MANCHESTER 1824
The University of Manchester

NICE
National Institute for Health and Care Excellence

How can I work collaboratively with NICE to increase my research impact?

Friday 28 February 2020

Time	Session title & Speakers
9:30 – 9:45	**Welcome and introductions** Rachel Elliott, Professor of Health Economics
9:45 - 10:15	**What is NICE, what does it do and what does the future hold?** Judith Richardson, NICE Deputy Medical Director & Programme Director
10:15 – 11:00	**From research to guidance to evidence gaps** Kay Nolan, NICE Associate Director
11:00 – 11:15	Coffee break
11:15 – 12:00	**Relationship between NICE and University researchers can be synergistic: here's how!** Peter Clayton, Deputy Dean of the Faculty of Biology, Medicine and Health Colm Leonard, NICE Consultant Clinical Adviser
12:00 – 12:45	**Case studies** • **How research has influenced NICE guidelines and changed public behaviour** Ann Webb, Professor of Atmospheric Radiation and Lesley Rhodes, Clinical Professor of Experimental Dermatology • **How Robot Analyst is addressing a service need within NICE** Sophia Ananiadou, Professor of Computer Science
12:45 – 13:00	**Closing remarks** Shaheen Hamdy, Associate Dean for REF and Impact, Professor of Neurogastroenterology
13:00 – 14:00	Networking lunch

NICE National Institute for Health and Care Excellence

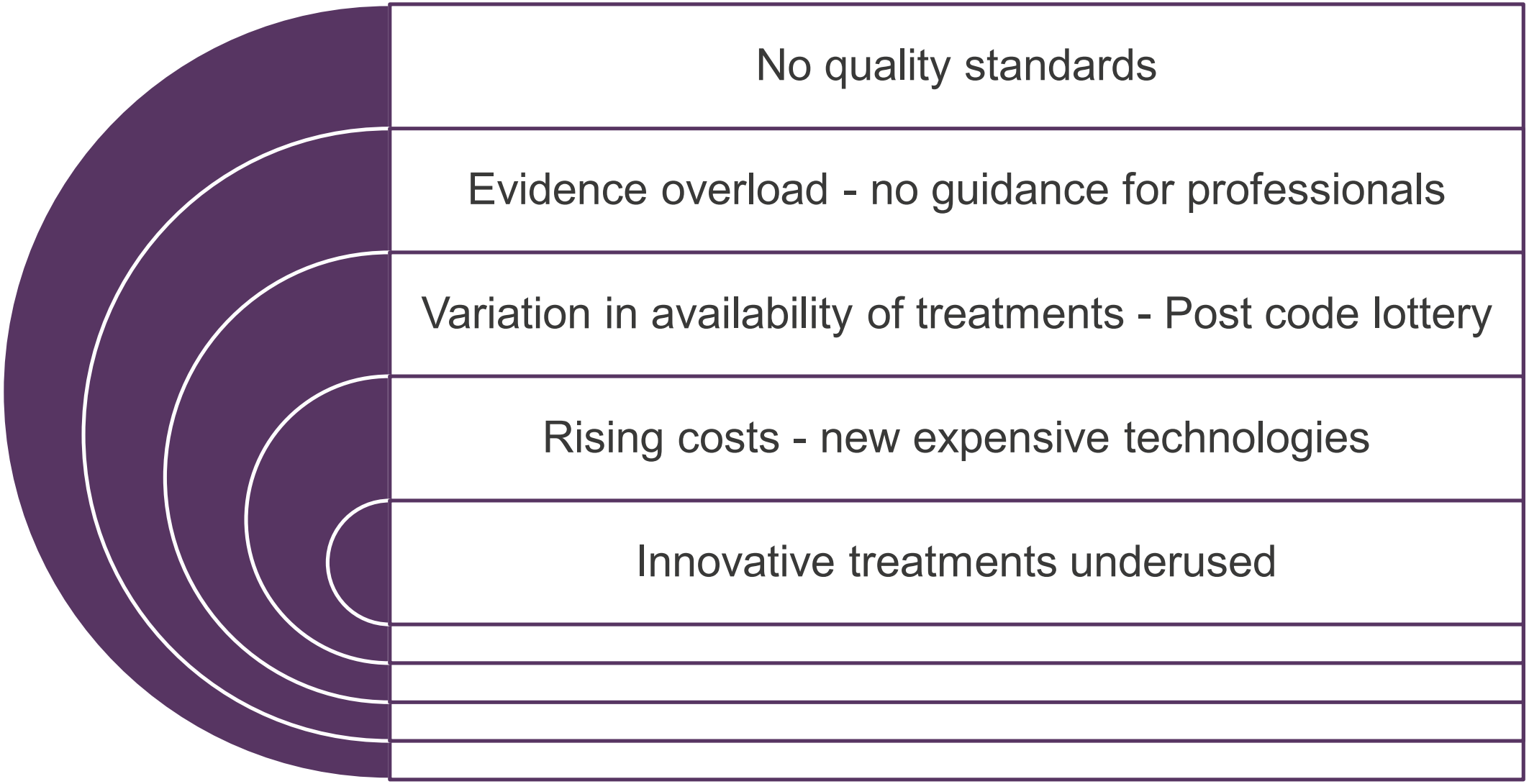
What is NICE, what does it do and what does the future hold?

28 January 2020
University of Manchester

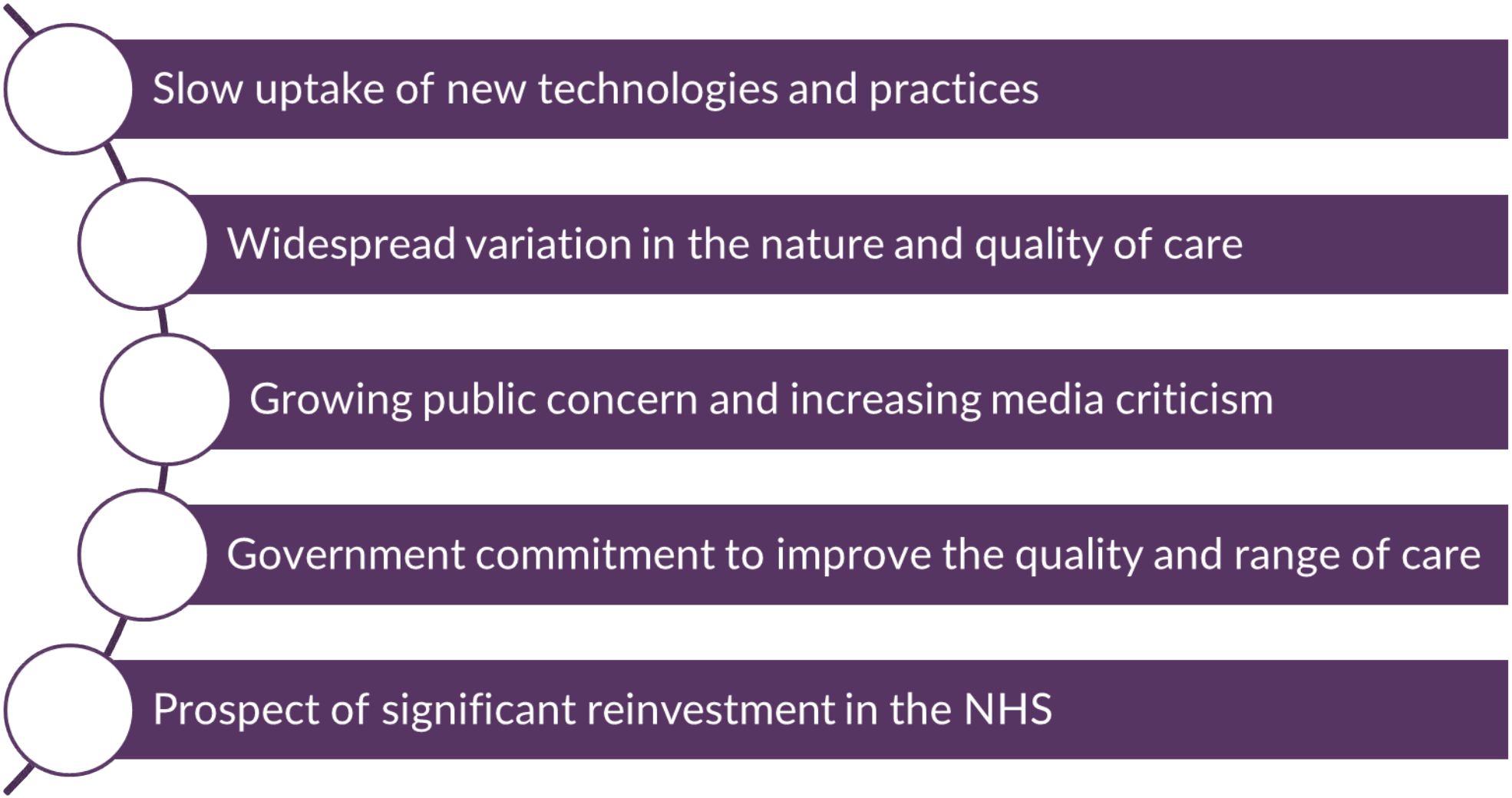
Judith.Richardson@nice.org.uk

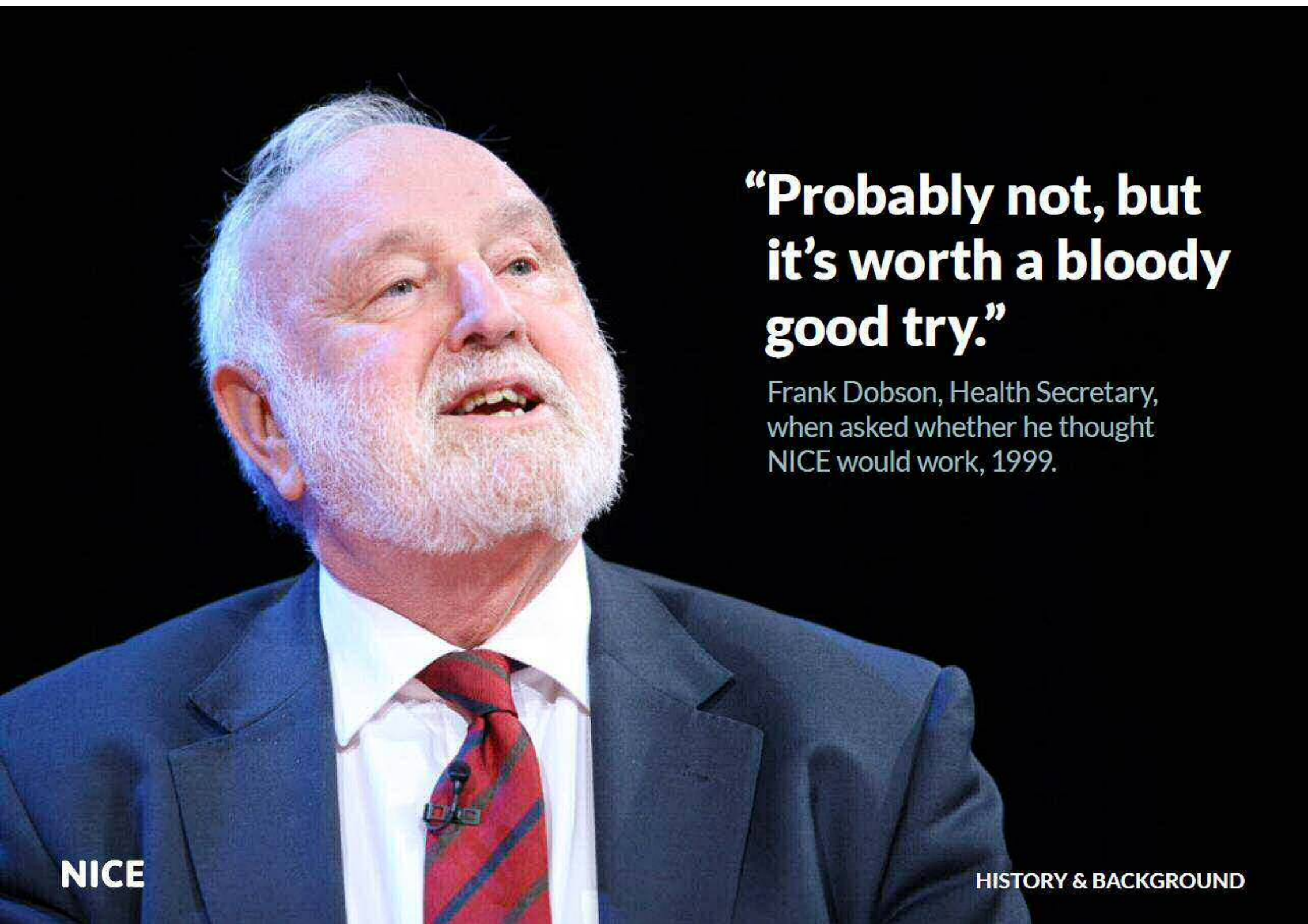
Dr Judith Richardson, Deputy Medical Director

Pre-1999: Before NICE



Why was NICE created?





"Probably not, but it's worth a bloody good try."

Frank Dobson, Health Secretary, when asked whether he thought NICE would work, 1999.

What’s the role of NICE?

NICE's role

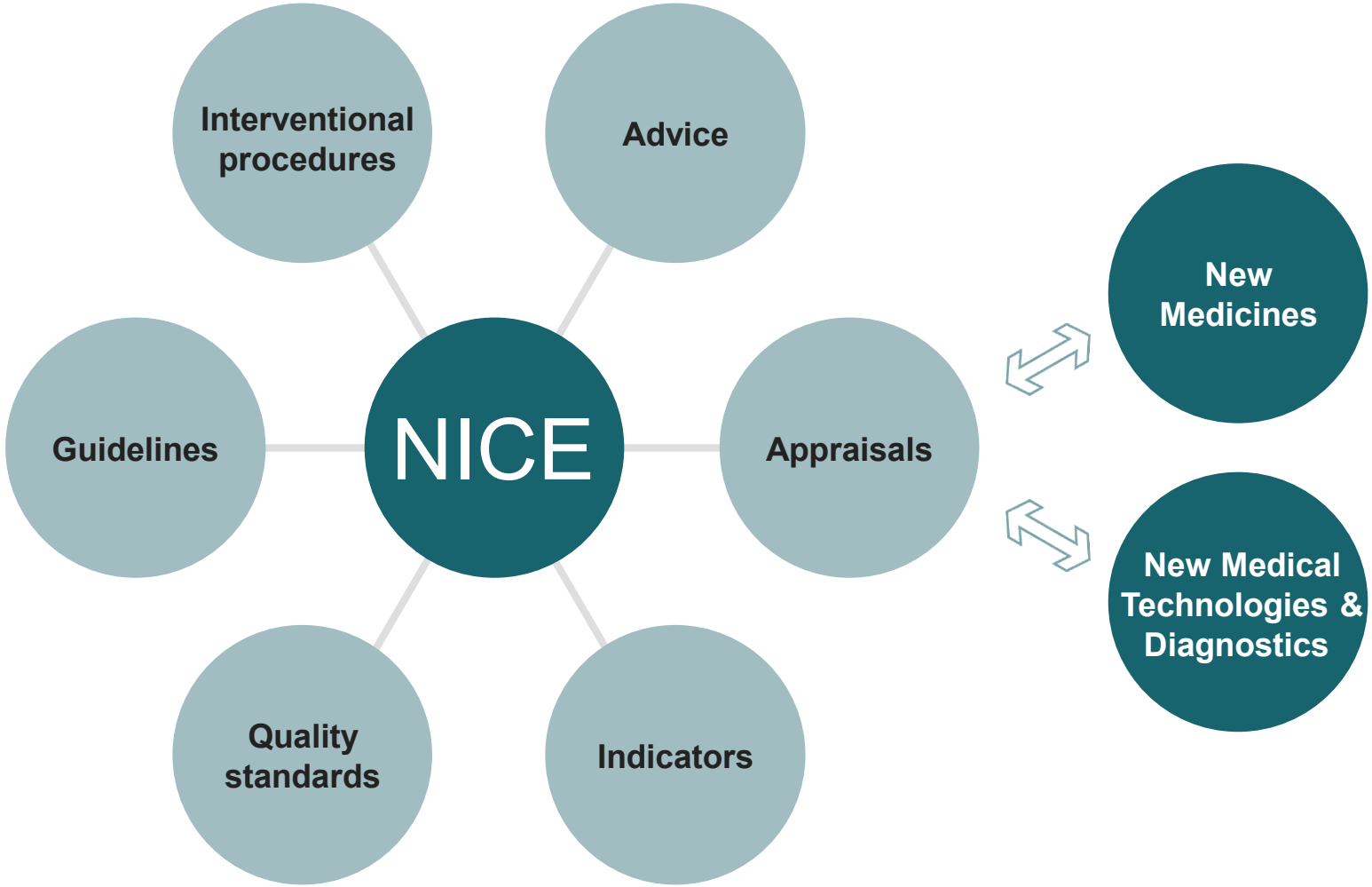
*The **national point of reference for advice on safe, effective and cost effective practice** in health and social care, providing guidance, advice and standards aligned to the needs of its users and the demands of a **resource constrained system.***

