

# Evaluating biomarkers: Creating an evidence base

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Pathology: the science behind the cure

# The National Pathology Catalogue

- Initiative from Department of Health, UK
- Driven by 'Connecting for Health'
- Priorities:
  - 'Order communications'
  - UK-wide entry of results into Electronic Patient Record
- Requires an agreed list of tests that can be used for NHS patients
- But there are consequences and possibilities...

# Consequences of a National Pathology Catalogue

- Agreed terminology
- Unified reference ranges
- **A system to agree what should be in the catalogue now**
- **A system to keep the catalogue up to date in the future**

# Catalogue content?

- **Test name and code**
- Sample type(s)
- Reference ranges
- When to use, when not to use, level of evidence
  - Clinical validity / utility in known populations
  - Current level of evidence, need for research
  - *Probably by hyperlink to other data repository(ies)*
- Recommendation for NHS use
  - Any limits on who may request
- Etc, etc.

# Possibilities of a National Pathology Catalogue

- Source of guidance
  - For doctors, on how (and how not) to use a test
  - For commissioners / managers, on whether to pay for it
  - For researchers, on where the evidence is lacking
  - For patients – especially re. direct to consumer tests
- Simplified route to market acceptance
  - Clarification of what evidence is needed
- Development of expert systems

***All depends on high-quality evidence and decision-making***

# Evaluation for clinical use

- Analytical validity
- Clinical validity
- Clinical utility
- Ethical, legal, social, financial...

# Current evaluation systems

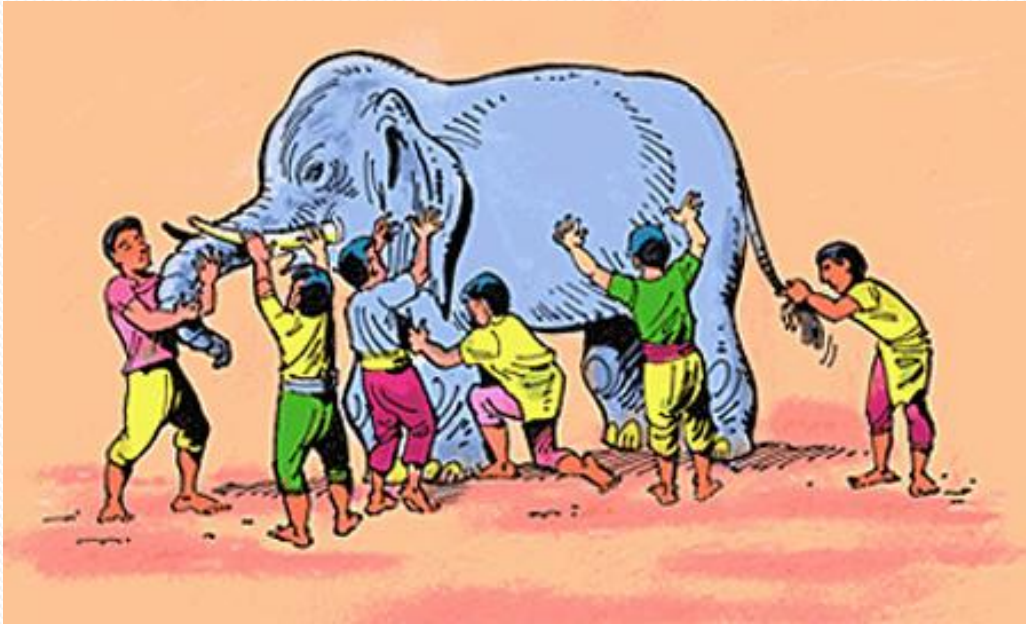
- FDA
  - Does not consider clinical utility
- AMA's Current Procedural terminology (CPT) programme
  - Does not consider clinical utility; opaque?
- Lists from commercial providers
  - Do not provide evidence
- NICE (UK)
  - Considers only a few 'big ticket' issues
- NHS Centre for Evidence-based Purchasing
  - Selective; concentrates mainly on purchasable devices
- Etc, etc...

