>2.4</td>
<td>26</td>
<td>Atrial fibrillation/flutter</td>
<td>0.8</td>
<td>1.2</td>
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<tr>
<td>12</td>
<td>Female genital check-up</td>
<td>1.5</td>
<td>2.4</td>
<td>27</td>
<td>Oral contraception</td>
<td>0.8</td>
<td>1.2</td>
</tr>
<tr>
<td>13</td>
<td>Acute bronchitis/ bronchiolitis</td>
<td>1.5</td>
<td>2.3</td>
<td>28</td>
<td>Solar keratosis/sunburn</td>
<td>0.8</td>
<td>1.2</td>
</tr>
<tr>
<td>14</td>
<td>Asthma</td>
<td>1.3</td>
<td>2.1</td>
<td>29</td>
<td>Ischaemic heart disease</td>
<td>0.7</td>
<td>1.1</td>
</tr>
<tr>
<td>15</td>
<td>Anxiety</td>
<td>1.2</td>
<td>2.0</td>
<td>30</td>
<td>Viral disease, not otherwise specified</td>
<td>0.7</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>Cumulative total top 15</td>
<td>34.6%</td>
<td>–</td>
<td></td>
<td>Cumulative total top 30</td>
<td>47.8%</td>
<td>–</td>
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