The NICE portfolio in 2019

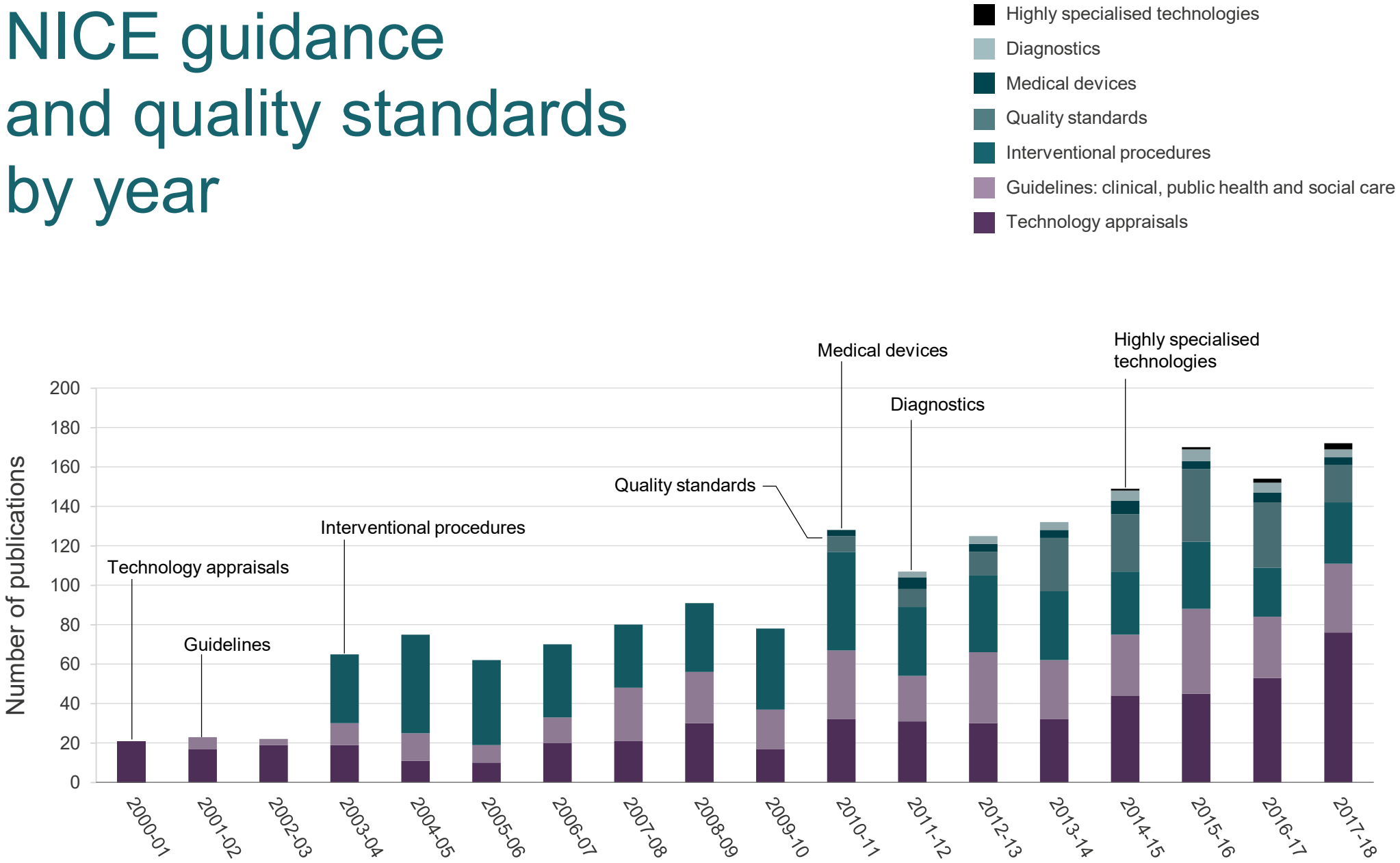
Health

Public Health

Social Care

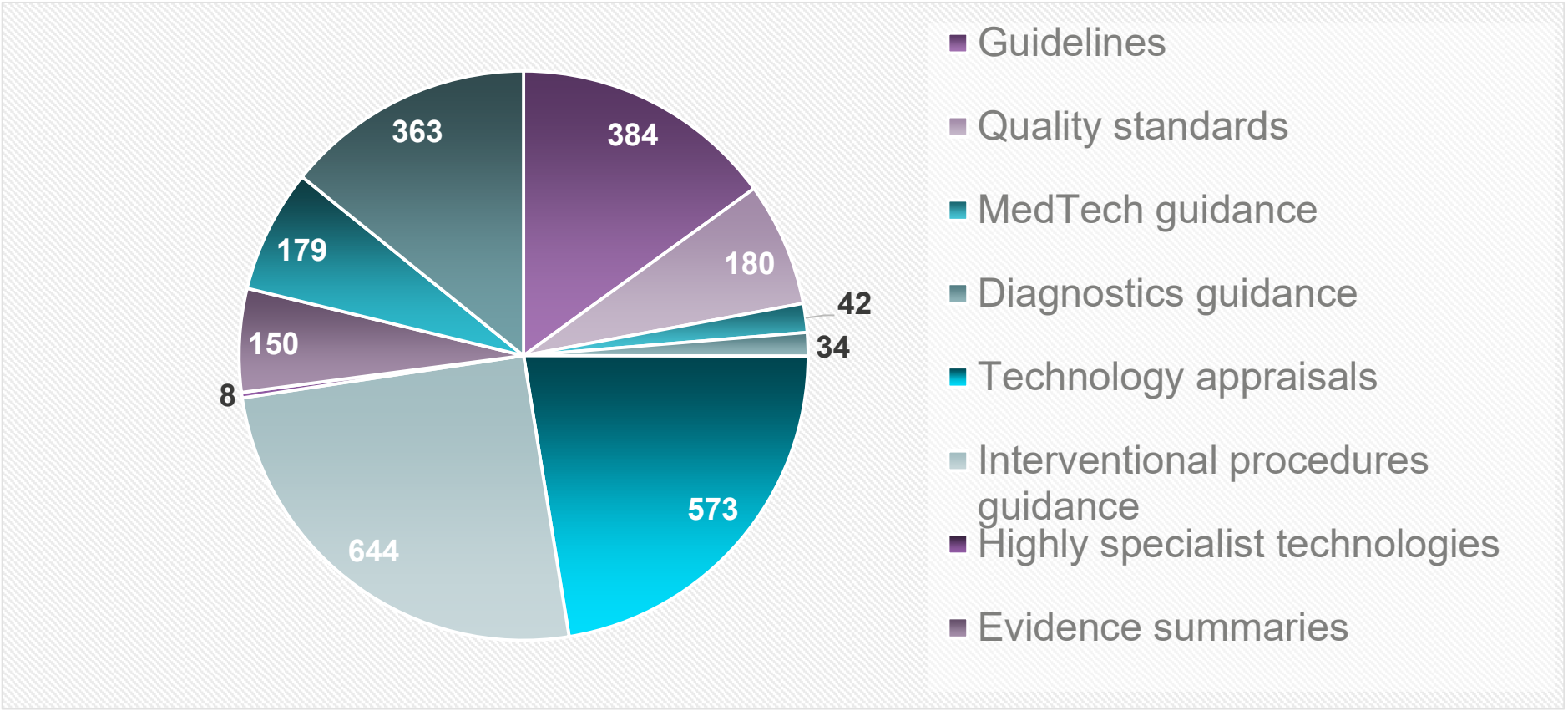


NICE guidance and quality standards by year

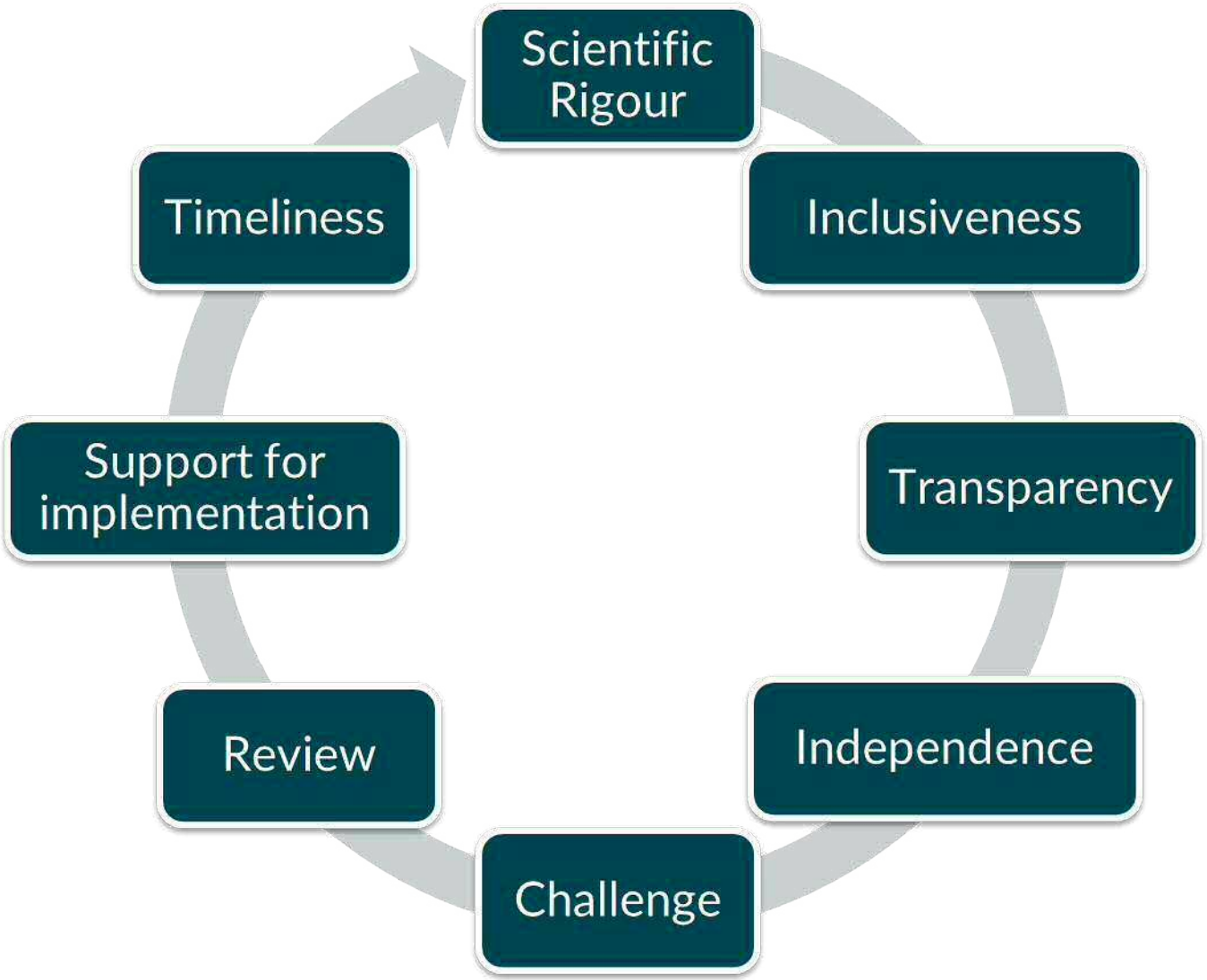


20 years of developing high quality advice and guidance

In total over 2500 separate products!



Procedural principles of NICE Guidance



Working in partnership

NICE

Who are we?
- the staff

- Funding - £60m (staff costs £35m)
- 700 staff directly employed in London and Manchester
- 2,000 experts –physicians, nurses, health economists, clinical epidemiologists, statisticians, lay people - across the UK

Encouraging uptake

Implementation strategy

Our aim is to drive and enable the effective use of NICE guidance and standards to support local initiatives, improve outcomes and reduce variation.

Five principles underpin the strategy:

- Guidance and standards are fit for our audiences' needs
- Audiences are aware of our guidance and standards
- Audiences are motivated to make changes and drive improvements
- Practical support is highlighted to support local adoption and implementation
- Impact and uptake is regularly evaluated


Work with national, regional and local organisations
Offer advice and support locally to facilitate problem solving
Provide practical tools and advice
Delivering the NICE implementation strategy
Fellows & Scholars ambassadors for NICE
Provide Shared Learning examples
Endorse external support tools
Collect and share impact data

NICE

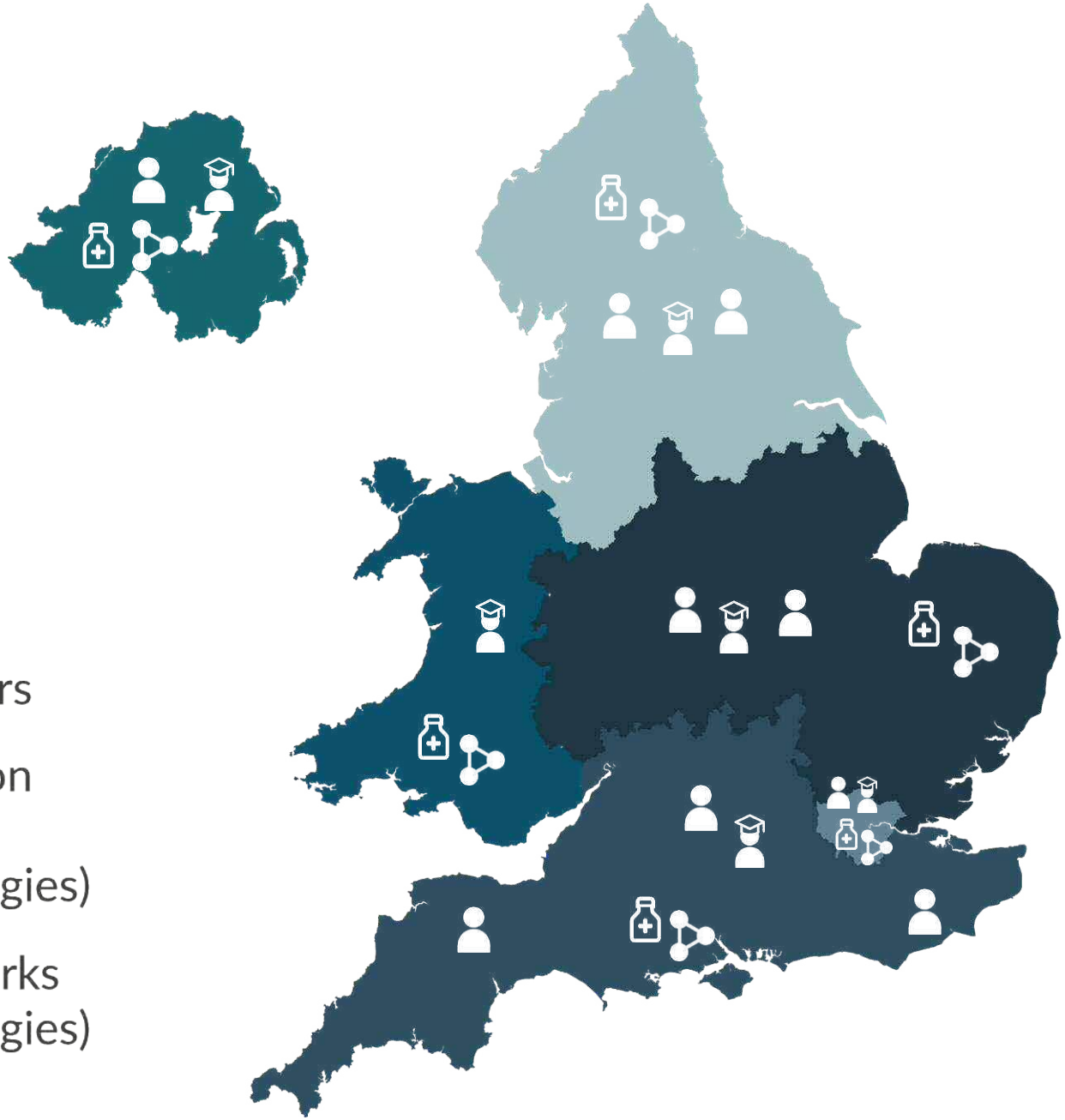
Resource Impact

Publication Date	Guidance short title		Type of guidance	Potential impact
June 2016	Adalimubab for treating moderate to severe hidradenitis suppurative (TA392)		Single Technology Appraisal	Low cost
Steady state resource impact for England (£000s)			Commissioner	Provider(s)
Costs (a)	Savings (b)	Total resource impact (a–b)	NHS England	Secondary care acute
7,334	0	7,334		

Resource Impact for England (£000s)				
2016/17	2017/18	2018/19	2019/20	2020/21
3,792	4,867	6,334	7,801	8,509

Potential resource impact areas (costs or savings)
Approx. 1,600 people with hidradenitis suppurativa eligible for treatment with adalimubab.
Costs will vary: peaking at around £8.5m in 2020/21 and reducing to a steady state of £7.3m from 2021/22.
Potential savings: reduced visits to wound care clinics and fewer wound dressings; reduced hospital admissions, surgeries and follow-ups; reduced need for other pharmacological treatments.

NICE Field Team and Medicines Implementation Consultants



- Field Team
- NICE Fellows and Scholars
- Medicines Implementation Consultants (Medicines and Technologies)
- Associate/affiliate networks (Medicines and Technologies)

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NICE Pathways – guidance at your fingertips

NICE Pathways bring together all NICE guidance, quality standards and support in easy-to-navigate flowcharts

pathways.nice.org.uk

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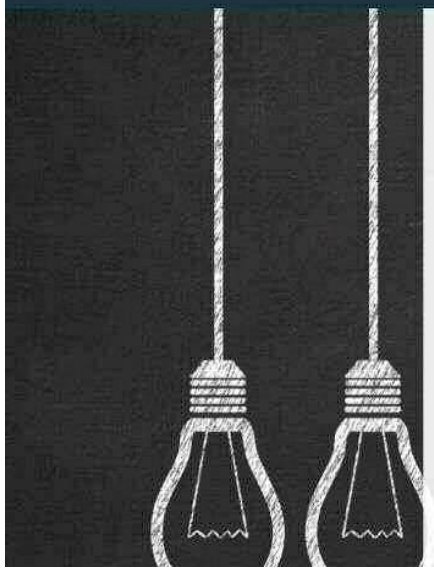
Support for transformation

NICE National Institute for Health and Care Excellence

Introduction | Support for transforming health and social care | Using our guidance | Redesigning pathways and improving services | Reducing unwarra

Other products and local support

Reducing unwarranted varia and standardising care



Ensuring people access the right care, in the right place, at the right time means the NHS and social care can help more people effectively, now and in the future. As Professor Matthew Cripps from RightCare explains, variation in care for different people can be the right thing. But it's unacceptable to see inconsistencies across the country in the quality of care people receive. Equally, if different organisations have joined together under one STP, you may want to make sure they're providing consistent care across similar services.

Our quality standards can help identify variation and areas for improvement in the care services provide in your STP, and make sure the best possible care is provided everywhere. By mapping these against the priorities in your STP plan, you can focus activity on areas that will have the greatest impact.

NICE National Institute for Health and Care Excellence

Making the case for action | Finding the right information | Support for improving quality | Shared learning case studies

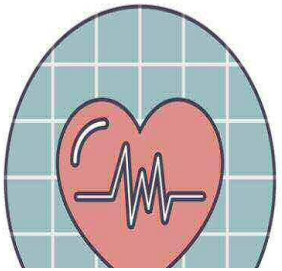
CVD prevention: detecting atrial fibrillation and anticoagulation

How NICE resources can support local priorities

Making the case for action

Atrial fibrillation (AF) increases the risk of stroke, heart attack and dementia, so is a priority for many sustainability and transformation partnerships (STPs).New analysis from Public Health England and NHS England shows that, over 3 years, achieving optimal treatment for people diagnosed with AF could prevent up to 14,220 strokes across England. This could save £240 million. They've used published data to produce infographics for each STP.

We've published guidance and quality standards on AF, and tools to help with putting it into practice. Our guidance is aligned with the NHS England RightCare and Public Health England cardiovascular disease (CVD) prevention pathway.



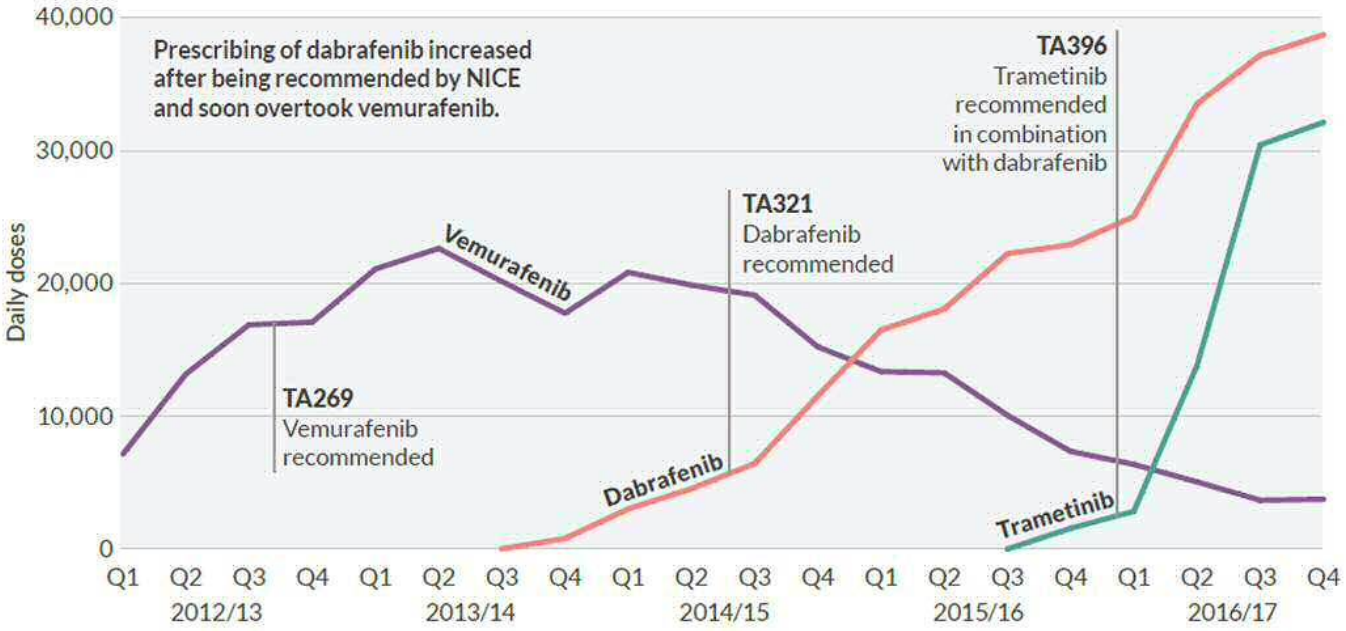
Does NICE make a difference?

Uptake of new drugs for melanoma

BRAF V600 targeted therapy

Vemurafenib was recommended by NICE in December 2012 for treating people with locally advanced or metastatic melanoma with a BRAF V600 mutation. In October 2014, another BRAF V600 inhibitor, dabrafenib, was recommended by NICE. These medicines do not differ in clinical effectiveness, but dabrafenib has a lower incidence of photosensitivity, which may be a major problem for some patients.