# The breadth of the problem

- Expensive expression array relevant to a common cancer
  - Needs thorough challenge-proof evaluation – NICE?
- Biomarker for appropriate drug use
  - Evaluate as part of drug evaluation
- Rare but expensive test (e.g. mass spectroscopy to identify amyloid type)
  - Limit to reference centre, only when specific treatment decision depends on it
- Single gene germline genetic test
  - UKGTN's 'Gene Dossier' system
- Rare but cheap test
  - Single antibody immunohistochemistry to confirm a rare tumour type
- Completely non-commercial test...



# The breadth of the problem



*It was six men of Indostan  
To learning much inclined,  
Who went to see the Elephant  
(Though all of them were blind),  
That each by observation  
Might satisfy his mind.*

*The First approached the Elephant,  
And happening to fall  
Against his broad and sturdy side,  
At once began to bawl:  
"God bless me! but the Elephant  
Is very like a wall!"*

## RECENT ADVANCES

# Skin biopsy: a new tool for diagnosing peripheral neuropathy

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**BMJ 2007;334:1159-62**  
doi:10.1136/bmj.39192.488125.BE

The prevalence of peripheral neuropathy is about 2% in the general population, but it rises to 12% and 17% in people with one or two recognised risk factors.<sup>1</sup> Diabetes is one such risk factor and the most common cause of this disorder—about half of patients who have had diabetes for 25 years have peripheral neuropathy. The early symptoms of diabetic neuropathy and other peripheral neuropathies are due to degeneration

thinly myelinated A $\delta$  fibres, which carry thermal and pain sensation from the skin to the spinal cord and eventually the brain. Pain induced by non-painful touch stimuli (dynamic mechanic allodynia) is due to large fibre dysfunction and thus is mild or absent in small fibre neuropathy.

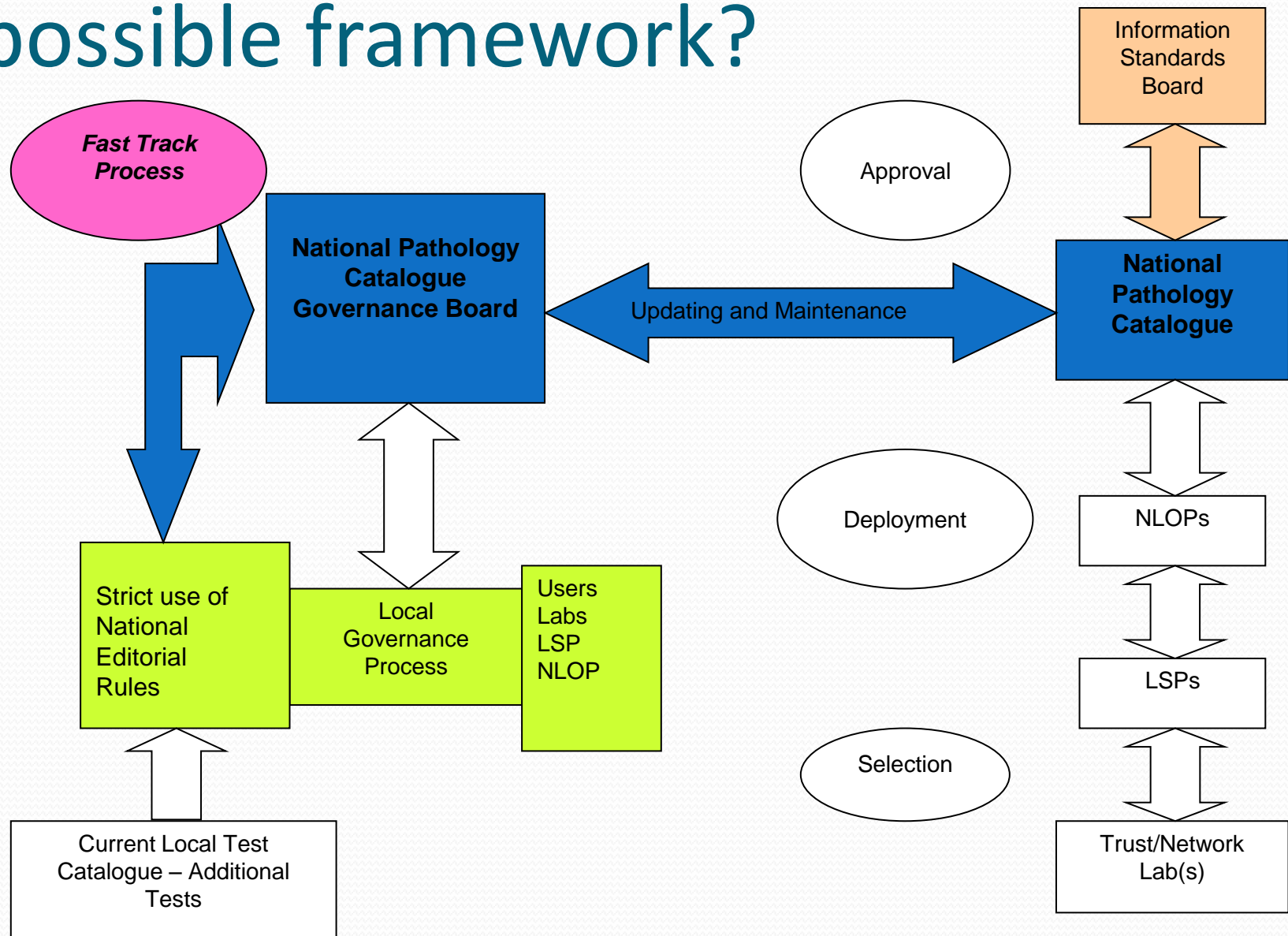
Pinprick and thermal sensation may be reduced in the feet or soles, while light touch and vibratory sense