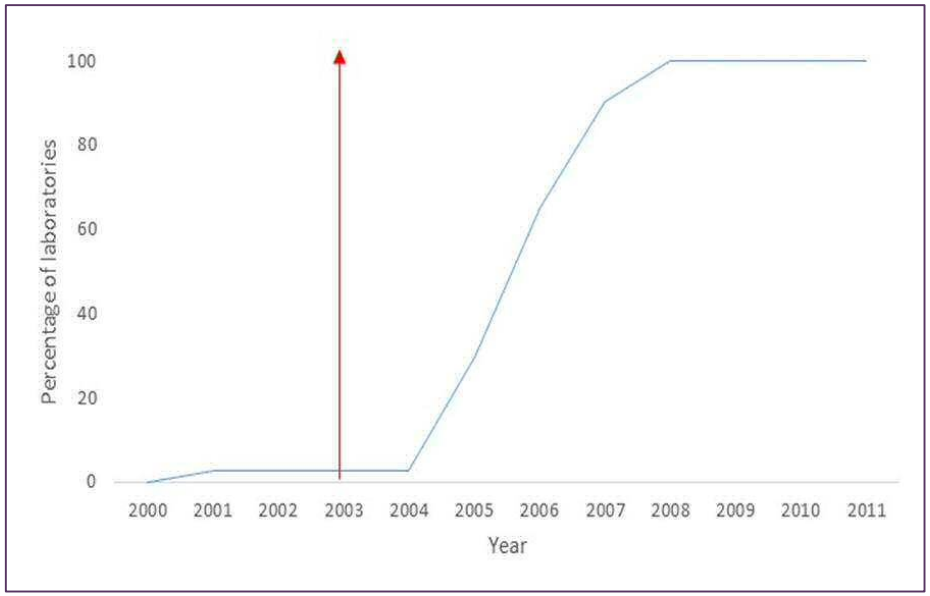
Prescribing of medicines for treating advanced BRAF V600 mutation-positive melanoma



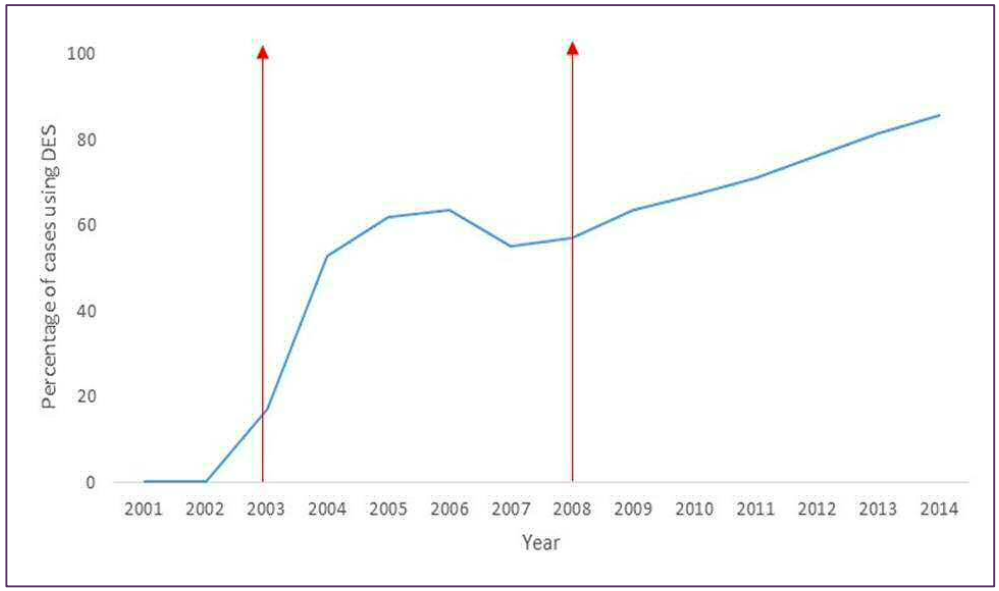
NICE

Uptake of recommended technologies

Report in BMJ Innovations

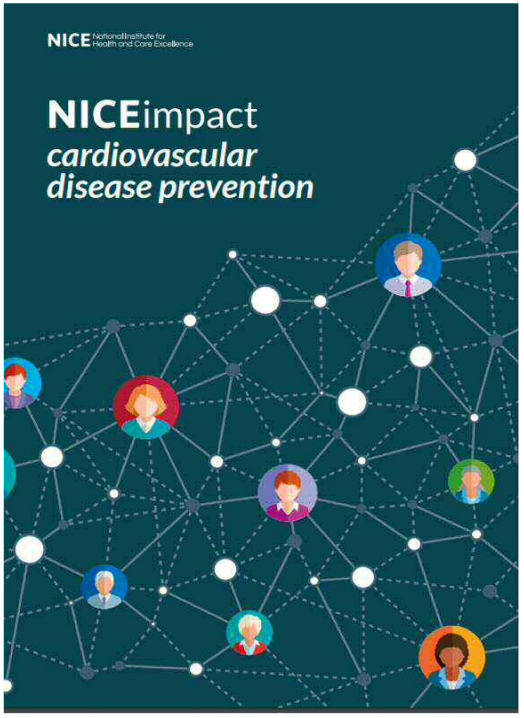


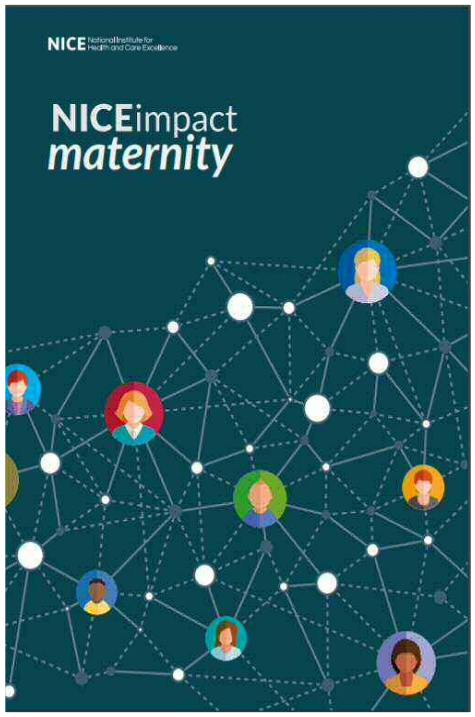
Percentage of laboratories fully converted to LBC. NICE guidance was published in 2003 (red arrow)

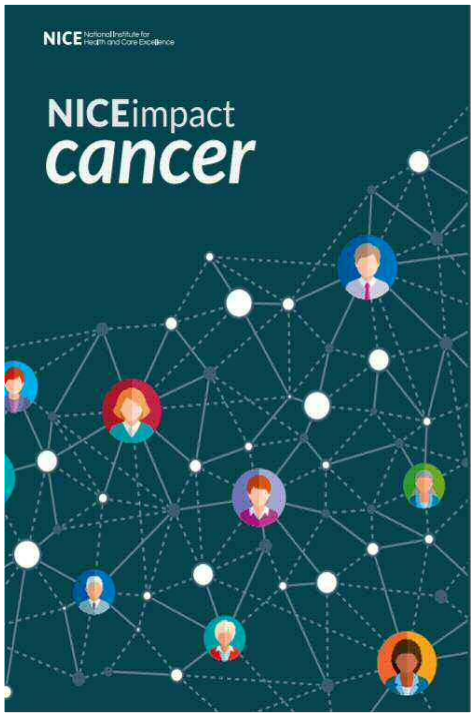


Percentage of percutaneous coronary interventions using drug eluting stents in an NHS setting in England. NICE guidance was published in 2003 and 2008 (red arrows)

Monitoring and supporting uptake



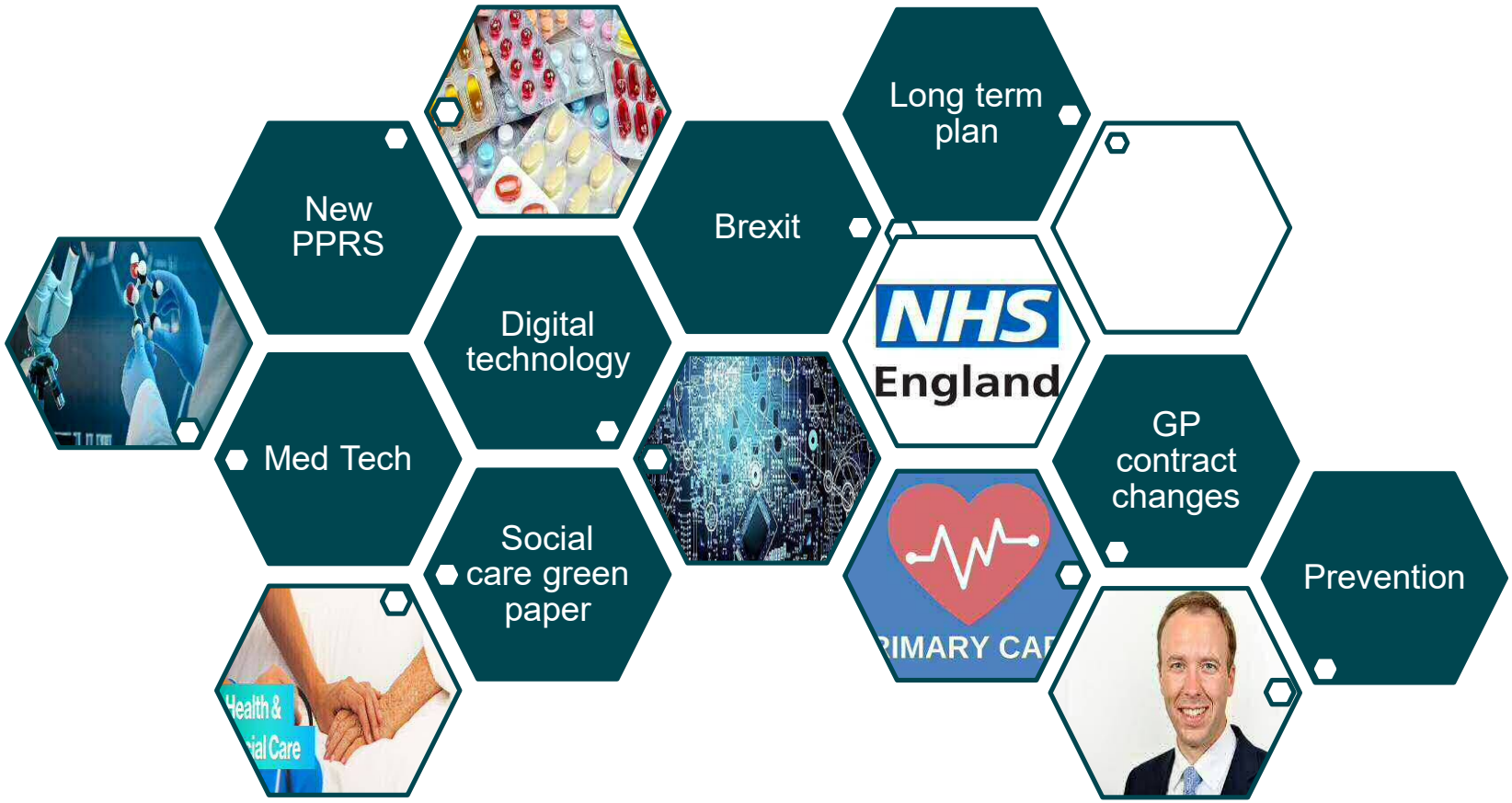




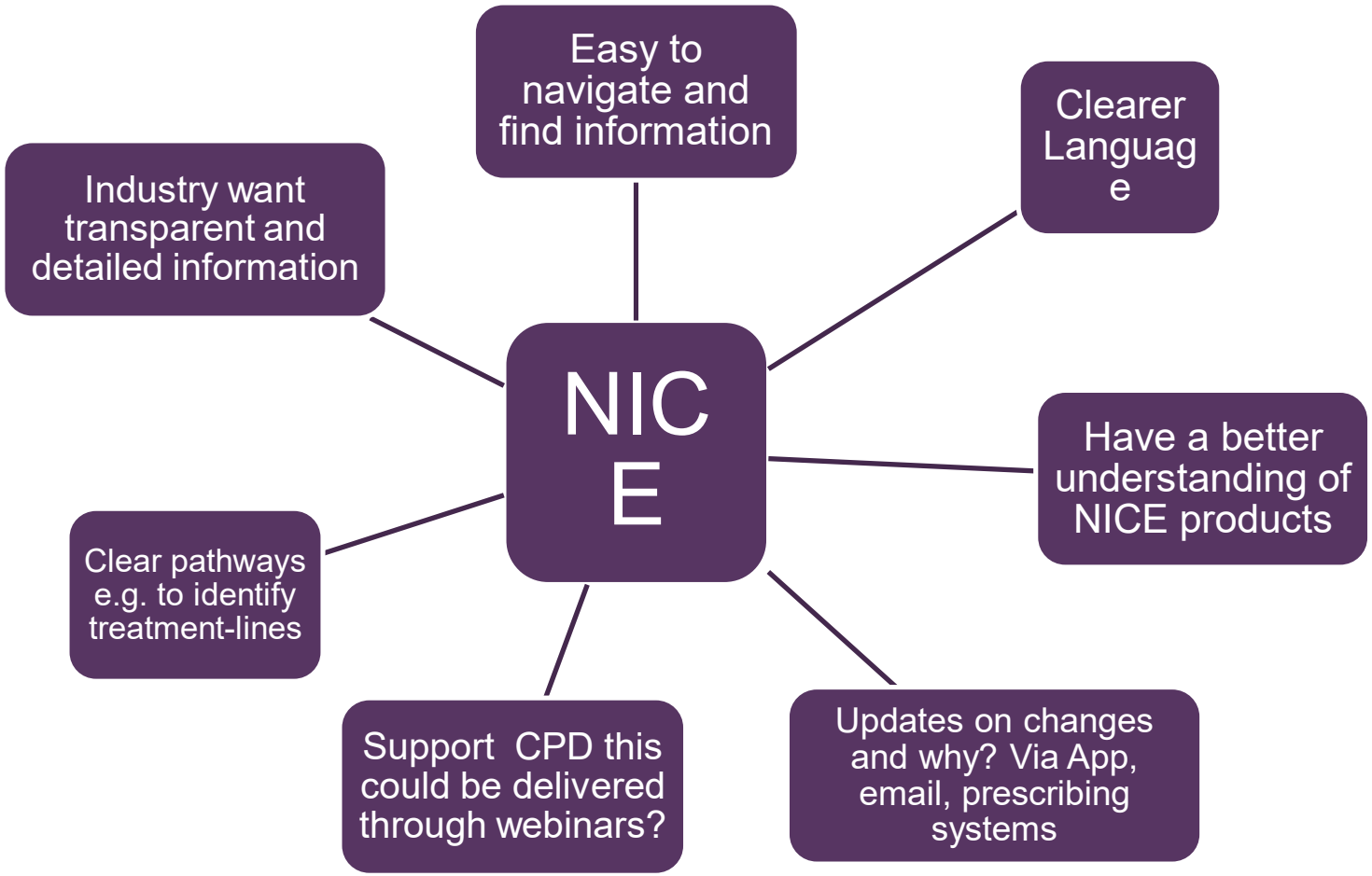
Search for
"NICE impact CVD"
at
www.nice.org.uk
to read

The future

Changes in the external environment



What do users want?



Problems with the evidence…

- Not enough
- Poor quality
- Conflicting
- Wrong sort

"Evidence is inherently uncertain, dynamic, complex, contestable, and rarely complete"

Lomas, J; Culyer T et. al

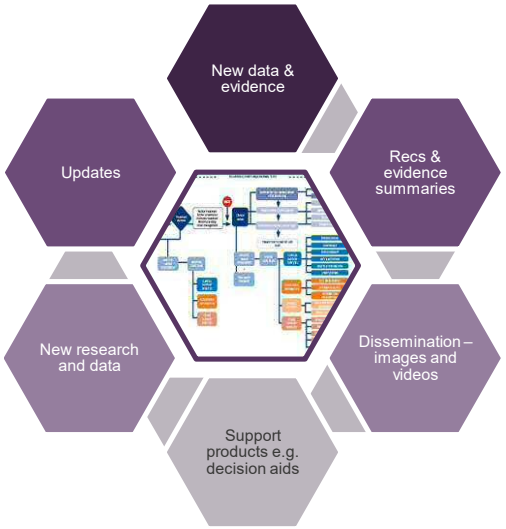
Conceptualizing & Combining Evidence For Health System Guidance; CHSRF, May 2005

Future vision

Building on the best – accessible, living, integrated guidance

To achieve this we will:

- Combine all our advice and guidance into an integrated product on the NICE website that follows the patient journey
- Rapidly sequence new drugs and technologies, so practitioners and commissioners can identify them and adopt more quickly
- Keep recommendations up to date, so care is always based on the best available evidence and data
- Integrate recommendations into IT systems, so it will be easier for practitioners to adhere to the evidence




NICE Connect
Our vision for accessible,
integrated and living guidance
NICE

Thank you and any questions?

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From research to evidence gaps

Kay Nolan

Associate Director, Centre for Guidelines

Kay.Nolan@nice.org.uk

Q1

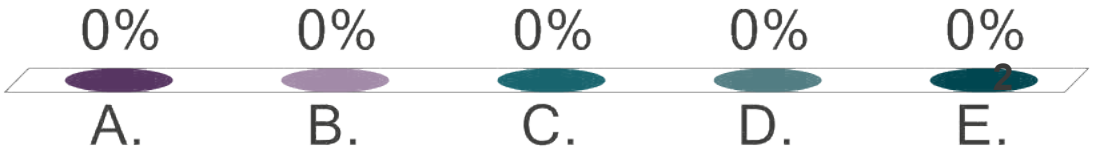
A. The first guidance issued by NICE was…..

B. Guidance on the use of inhaler systems (devices) in children under the age of 5 with chronic asthma

C. Guidance on the use of trastuzumab for the treatment of breast cancer

D. Guidance on the extraction of wisdom teeth

E. Improving outcomes in urological cancers



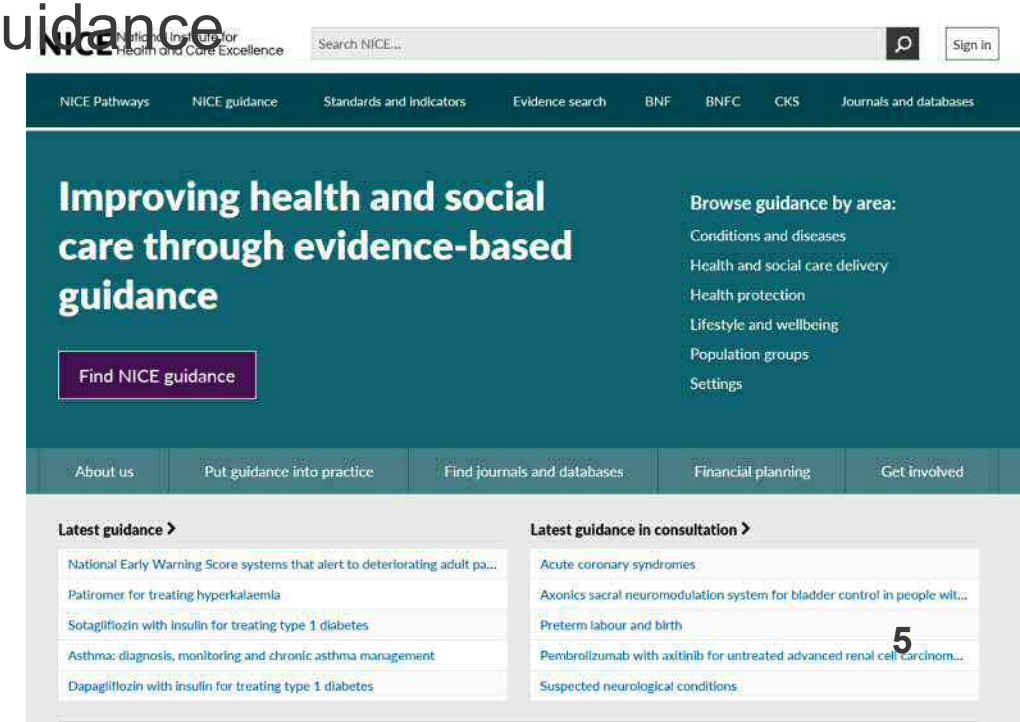
Overview

- Principles of guidance development
- Overview of approach to guidance development – journey from evidence-guidance-gaps
- Opportunities for researcher interaction

NICE guidance

NICE Guidance Portfolio

- NICE guidelines
- Diagnostics guidance
- Interventional procedures guidance
- Technology appraisal guidance
- Highly specialised technology guidance
- Medical technologies guidance



Q2

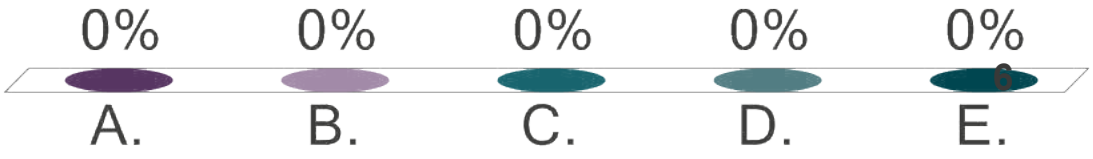
A. Approximately - how many guidance products has NICE produced?

B. 800

C. 1100

D. 1500

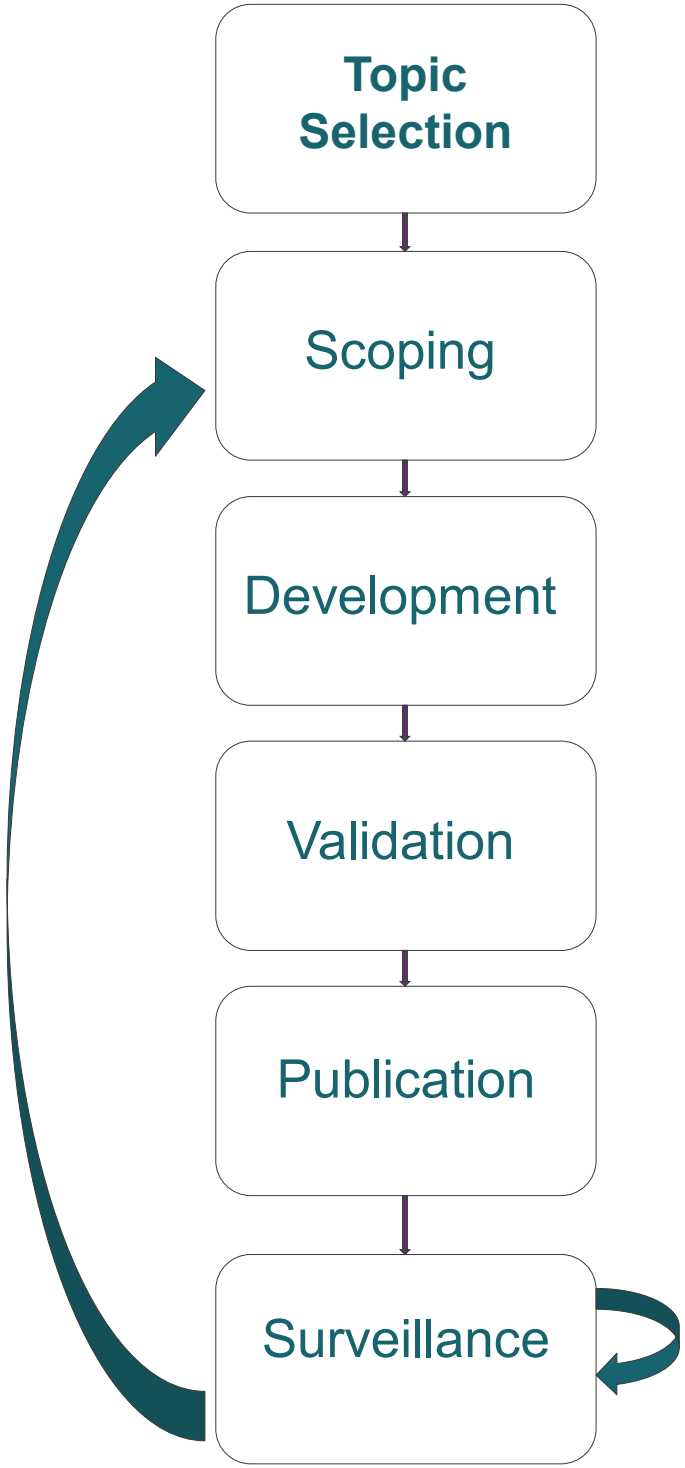
E. 2000



Key principles for guidance development

Guidance development cycle

Example of guidelines


Topic Selection
Scoping
Development
Validation
Publication
Surveillance

NICE

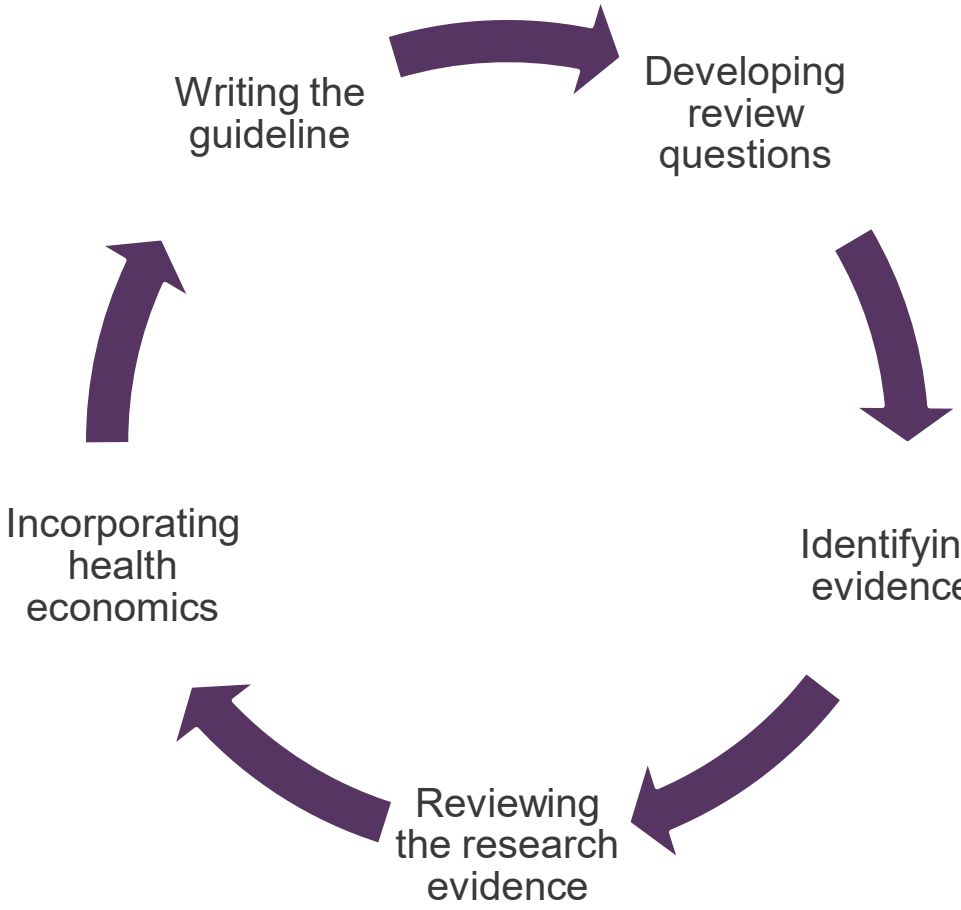
Topic selection

- Key considerations:
    - System need (priority given by professional bodies, commissioners, organisations for people using services)
    - Health and Care burden
    - Potential to improve outcomes and quality of life
- Internal Topic Selection Oversight Group
- Discuss with commissioners
    - Department of Health and Social Care and NHS England
- Formal referral

Scoping

- Sets out what the guideline will and won't cover
- Sets a framework for the development work
- Is modified in response to consultation feedback

Development



Outcomes

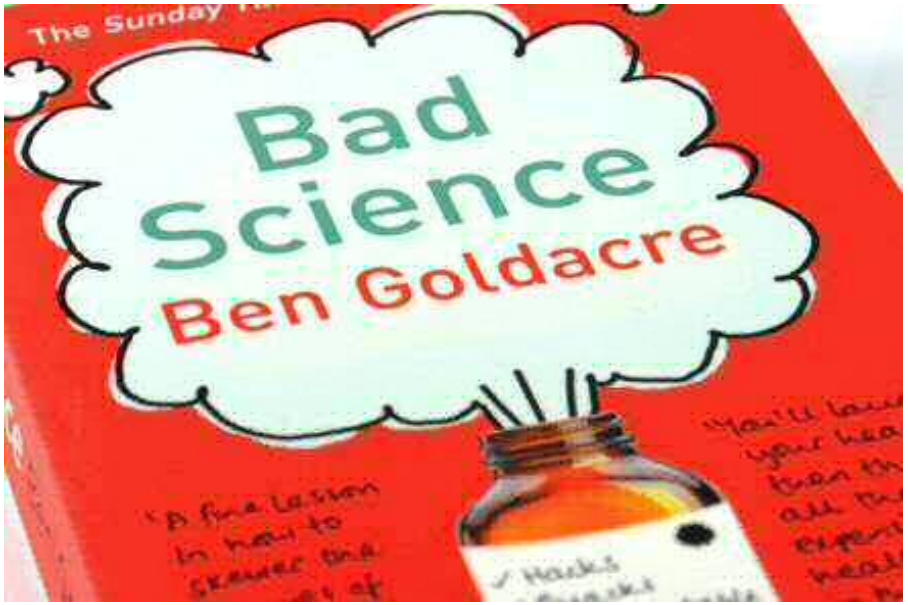
Is your research relevant?

Q3

True or False
NICE is primarily interested in RCTs for guidance development?

A. True

B. False



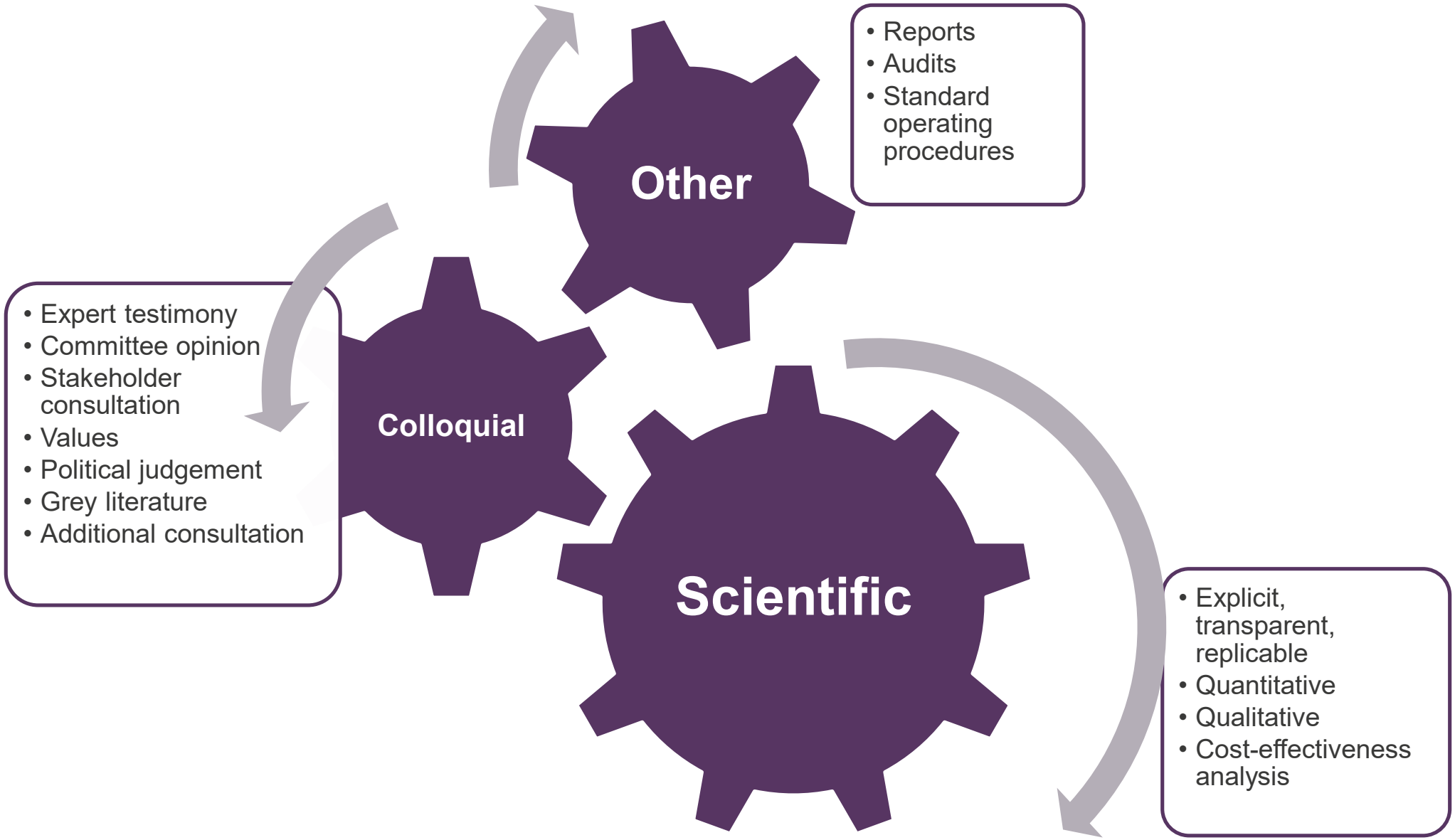
Q4

NICE always does a cost effectiveness analysis for everything it recommends

A. True

B. False

Evidence



NICE

Types of questions covered in guidelines

Effectiveness

- What are the effective occupant behaviour interventions to reduce or prevent the health impacts of poor indoor air quality at home?
- Which first-line opioid maintenance treatments are effective and cost effective in relieving pain in patients with advanced and progressive disease who require strong opioids?

Diagnostic test/test strategy

- What is the accuracy of D-dimer assay for diagnosing deep vein thrombosis compared with compression ultrasonography?

Prognosis (likelihood of outcome)

- Which people having neoadjuvant chemotherapy or chemoradiotherapy for rectal cancer do not need surgery?

Types of questions covered in guidelines

Prediction

- Which risk assessment tools are the most accurate in predicting the risk of fragility fracture in adults with osteoporosis or previous fragility fracture? (e.g prognostic prediction)

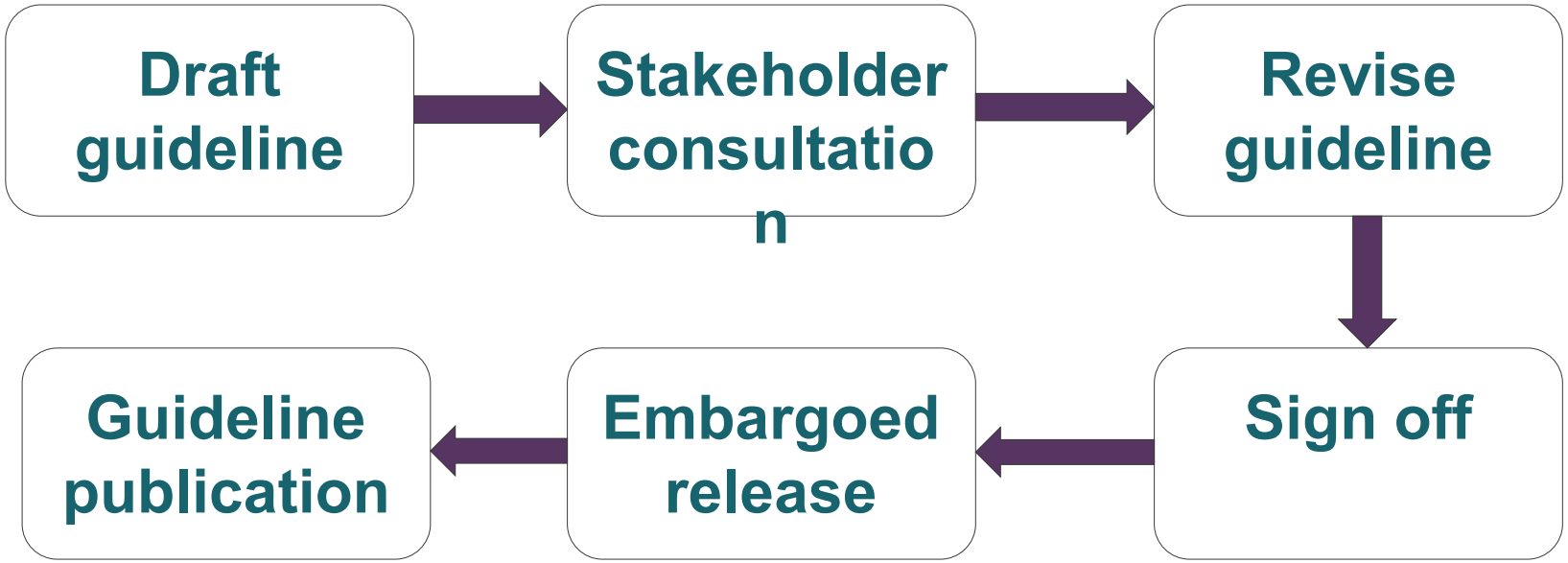
Views/Experiences – Qualitative

- How does culture affect the need for and content of information and support for bottle or breastfeeding?
- What elements of care on the general ward are viewed as important by patients following their discharge from critical care area?

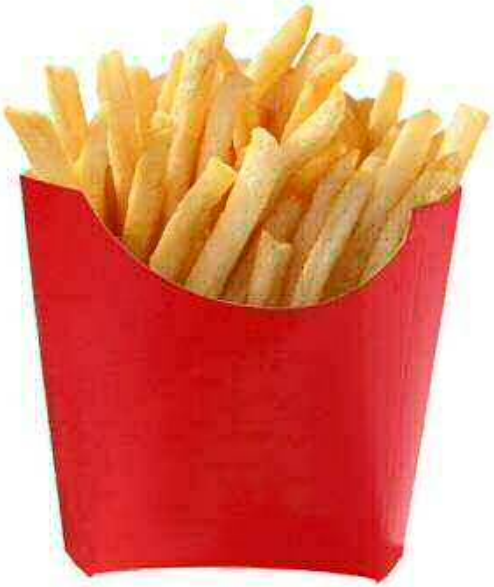
Writing the guideline

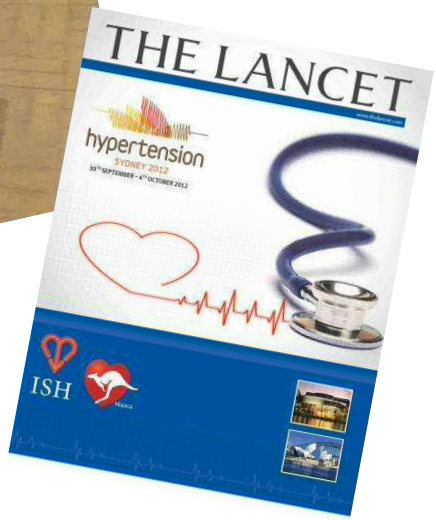
- Recommendations
  - Quality of evidence
  - Trade off between benefits and harms
  - Trade off between economic considerations and resource use
  - Indirect evidence
  - Evidence to support implementation
  - Size of effect and potential impact on population health
  - Judgements – social value, equality
  - Strength of recommendation – assessment of balance between benefits and harms
- Insufficient evidence/uncertainty - Research recommendations

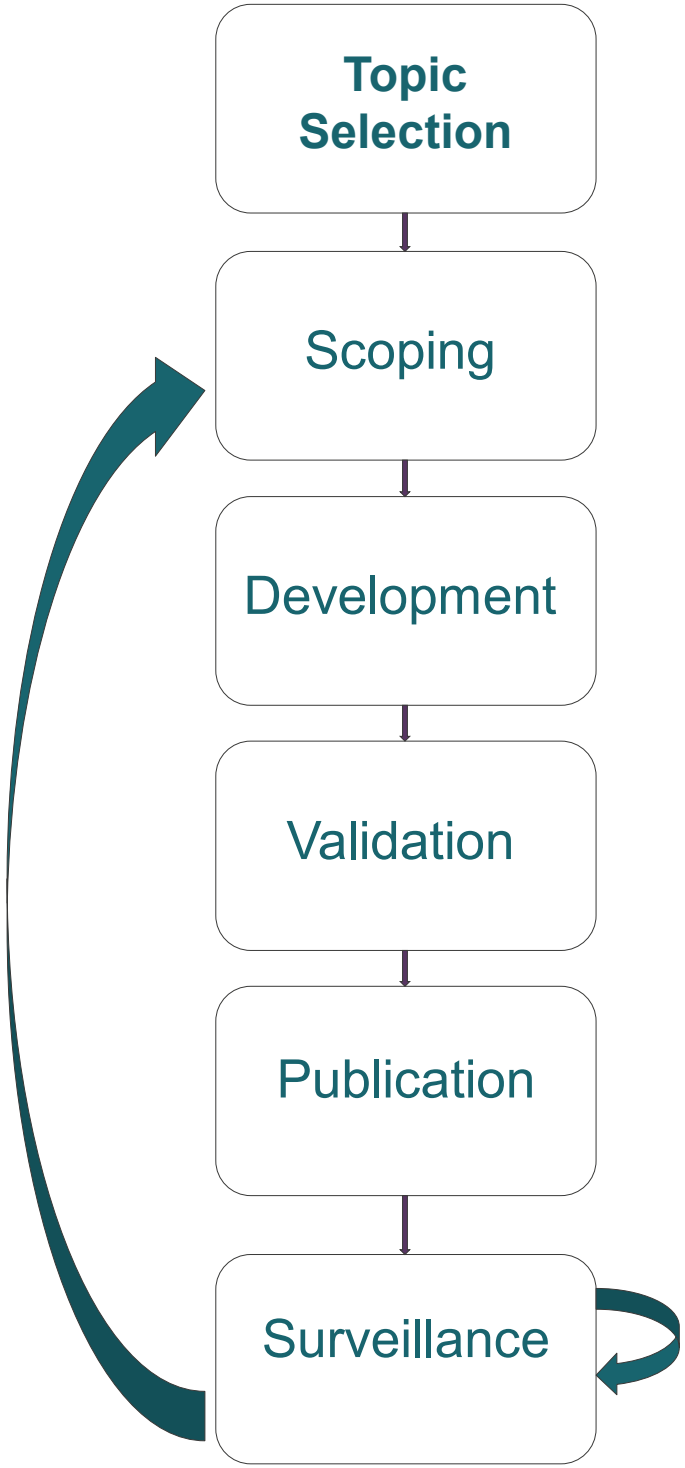
Validation & publication



Implementation!