Purely 'academic' suggestion

No patent, no CE mark, no financial backing, no commercial possibilities

Evidence debateable; no discussion or evaluation of clinical utility.

# Pathology catalogue governance: A possible framework?



# How to collect data?

## – Current tests

- Huge task
- Arguably unnecessary for inclusion in catalogue
- But vital for ‘added value’ functions
- **Model on & link to current ‘E-Learning for Health’ project in pathology**
  - Heavily moderated ‘Wiki’ approach
  - Involve trainees
  - Moderated input from anyone

# RCPATH 'Pathopedia':

- **Editorial Board**

- An Editorial Board has been recruited from the College Fellows and represents experts from all seven major college disciplines (histopathology, haematology, microbiology, biochemistry, virology, immunology and genetics).

- **Creating the initial critical mass of content**

- To be of value the Pathopedia needs a critical mass of content at the launch. To achieve this we plan to recruit all the current trainees across all specialties to help write the initial material.

There are over 1000 trainees and we would require that they each write two pages of content within three months and a total of four within a year.

# Repository for information collected?

The screenshot shows the Lab Tests Online UK website. The browser's address bar displays "Lab Tests Online UK: Welcome!". The website header features the "Lab Tests Online UK" logo, a tagline "A public resource on clinical lab testing from the laboratory professionals who do the testing", and the values "Peer-reviewed", "Non-commercial", and "Patient-centred". A navigation bar includes a "HOME" link and flags for other countries: AU, ES, DE, HU, IT, PL, and US. A search box with the text "Search Here" and a "GO" button is present. The main content area is divided into a left sidebar with links like "in the news", "understanding your tests", "inside the lab", "about this site", "site map", "send us your comments", and "home". The central text area is titled "Lab Tests Online goes Multi-Lingual" and discusses the launch of new websites in Spanish, German, Polish, Hungarian, Italian, and Australian sites. It also mentions that several other European countries have recently decided to provide LTO in their language, including France, Greece, and most recently Portugal. A "Tests" dropdown menu is visible, listing "5-HIAA", "test not listed?", "ACE", "ACTH", and "AFB Smear and Culture". Below it, a "Conditions & Diseases" dropdown menu lists "Alcoholism", "Allergies", "Alzheimer's Disease", "Anaemia", and "Angina Pectoris". The browser's status bar at the bottom shows "Done", "Internet", and "100%".

Lab Tests Online UK: Welcome!