Topic Selection
Scoping
Development
Validation
Publication
Surveillance

NICE

Surveillance process - Aim

Check that guidelines are up to date

- Explore impact of any new evidence

Identify new technologies and interventions

- Within the parameters of the referral

Explore changes in contextual factors

- Policy, infrastructure, legislation or costs

2 approaches – proactive and reactive

Standard surveillance	Exceptional review
At least every 5 years	Triggered by an event
Try to review in themes	Reactive approach
Covers all recommendations within guideline	Scope is determined by event
Key steps • Intelligence gathering • Evidence review (abstract) • Consultation • Publication of decision	Flexible approach dependent on event

Researcher interaction

Research recommendations

Implementation/uptake

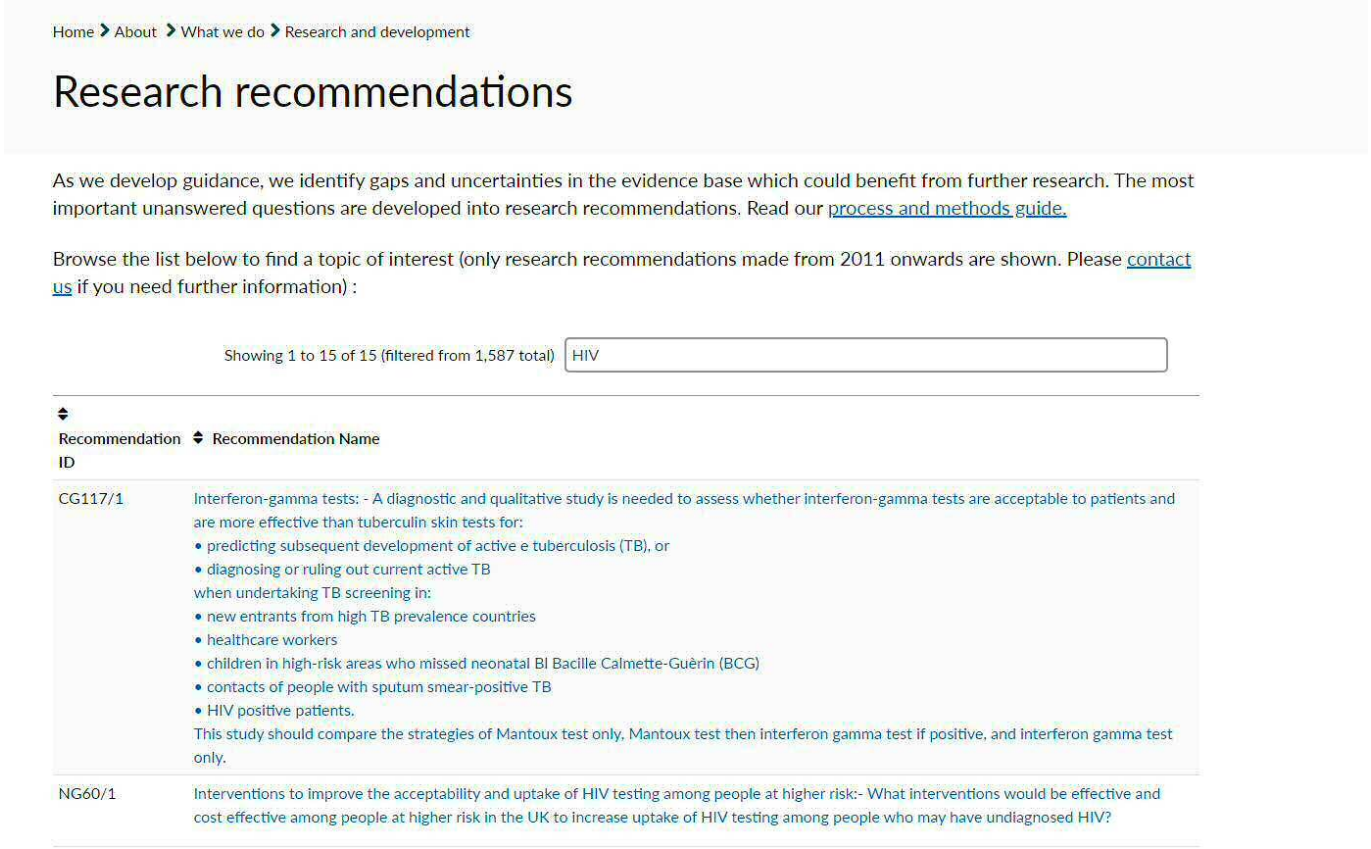
New evidence (surveillance)

Process and methods (RobotAnalyst)

Research recommendations

Database of research recommendations

https://www.nice.org.uk/about/what-we-do/science-policy-research/research-recommendations



Home › About › What we do › Research and development

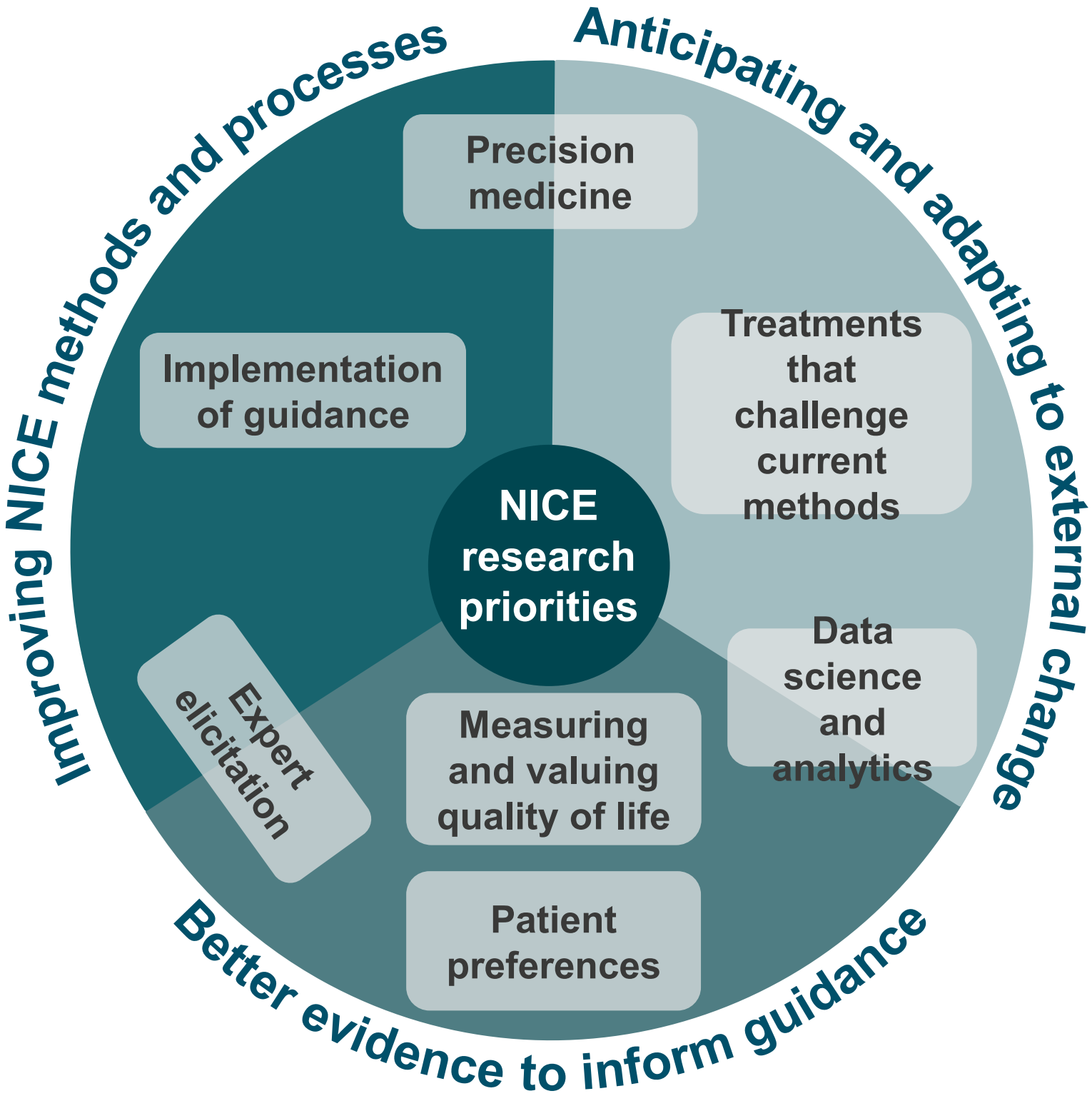
Research recommendations

As we develop guidance, we identify gaps and uncertainties in the evidence base which could benefit from further research. The most important unanswered questions are developed into research recommendations. Read our process and methods guide.

Browse the list below to find a topic of interest (only research recommendations made from 2011 onwards are shown. Please contact us if you need further information) :

Showing 1 to 15 of 15 (filtered from 1,587 total) HIV

Recommendation ID	Recommendation Name
CG117/1	Interferon-gamma tests: - A diagnostic and qualitative study is needed to assess whether interferon-gamma tests are acceptable to patients and are more effective than tuberculin skin tests for: • predicting subsequent development of active e tuberculosis (TB), or • diagnosing or ruling out current active TB when undertaking TB screening in: • new entrants from high TB prevalence countries • healthcare workers • children in high-risk areas who missed neonatal Bl Bacille Calmette-Guèrin (BCG) • contacts of people with sputum smear-positive TB • HIV positive patients. This study should compare the strategies of Mantoux test only, Mantoux test then interferon gamma test if positive, and interferon gamma test only.
NG60/1	Interventions to improve the acceptability and uptake of HIV testing among people at higher risk:- What interventions would be effective and cost effective among people at higher risk in the UK to increase uptake of HIV testing among people who may have undiagnosed HIV?


Improving NICE methods and processes
Anticipating and adapting to external change
Better evidence to inform guidance
Precision medicine
Implementation of guidance
Treatments that challenge current methods
NICE research priorities
Data science and analytics
Expert elicitation
Measuring and valuing quality of life
Patient preferences

NICE

Any questions?

Kay.Nolan@nice.org.uk

Research & Opportunities to Interact with NICE: Understanding the landscape

- Health Priorities
- Faculty of Biology, Medicine & Health
- *Manchester Academic Health Science Centre* - Discovery
- *GM Academic Health Science Network*- Development & Deployment
- *GM Applied Research Collaboration* – Evaluation & Implementation

Health Innovation Manchester

Health Innovation Manchester

Memorandum of Understanding – UoM, Health Innovation Manchester, NICE 2019

A shared commitment to improving the overall health of the population through research and informing health policy and practice, as well as through the development and evaluation of health technologies.

Example:
Exploring how routinely collected information, such as anonymised data derived from patient records, may be used to evaluate the effectiveness of medicines, new technologies and interventions in the development of NICE guidance.

“using data for research purposes is vital to provide modern day healthcare that radically improves the health and wellbeing of our citizens”

Manchester Academic Health Science Centre

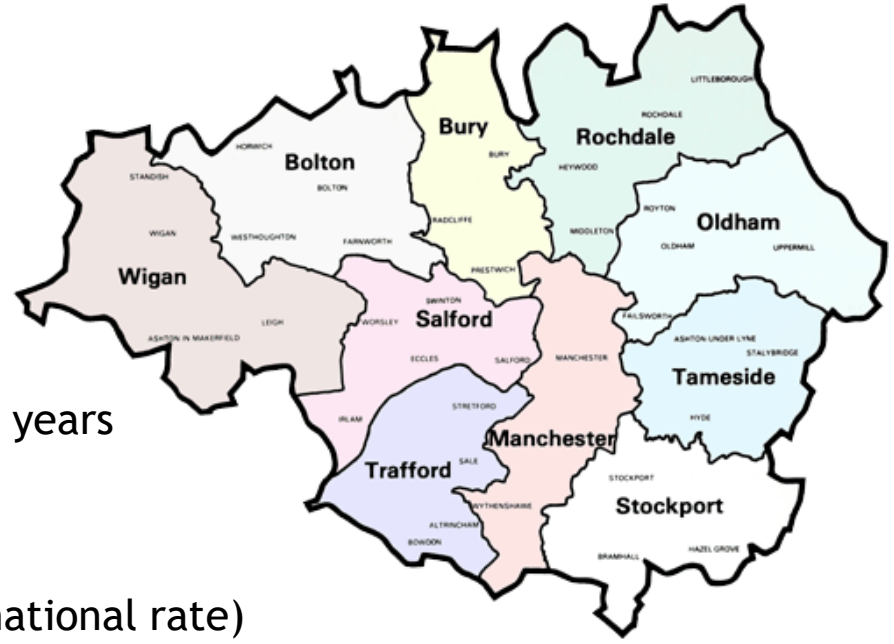
Manchester – our priorities

2.8 Million Population:
200+ languages spoken

434,000
ethnic minority population
Growth of 200,000+ in last 10 years

104,000
Unemployed (7.8% vs 5.5% national rate)

12,000
children not ready for school



Population Outcomes

are below national averages against a range of disease and mortality figures

77.8 yrs
men's life expectancy
Below England average of 79.5

81.3 yrs
women's life expectancy
Below England average of 83.1

4000 people in GM in contact with mental health services
for every 100,000 of the population

National average 2200

More homeless people died in Manchester than in any other local authority area in England and Wales in 2017

Start Well | Live Well | Age Well

MANCHESTER 1824
The University of Manchester

UoM Faculty of biology, medicine and health

3000 staff

10,000 students

£336m income

Schools Divisions	Biology 6	Medicine 6	Health 6

9 Research Domains

- Cardiovascular endocrine and metabolism
- Infection, inflammation, immunity and repair
- Cellular and development systems
- Evolution systems and genomics
- Cancer
- Neuroscience and mental health
- Digital Health
- Applied Heath
- Research technologies

UoM research - interface with Manchester Academic Health Science Centre

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9 Research Domains

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- Digital Health
- Applied Heath
- Research technologies

MAHSC domains & Trusts

- Cardiovascular — MFT
- Inflammation and repair — MFT
- Women's and Children's — MFT
- Cancer — The Christie
- Mental Health — MMH
- Neuroscience — SRFT

Enablers

- Digital
- Precision Health
- ARC

GM Research infrastructure overview

Faculty of Biology Medicine and Health | Research domains and divisions | BRC | MAHSC - Domains | Trust R&I | NHS Trusts, CCGs, HSCP

Discover → Develop → Deploy

Priorities

- Novel biological mechanisms
- Prevention, early detection and novel diagnostics
- Next generation therapy and care pathway intervention

Funders

- UKRI
- Charities
- NIHR
- NHSE/NHSI

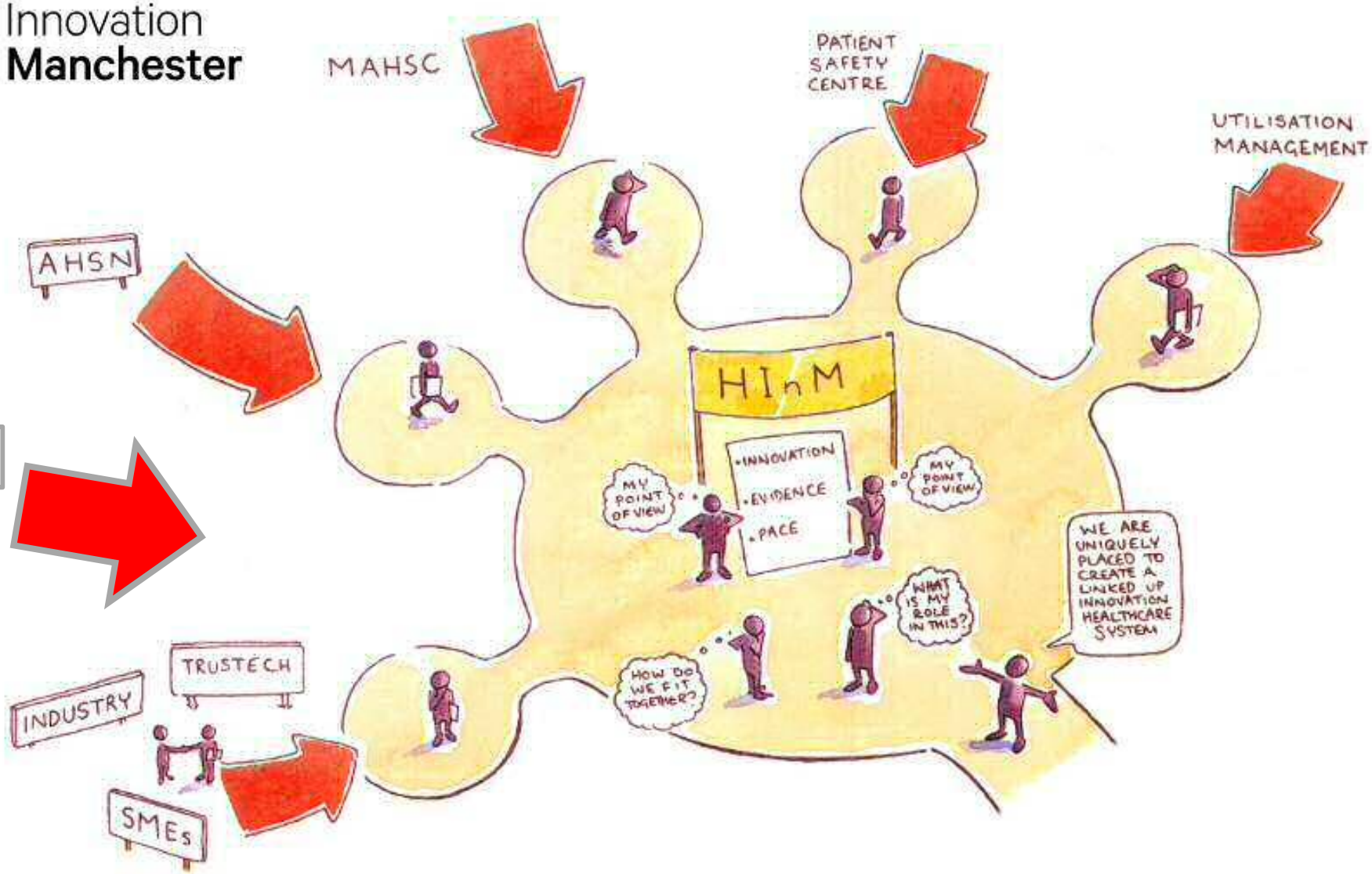
Enablers

- Core Facilities
- CRN, CRFs, CTU
- Data Digital, Omics
- HInM ARC, AHSC AHSN

Research-based teaching

- Undergraduate
- Postgraduate
- Continuing professional development

Health Innovation Manchester



Strategic aims of HInM

Ensure a constant innovation pipeline into health and social care.

Prioritise and monitor innovation activities that meet the needs of GM.

Accelerate delivery of innovation into health, care and wellness delivery.

Amplify existing academic and industry value propositions.

Influence national and international policy.

GM's academic health science innovation system

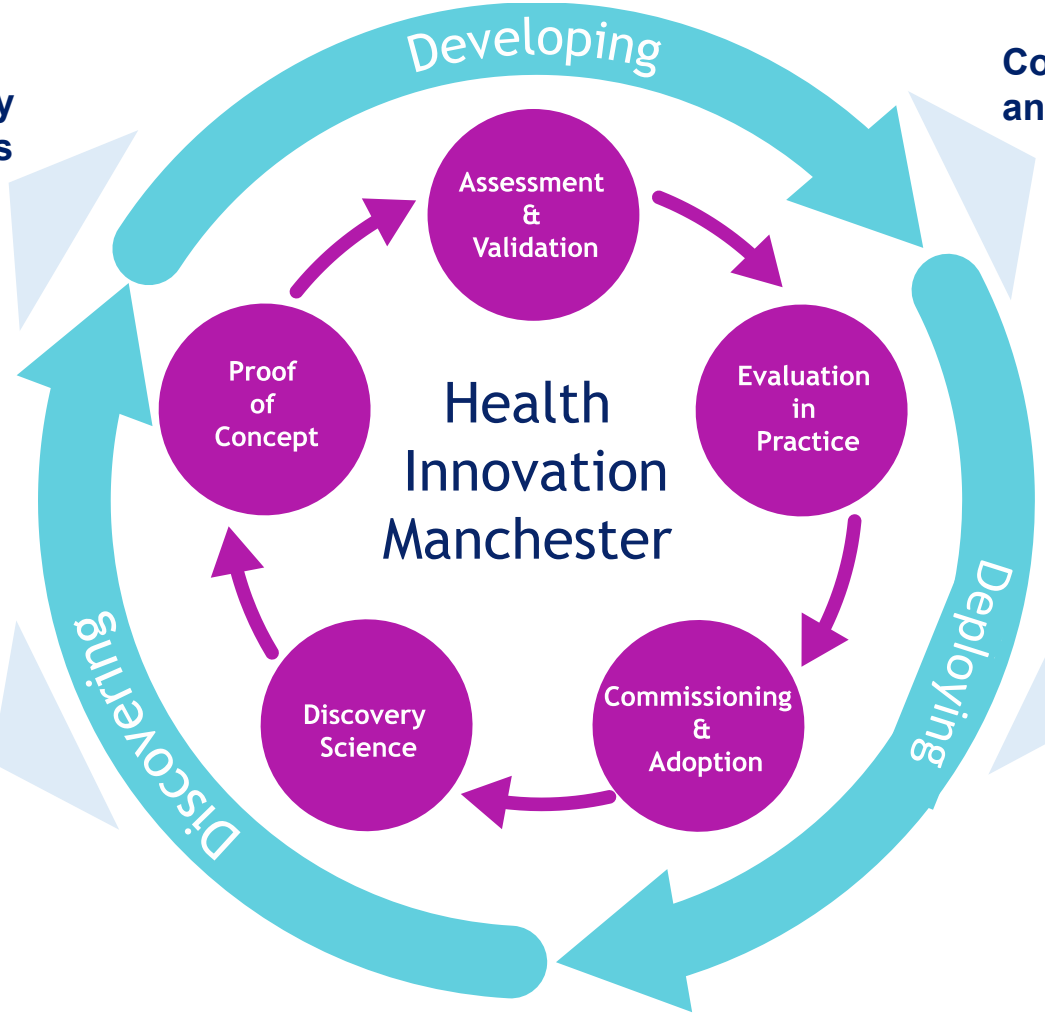
Health Innovation Manchester is a system and an organisation that represents a new way of working

Industry partnerships

abpi — Bringing medicines to life

abhi

nhsa — Northern Health Science Alliance



Commissioners and providers

NHS in Greater Manchester

GMCA Greater Manchester Combined Authority

Academia and research

Manchester Metropolitan University

University of Bolton

University of Salford Manchester

MANCHESTER 1824 The University of Manchester

National agencies and government

NHS England

NICE National Institute for Health and Care Excellence

Office for Life Sciences

NHS National Institute for Health Research

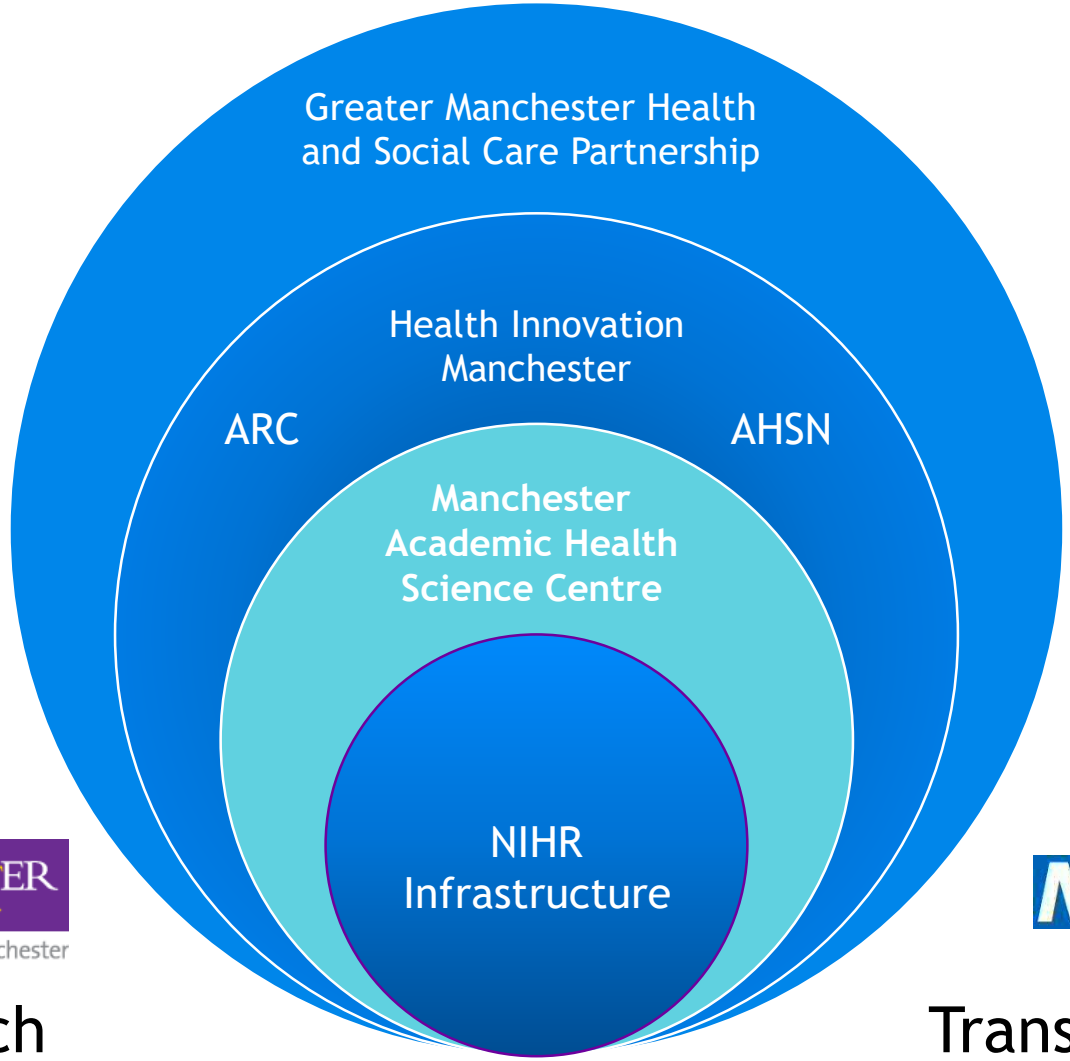
Manchester Academic Health Science Centre

Population Benefit and Wider Economic Gain: At Pace and Scale with Equity

Cardiovascular Domain
Chair: CEO Manchester University FT (MFT)

Inflammation & Repair Domain
Chair: CEO MFT

Women & Children Domain
Chair: CEO MFT



Cancer Domain
Chair: CEO Christie FT

Neuroscience Domain
Chair: CEO Salford Royal FT

Mental Health Domain
Chair: CEO GM Mental Health FT

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The University of Manchester

Research Power

Citizen involvement

NHS

Translational Excellence

Relationship between NICE & University of Manchester research can be synergistic: Here's how!

Prof. Colm Leonard

Consultant Clinical Adviser, NICE Centre for Health Technology Evaluation

Consultant Thoracic Physician/Honorary Professor of Respiratory Medicine

Manchester University NHS Foundation Trust

Colm.Leonard@nice.org.uk; Colm.Leonard@Manchester.ac.uk


SYNERGY
1+1>2

Where might synergy be relevant?

- Grant applications, review, follow-on applications
- Career & personal development (committee membership)
- NICE has an international reach (Network-building potential)
- Benefitting from and/or contributing to NICE's expertise/work in Real World Evidence & other research priorities
- Medtech database of emerging new medical technologies (Health Tech Connect)

Grants- not just about NICE-identified evidence gaps

- Academic in University of St Elsewhere submitting grant application to UK funding body for rare neurological disease
- A trial embedded in this of a repurposed drug for rare disease exploring some biomarkers and tolerability and proof of concept
- Contacts NICE & leads to discussion with NICE Scientific advice around how to think beyond the grant if pilot trial successful & what type of help/input NICE could offer with next stage of evidence generation
- Successful grant and feedback to Academic was very positive about engagement with NICE

Career development & Network building

- Committee membership (technology appraisals, Medtech, diagnostics, interventional procedures, clinical guidelines…), or informal clinical adviser on relevant topics

- NICE Fellows and Scholars Programme

Fellows

Are you an experienced leader in health and social care? Could you build an influential network that helps us to implement our guidance?

NICE fellows are experienced leaders from the field of health and social care who are our ambassadors at regional and national levels.

Applications for 2020 are now closed. Recruitment will open again in September 2020.

Scholars

Would you like the opportunity to improve the quality of care and contribute to your professional development?

NICE Scholarships are one-year opportunities to find out about the inner workings of NICE. You'd undertake a supported improvement project, related to our guidance, within a local organisation, national charity or voluntary sector organisation.

View examples of potential projects (word) that might be suitable activities for scholars.

Applications for 2020 are now closed. Recruitment will open again in September 2020.

Career development & Networking – a personal experience

- Case example: clinician/honorary academic & Clinical adviser to NICE CHTE (core role is filtering new pharma products for potential technology appraisal & providing clinical advice to Medtech programme)
- Due to Clinical & NICE role- asked to contribute to UK work on novel value assessment & delinked reimbursement to incentivise antibiotic development pipeline
- Speaking engagements internationally (NICE reach is very broad)
- Now clinical lead for UK AMR project to develop & test novel value assessment & reimbursement for new antimicrobials
- Invited onto consortium for EU-funded (>Euro 10 million) multicountry research project called VALUE-Dx looking at novel assessment of diagnostics in community respiratory infection

VALUE-Dx

VALUE-Dx

VALIDATING DIAGNOSTICS TO
COMBAT ANTIMICROBIAL RESISTANCE
BY OPTIMISING ANTIBIOTIC USE

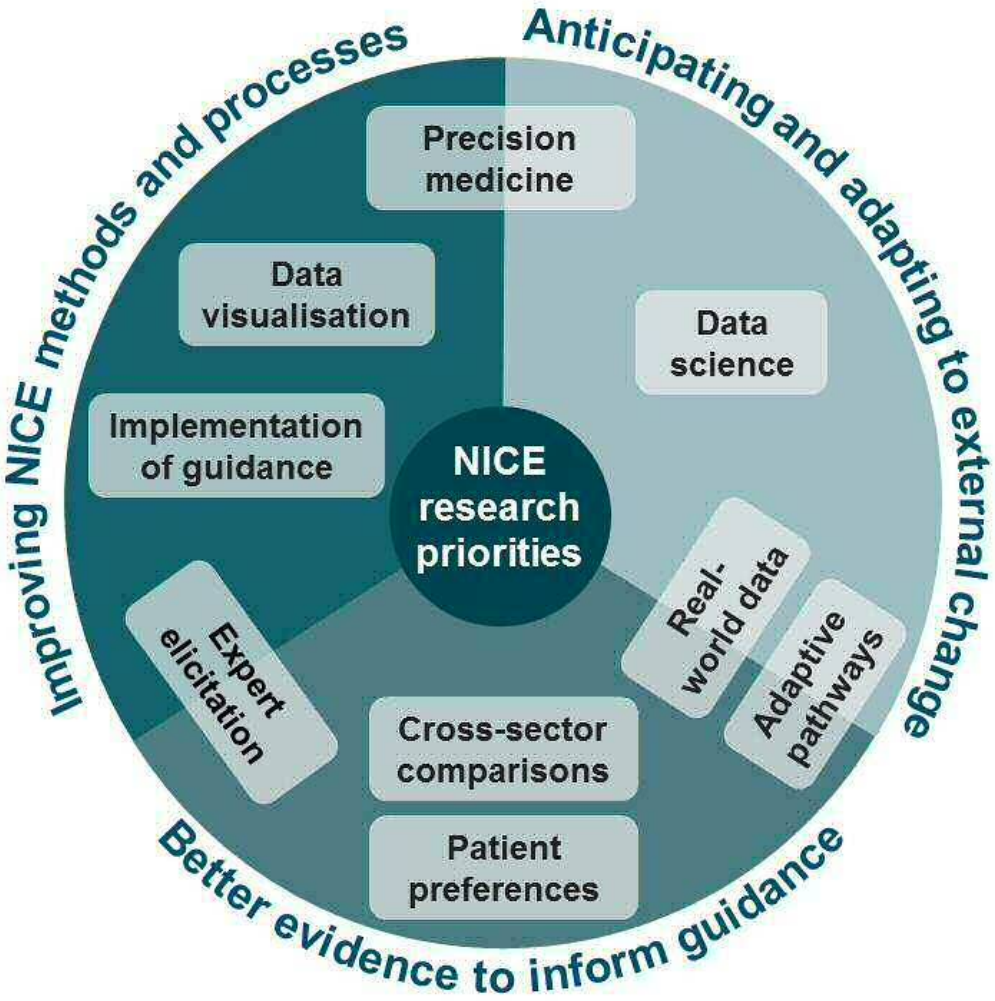
WWW.VALUE-DX.EU

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 820755. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and bioMérieux SA, Janssen Pharmaceutica NV, Accelerate Diagnostics S.L., Abbott, Bio-Rad Laboratories, BD Switzerland Sàrl, and The Wellcome Trust Limited.

www.imi.europa.eu

www.value-dx.eu

NICE’s priority research areas



More info: https://www.nice.org.uk/about/what-we-do/our-research-work/methodological-research-areas

What is HealthTech Connect?

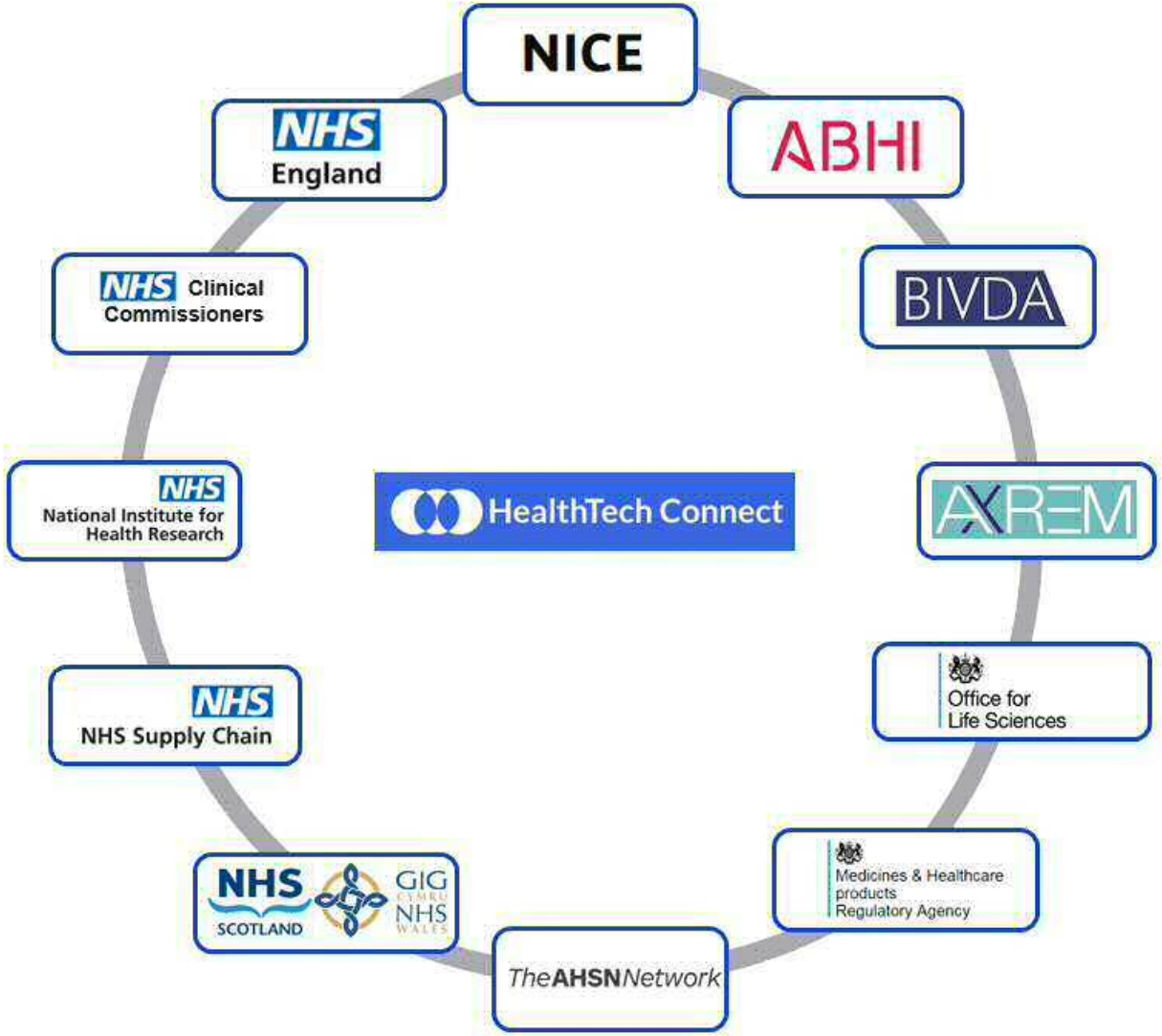
- A secure online system www.healthtechconnect.org.uk
    - store and maintain data
    - find accurate information
    - access national programmes and support
    - reduces duplication
    - streamlines processes

- Its not a catalogue

- For technologies with measurable additional benefits (in comparison to routine practice)

What is HealthTech Connect?

- Funded by NHS England
- Developed and hosted by NICE
- Developed in partnership with:
  - Innovators
  - National organisations
  - Trade associations



HealthTech Connect

January 2020

Launched in April 2019

Over 600 registered users...

...have submitted 160 technologies

65% selected

Health technology assessment

Assessment of the evidence to provide the health and care system with

- Guidance
- Policies
- Advice

Help and Support

- Funding
- Commercialisation
- Clinical & academic expertise
- Economics
- Evidence generation
- Validation
- Spread & adoption

NHS England

NICE National Institute for Health and Care Excellence

Technoleg Iechyd Cymru Health Technology Wales

Healthcare Improvement Scotland | SHTG Advice on health technologies

GIG CYMRU NHS WALES | Tîm Gwasanaethau Iechyd Arbenigol Cymru Welsh Health Specialised Services Team

The AHSN Network

NIHR | National Institute for Health Research

NHS Supply Chain

NHS England

Hwb Gwyddorau Bywyd Life Sciences Hub | Cymru Wales

Department for International Trade

NICE National Institute for Health and Care Excellence

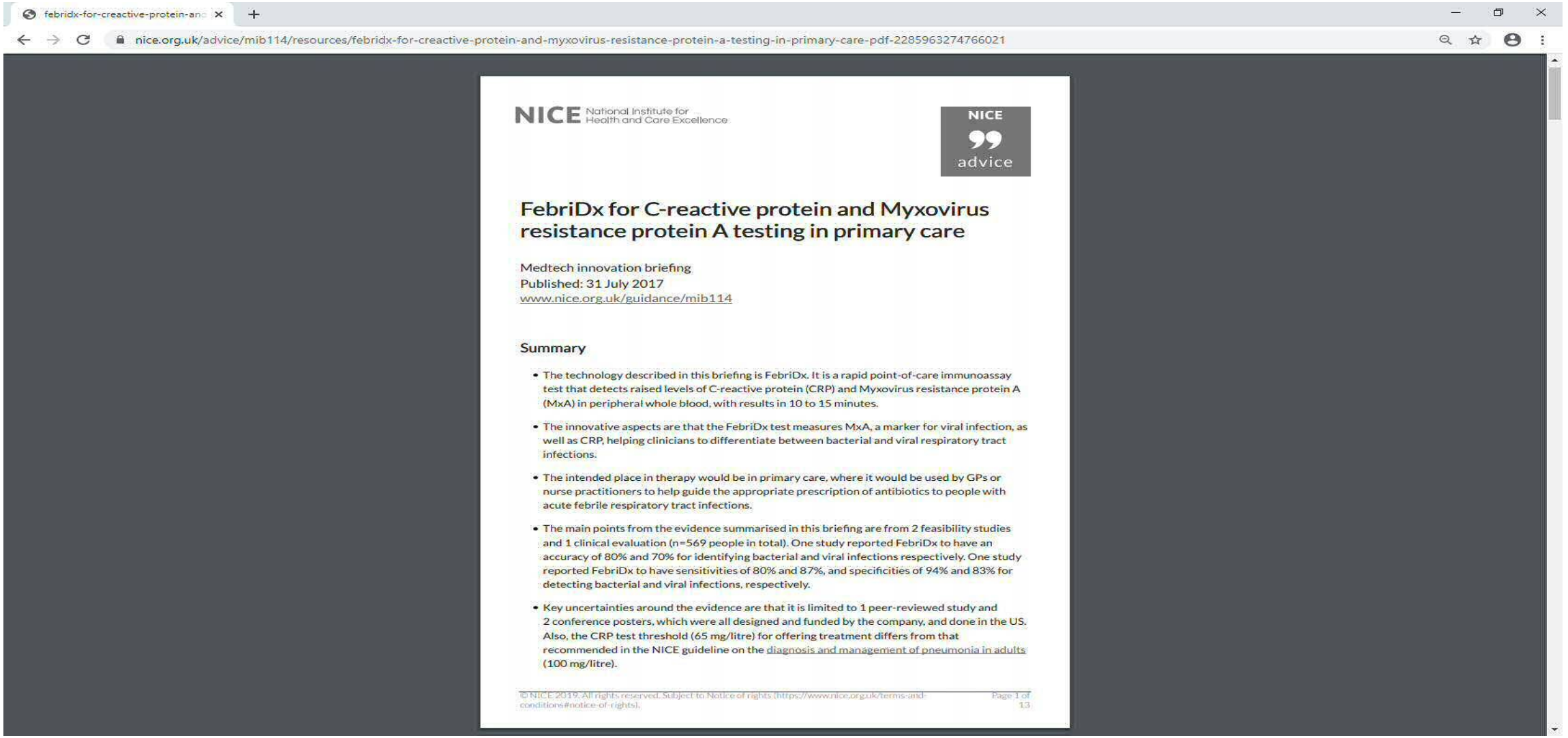
ABHI BIVDA BHTA British Healthcare Trades Association

AXREM Association of Healthcare Technology Providers for Imaging, Radiotherapy & Care

www.HealthTechConnect.org.uk

Contactus@HealthTechConnect.org.uk

NICE Medtech Innovation briefing



Viral or Bacterial Infection?

The symptoms can be very similar.

An acute respiratory infection (ARI) is the most common single reason for **outpatient office visits** and **antibiotic prescriptions**.[1-5]

More than **90%** of patients who present to their healthcare providers with the most common symptom of an ARI—an acute cough—have a syndrome caused by a **virus**.[6-7]

Unnecessary use of antibiotics leads to **antibiotic resistance, causing more than 25,000 deaths** in the EU, and 700,000 globally.[8-9] Antibiotic resistance results in costs over €1.5 billion in the EU and $20 billion in the U.S. annually.[1,2,8]

WHAT IF THERE WAS A RAPID TEST TO DIFFERENTIATE A VIRAL FROM A BACTERIAL INFECTION?

Introducing FebriDx® Point-of-Care Test Device

The ***first and only*** rapid, all-in-one point-of-care test device that can identify a clinically significant acute respiratory infection and differentiate viral from bacterial causes.

FebriDx® can be used to help triage patients at the point of care to reduce uncertainty and avoid unnecessary antibiotics.

- **Results within 10 minutes** increases confidence in whether or not to prescribe an antibiotic.
- **All-in-one test device** allows doctors or nurses to test during triage.
- **Instrument-free** means no expensive equipment and a fully portable solution.
- **Highly sensitive/specific** dual biomarker technology provides reliable differentiation of viral and bacterial infections.

NICE

Researchers wanted to study the public's views of health-related quality of life

Applications close on Wednesday 4 March 2020

12 February 2020

Appeal panel rules that NICE needs to request evidence for erenumab effectiveness in subgroup of people with chronic migraine

NICE has today (4 February 2020) published the outcome of the appeal against its final draft guidance (FAD) on erenumab (also called Aimovig and made by Novartis) for preventing chronic migraine.