**Lab Tests Online UK**  
A public resource on clinical lab testing from the laboratory professionals who do the testing

Peer-reviewed  
Non-commercial  
Patient-centred

HOME AU ES DE HU IT PL US

Use the search box and menus below to quickly navigate the Lab Tests Online site:

**in the news**

**understanding your tests**

**inside the lab**

**about this site**

**site map**

**send us your comments**

**home**

**Lab Tests Online goes Multi-Lingual**

New Lab Tests Online websites have been launched over the last few months on Spanish, German, Polish, Hungarian, Italian and Australian sites. Several other European countries have recently decided to provide LTO in their language including France, Greece and most recently Portugal.

The content on these new sites reflects the practice of medicine and laboratory science in these countries and therefore may be different to that on the UK site. Lab Tests Online UK is designed to help you, the patient, understand the way lab tests are used to diagnose, monitor and screen for a broad range of conditions and diseases. It was made possible by a unique collaborative partnership between the Association for Clinical Biochemistry and the American Association for Clinical Chemistry.

Search Here GO

**Tests**

- 5-HIAA
- test not listed?
- ACE
- ACTH
- AFB Smear and Culture

**Conditions & Diseases**

- Alcoholism
- Allergies
- Alzheimer's Disease
- Anaemia
- Angina Pectoris

Done Internet 100%

# How to collect data?

## – New tests

- Initial submission of argument and evidence
- Decision on how to evaluate
  - Proportionate to nature of test
- Call for other views
- Literature search and analysis
- Publication of conclusion (INCLUDING tests rejected for NHS use) with strength of evidence
- Calls for new research
- Ongoing ‘moderated Wiki’ and review of evidence

***Foreseeable problems???***

# Don't be defeatist. It's been done before.

The screenshot shows a web browser window displaying the British National Formulary (BNF) website. The browser's address bar shows "Log in: British National Formulary". The website header includes the BNF logo, the text "British National Formulary", and a search bar. Below the header is a navigation menu with links for Home, Contents, Print, Feedback, and Help. The main content area features a breadcrumb trail "Home > British National Formulary" and a prominent "Please log in" heading. A message explains that additional authentication is required for access. A "Sections" section contains a link for "What's new?". A purple box contains a "Log in" heading and a form with fields for "Email" and "Password", a "Login" button, and a link to "terms and conditions". A footer link says "Login via Athens or your home". The browser's taskbar at the bottom shows the "Internet" icon and a 100% zoom level.

Log in: British National Formulary

BNF  
56  
British National Formulary

Search  
Interactions

Home Contents Print Feedback Help

Home > British National Formulary

## Please log in

The page you have requested to view requires additional authentication. Access to the publications on this website requires registration and login.

### Sections

[What's new?](#)

Published jointly by the BMJ Group and RPS Publishing (a wholly-owned publishing organisation of the Royal Pharmaceutical Society of Great Britain)

Compiled with the advice of clinical experts, the *British National Formulary (BNF)* provides up-to-date guidance on prescribing, dispensing and administering medicines.

### Log in

Please log in or choose from the options below.

Email

Password

Login

By logging in you are agreeing to abide by our [terms and conditions](#).

• [Login via Athens or your home](#)

Internet 100%



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## 3.9 Cough preparations

### 3.9.1 Cough suppressants

The drawbacks of prescribing cough suppressants are rarely outweighed by the benefits of treatment and only occasionally are they useful, as, for example, if sleep is disturbed by a dry cough. Cough suppressants may cause sputum retention and this may be harmful in patients with chronic bronchitis and bronchiectasis.

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Cautionary label wordings, see inside back cover

## PHOLCODINE

*Indications:* dry or painful cough

*Cautions; Contra-indications; Side-effects:* see under Codeine Phosphate

### Pholcodine Linctus, BP

*Linctus*, pholcodine 5 mg/5 mL in a suitable flavoured vehicle, containing citric acid monohydrate 1%. Net price 100 mL = 25p

*Dose:* 5–10 mL 3–4 times daily; CHILD 5–12 years 2.5–5 mL

Available from APS, Boehringer Ingelheim (Pavacol-D<sup>®</sup>, sugar-free), Galen (Galenphol<sup>®</sup>, sugar-free), Norton

Prices are **net**, see p.1