04 February 2020

Broader types of data to be used in development of NICE guidance

An expanded evidence base could allow NICE to address evidence gaps and enhance reviews of the impact of our guidance

04 February 2020

Summary

- Various synergies around grants (NICE evidence gaps; NICE letters of support; looking beyond grant with NICE Scientific advice)
- Career development, personal development & networking (committees, advisers, fellows, scholars)
- Clinical excellence awards- NICE involvement helps!
- NICE has abroad remit (pharmaceuticals, MedTech, Clinical Guidelines, Public Health, Social Care, interventional procedures)
- NICE has expertise in real world evidence & other research areas
- NICE has an international reach & brand strength

Colm.Leonard@nice.org.uk; Colm.Leonard@Manchester.ac.uk

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The University of Manchester

NICE Guidance on Sunlight Exposure: Risks and Benefits (NG34)

Ann R. Webb

Lesley Rhodes

University of Manchester

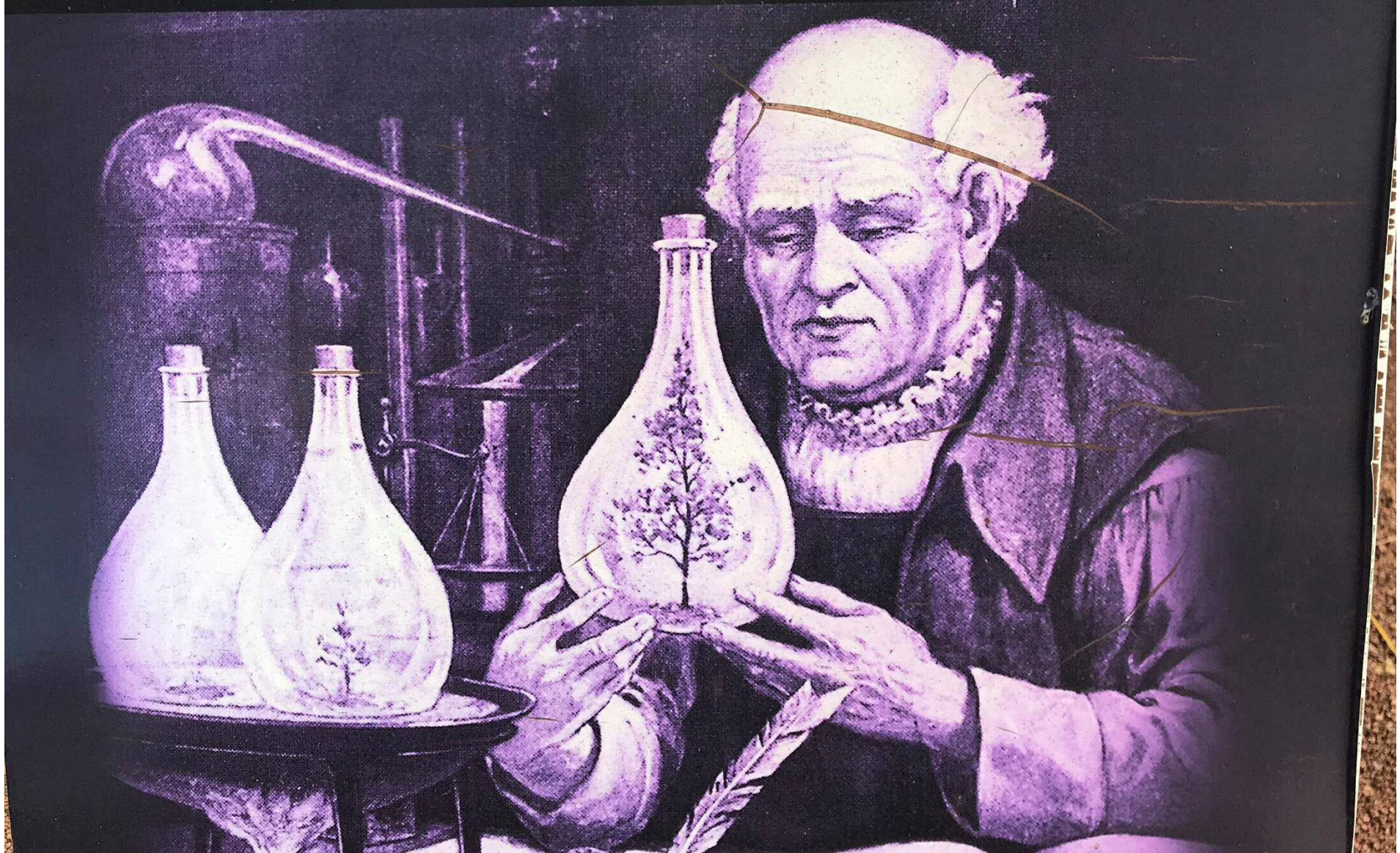
NICE Public Health Advisory Committee on Sunlight and Vitamin D

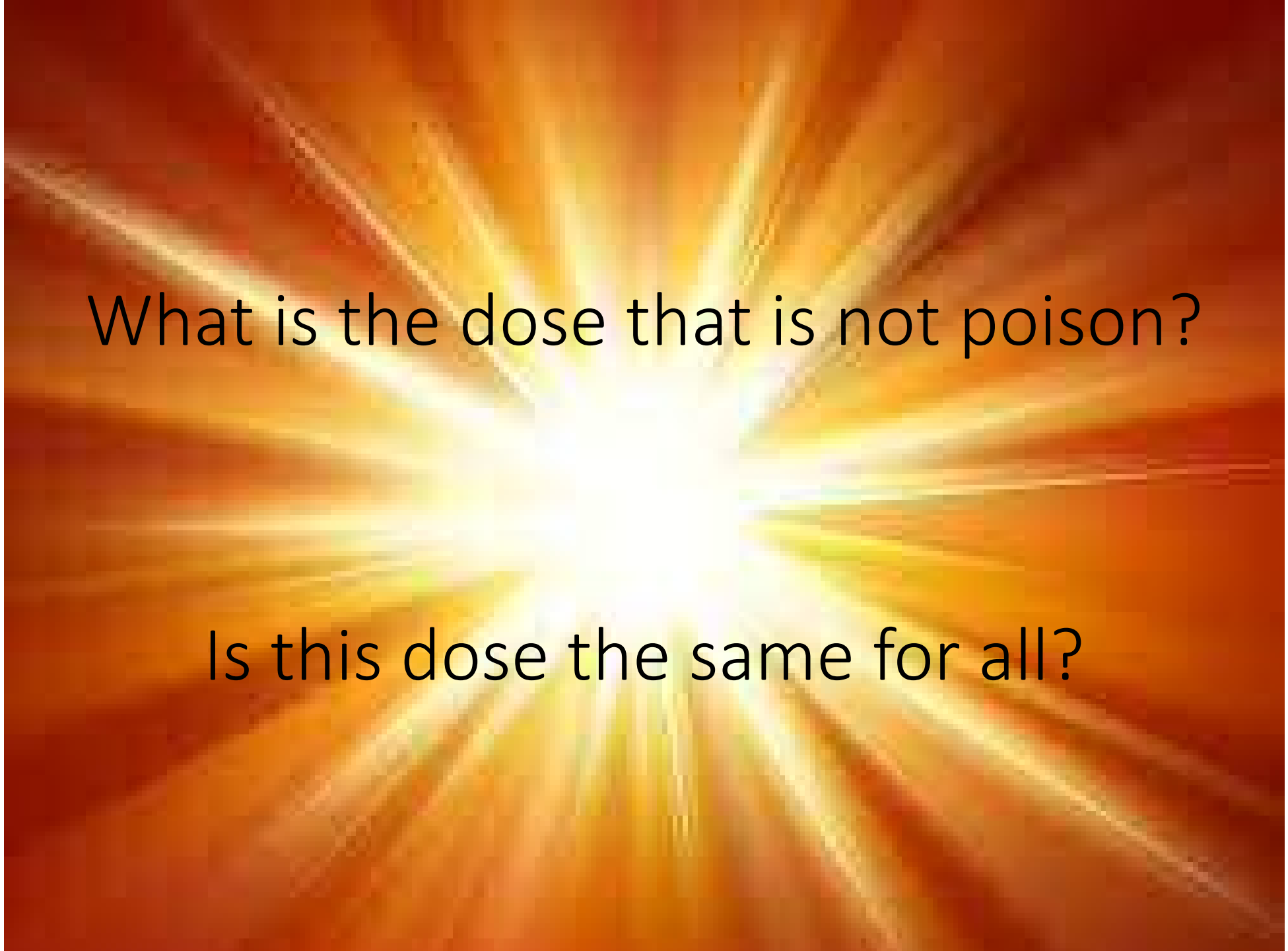
Member of PHAC – Professor Lesley Rhodes

Overview: This guideline covers how to communicate the risks and benefits of natural sunlight exposure (specifically, the ultraviolet rays UVA and UVB) to help people understand why they may need to modify their behaviour to reduce their risk of skin cancer and vitamin D deficiency.

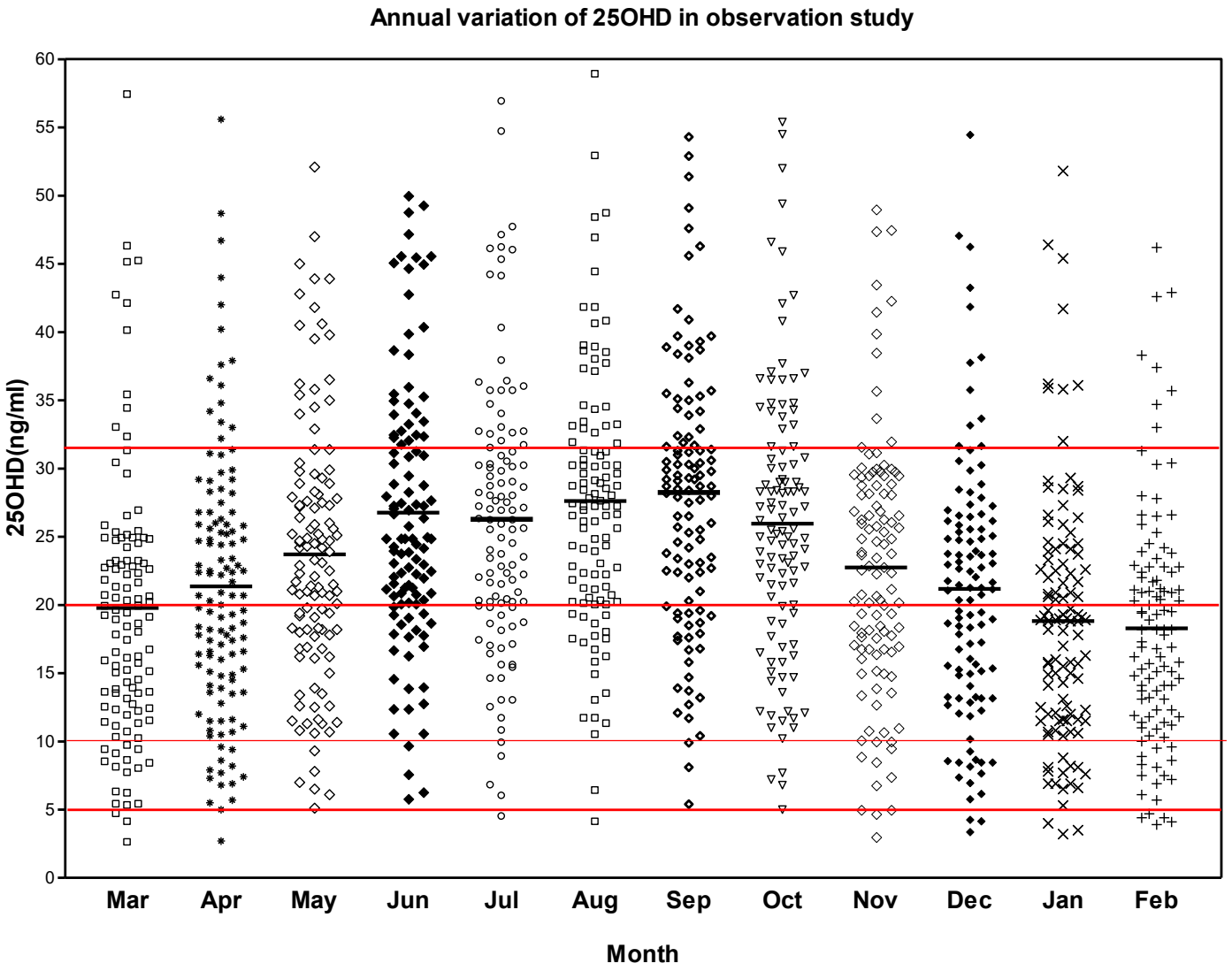
This guideline replaces recommendations 1–5 in skin cancer prevention NICE guideline PH32 (2011). The guideline should be read together with NICE's guideline on vitamin D: increasing supplement use among at-risk groups and any recommendations made by the Scientific Advisory Committee on Nutrition (SACN) on vitamin D (input from Professor Ann Webb)

Paracelso:
"… sólo la dosis determina que una cosa no sea un veneno."
Paracelsus: "…only the dose permits something not to be poison."
Paracelsus: "… allein die Dosis machts, dass ein Ding kein Gift sei."




What is the dose that is not poison?
Is this dose the same for all?

Vitamin D levels by month



Example of white Caucasian adults

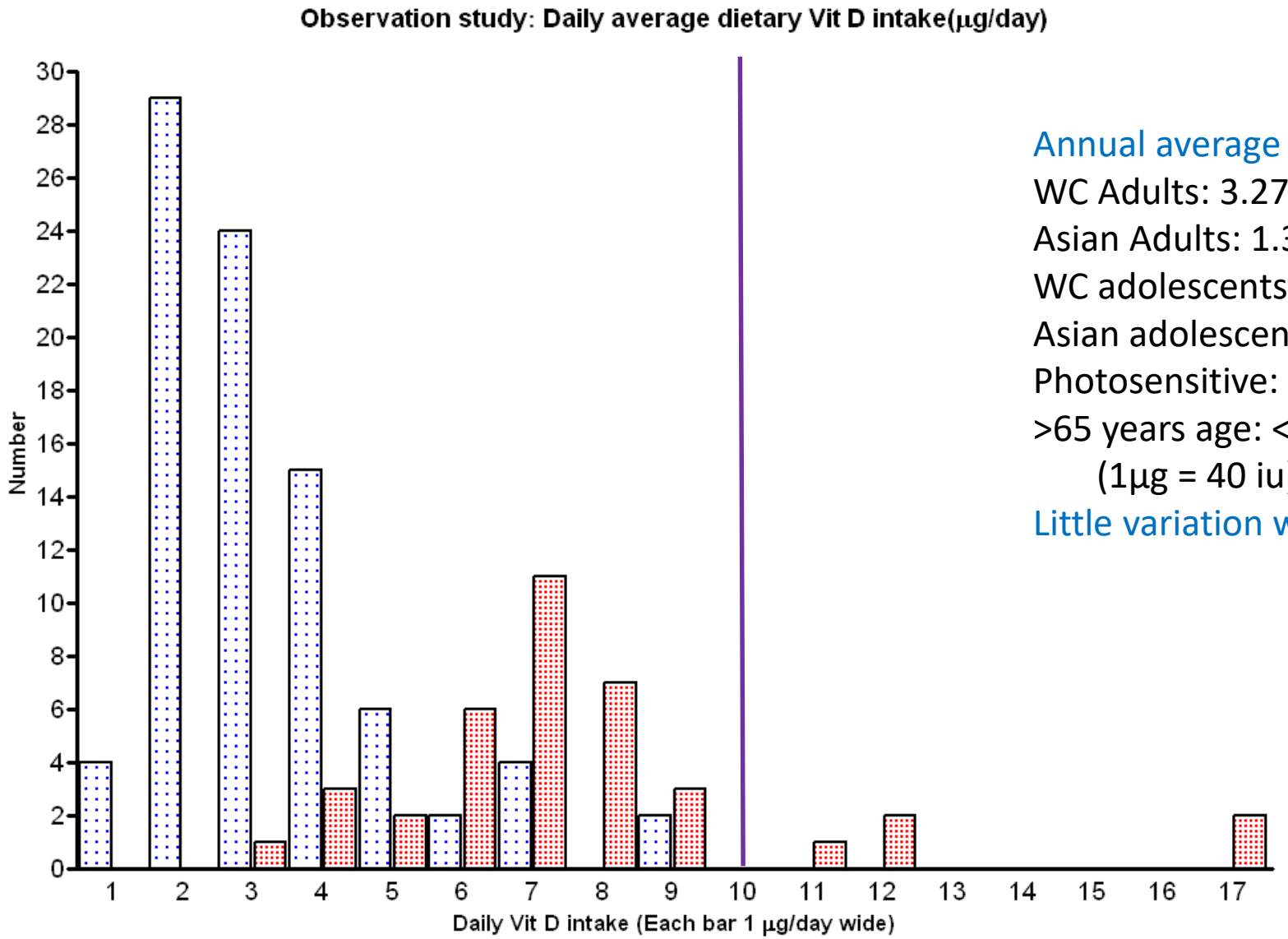
Data from Manchester, UK.

Amplitude of seasonal cycle in median 25OHD levels is about
10 ng/ml (25 nmol/L), with maximum in September and minimum in February.

Red lines at 5, 10, 20 and 32 ng/ml
12.5, 25, 50 and 80 nmol/L

Webb et al. (2010) BJD 163; 1050-1055

Dietary intake – low!



Annual average daily intake (µg/day)

WC Adults: 3.27

Asian Adults: 1.32

WC adolescents: 1.92

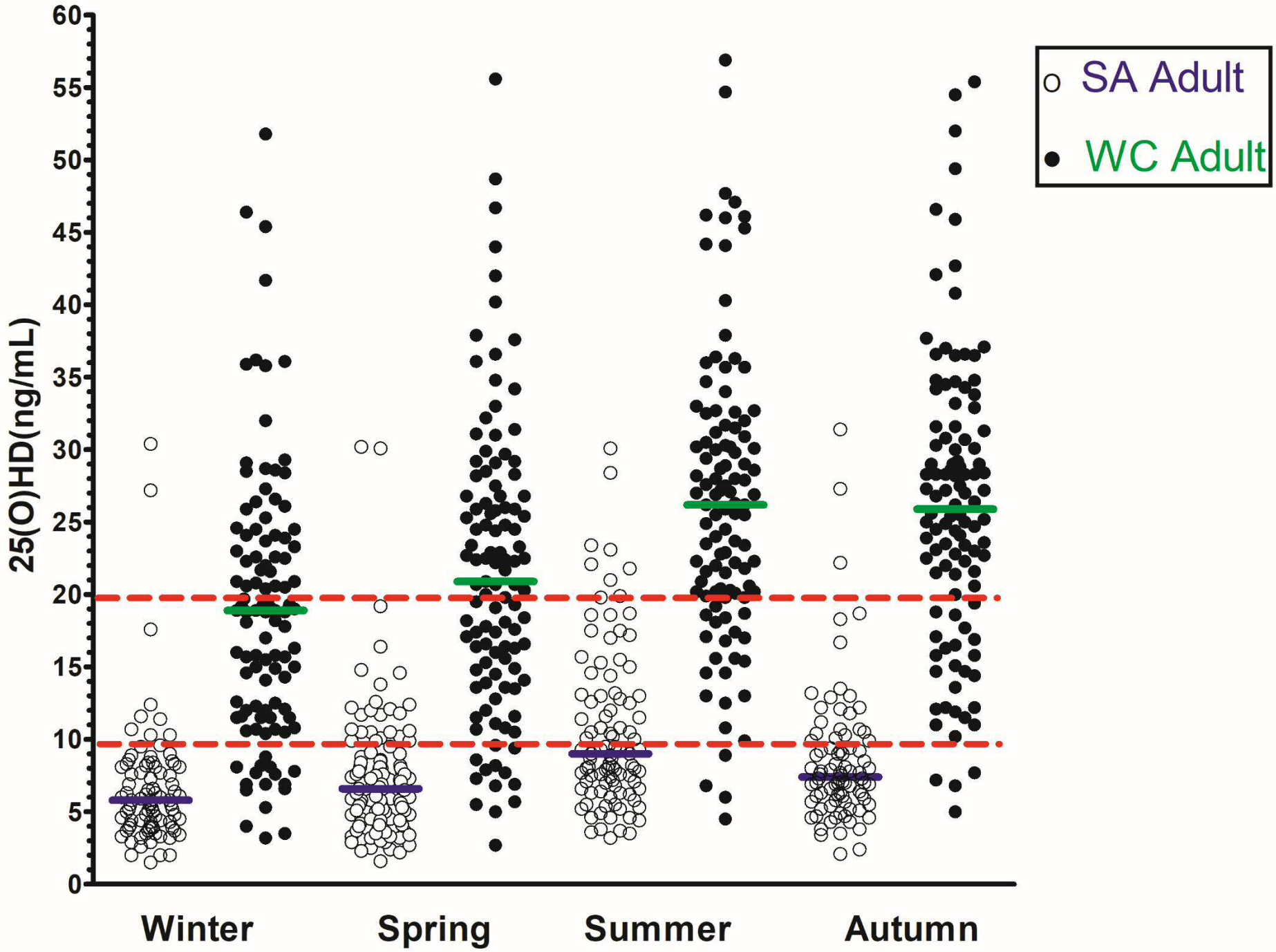
Asian adolescents: 1.75

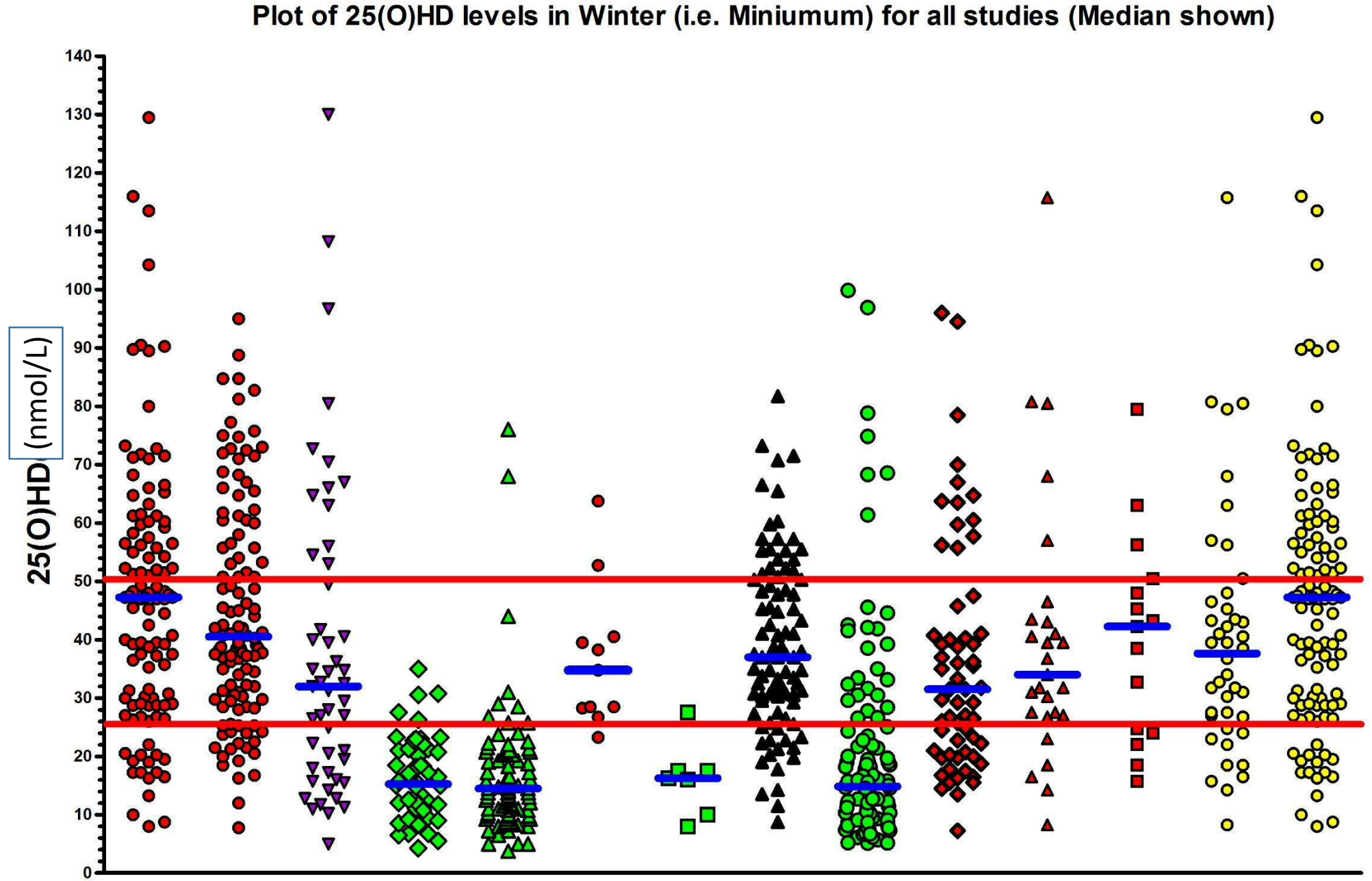
Photosensitive: 3.25

>65 years age: < 5

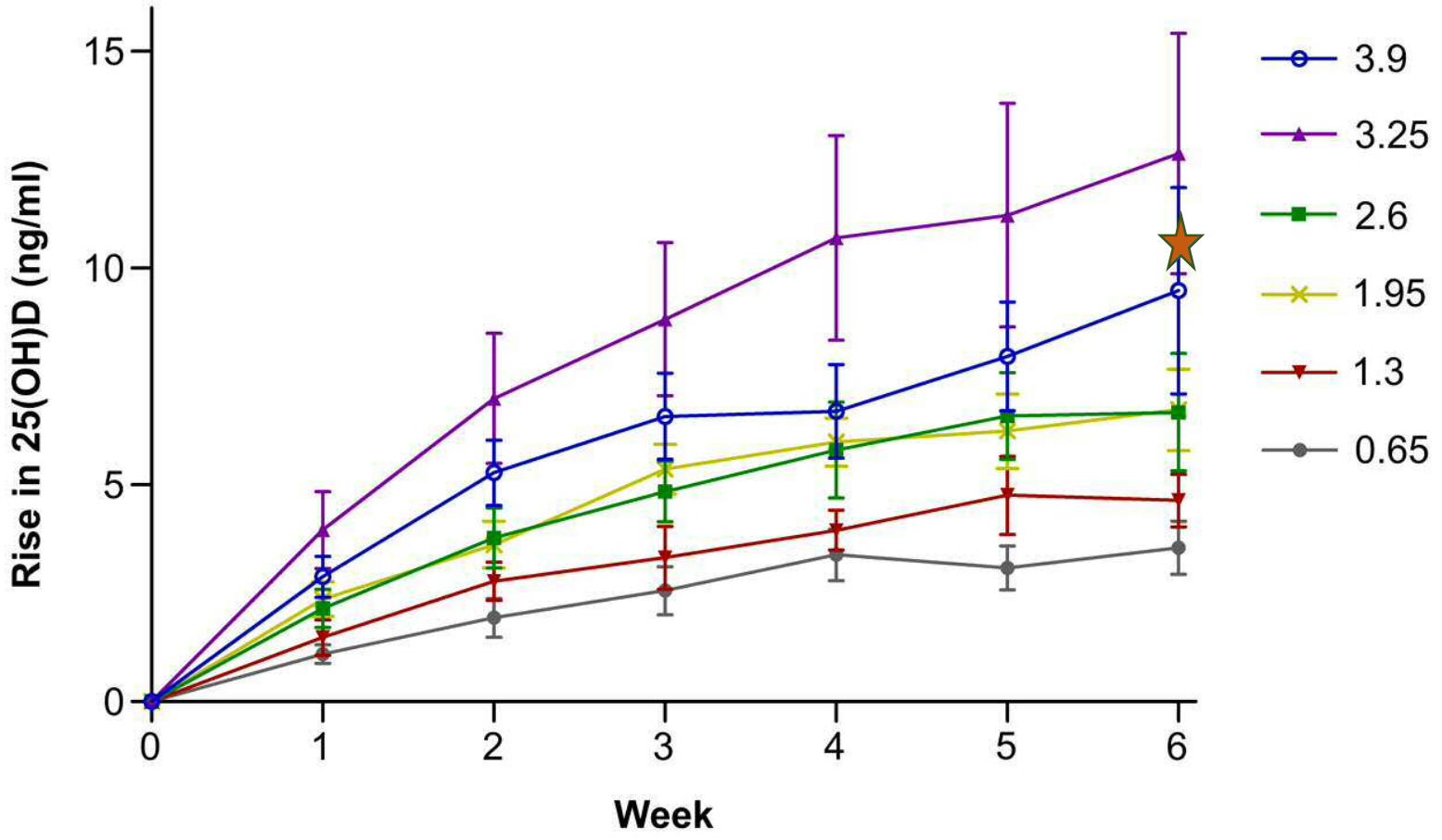
(1µg = 40 iu)

Little variation with season


SA Adult
WC Adult
25(O)HD(ng/mL)
60
55
50
45
40
35
30
25
20
15
10
5
0
Winter
Spring
Summer
Autumn

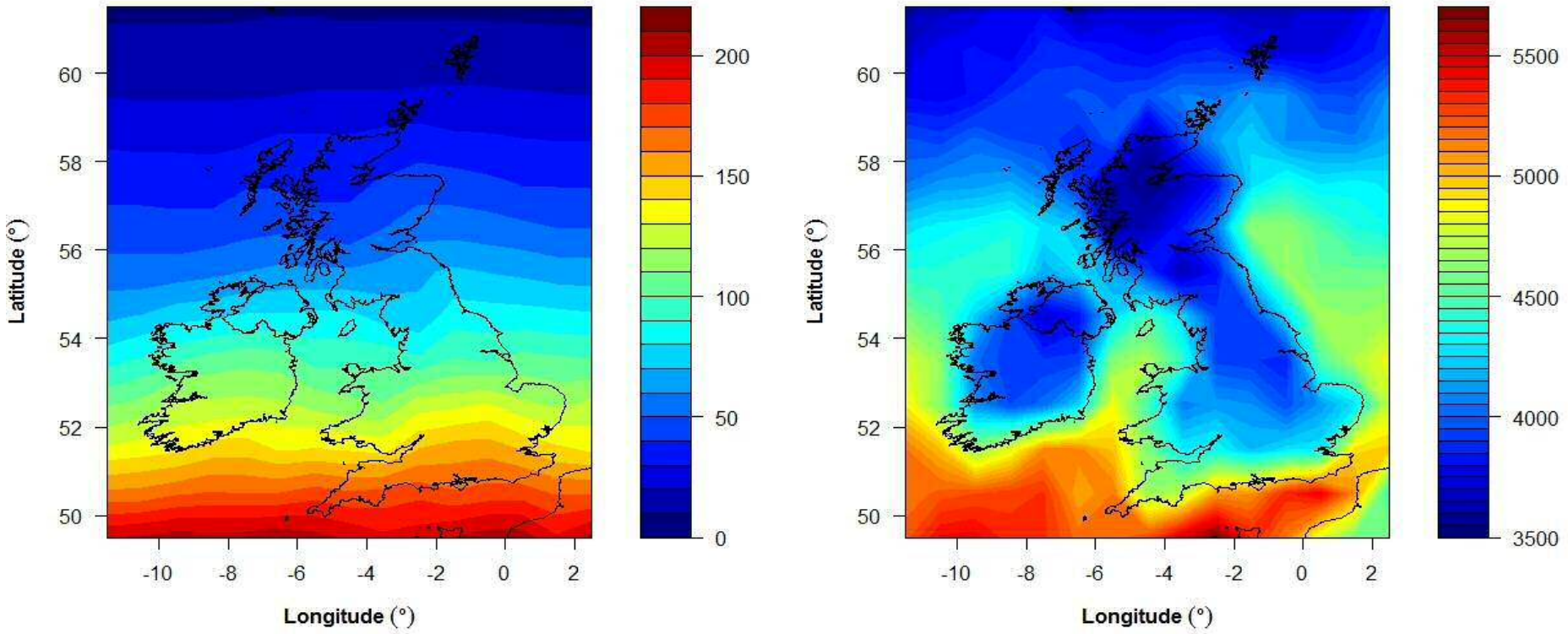

Plot of 25(O)HD levels in Winter (i.e. Miniumum) for all studies (Median shown)
25(O)HD (nmol/L)
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

Effect of skin pigmentation, controlled exposures, skin type V, ★ skin type II/III



UK climatology (expectation)

Pre-vitamin D weighted, monthly average of daily UV (Jm^{-2}) for period 2003-2012, inputs ozone, cloud, aerosol, albedo and elevation. January (LHS) and July (RHS)



Kazantzidis et al. (2015) Photochem. Photobiol. Sci. 14, 1073-81

A pragmatic approach

- How much vitamin D do we need?

  97.5% population > 25 nmol/L by end February (SACN)

- How much sun exposure required to make this amount of vitamin D?

  Safety criteria: <1 SED per day at any time and place

- Can we achieve this level of exposure?

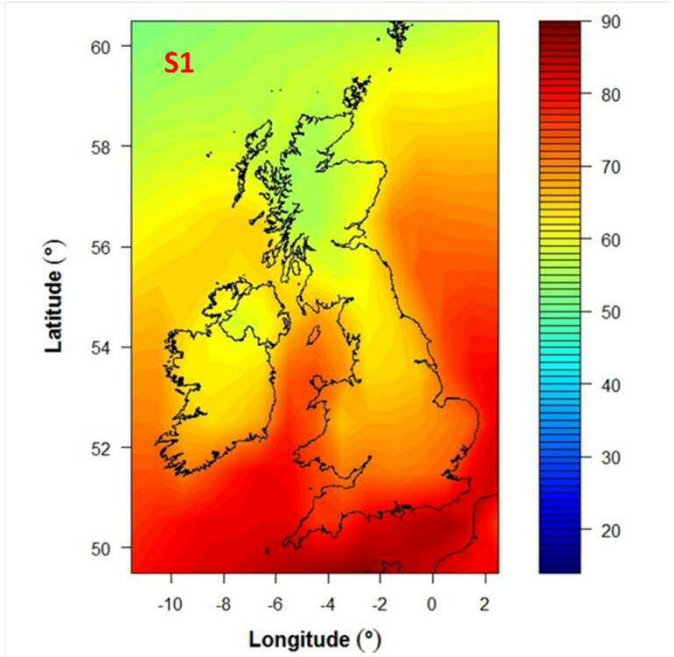
  Yes, in principle

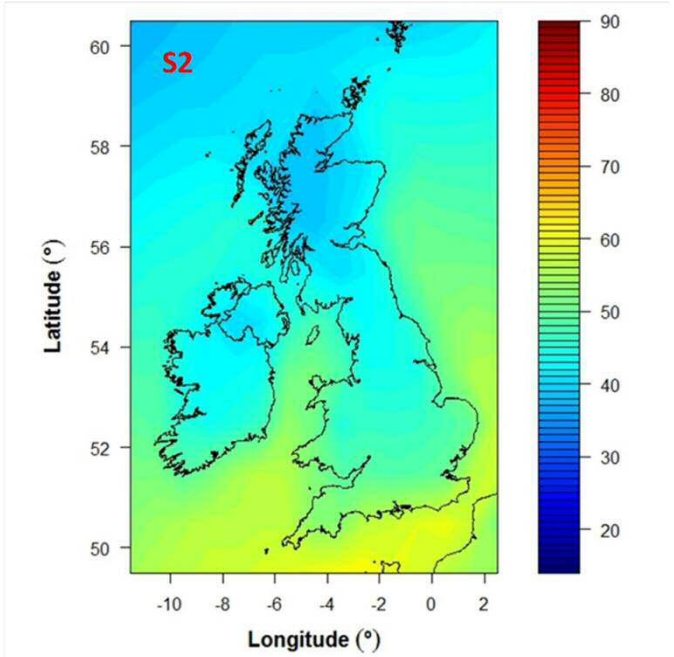
  9 (25) minutes at lunchtime every day in season appropriate clothing

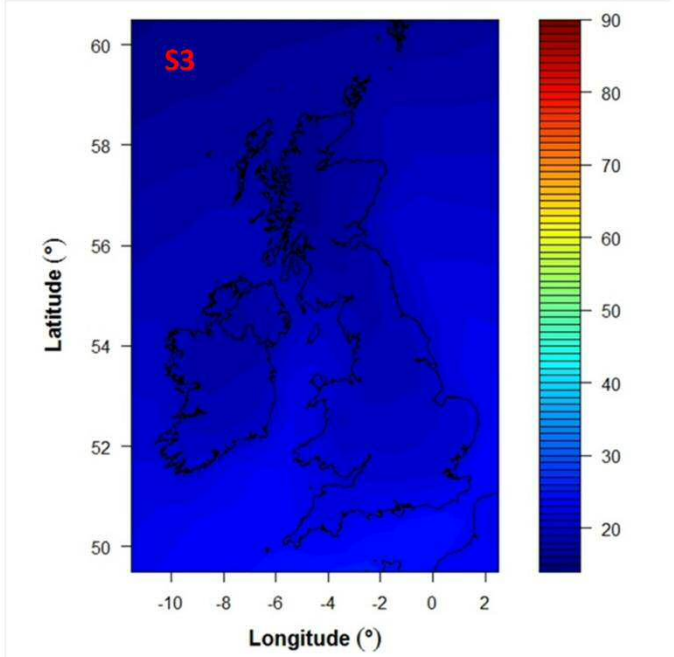
  Realistically, 10-15 (25-40) minutes.

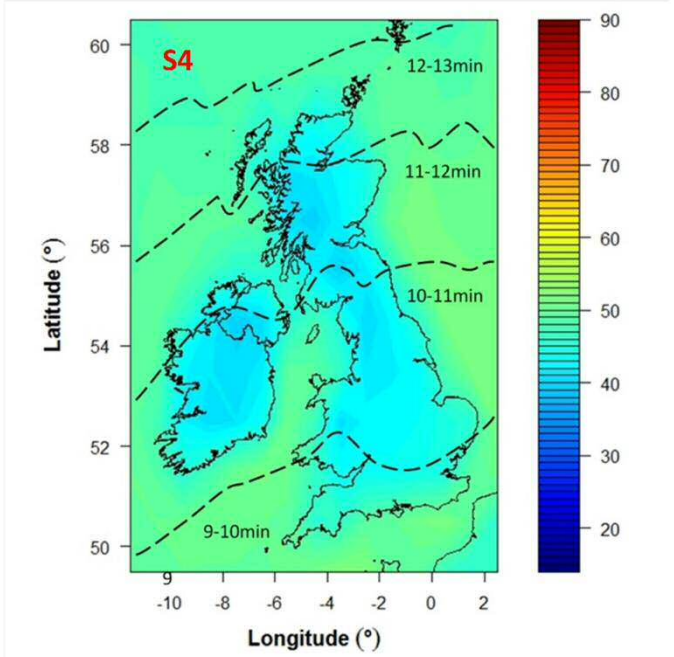
- Do we achieve this level of exposure?

  Data from sub-sets of the Manchester population









UV climatology 2003-2012
Summer half year (March-September)
Total for 9 minutes at solar noon every day (units SED)

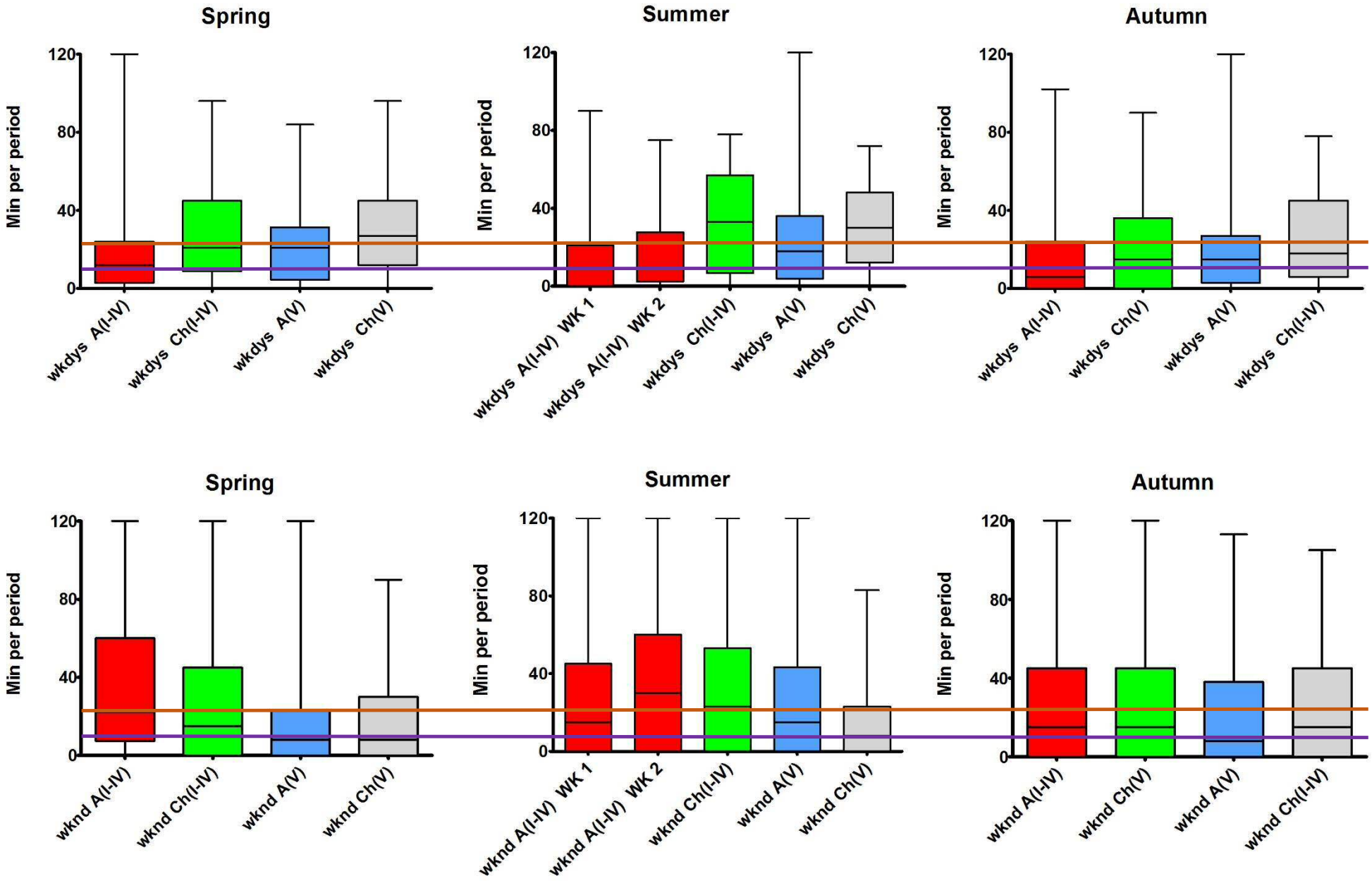
Weighted by skin area exposed:
S1 35% skin area all summer
S2 35% June-August, 10% otherwise
S3 10% skin area all summer

S4 June-August total, 35% skin area, exposure time for 1SED on clear day at summer solstice

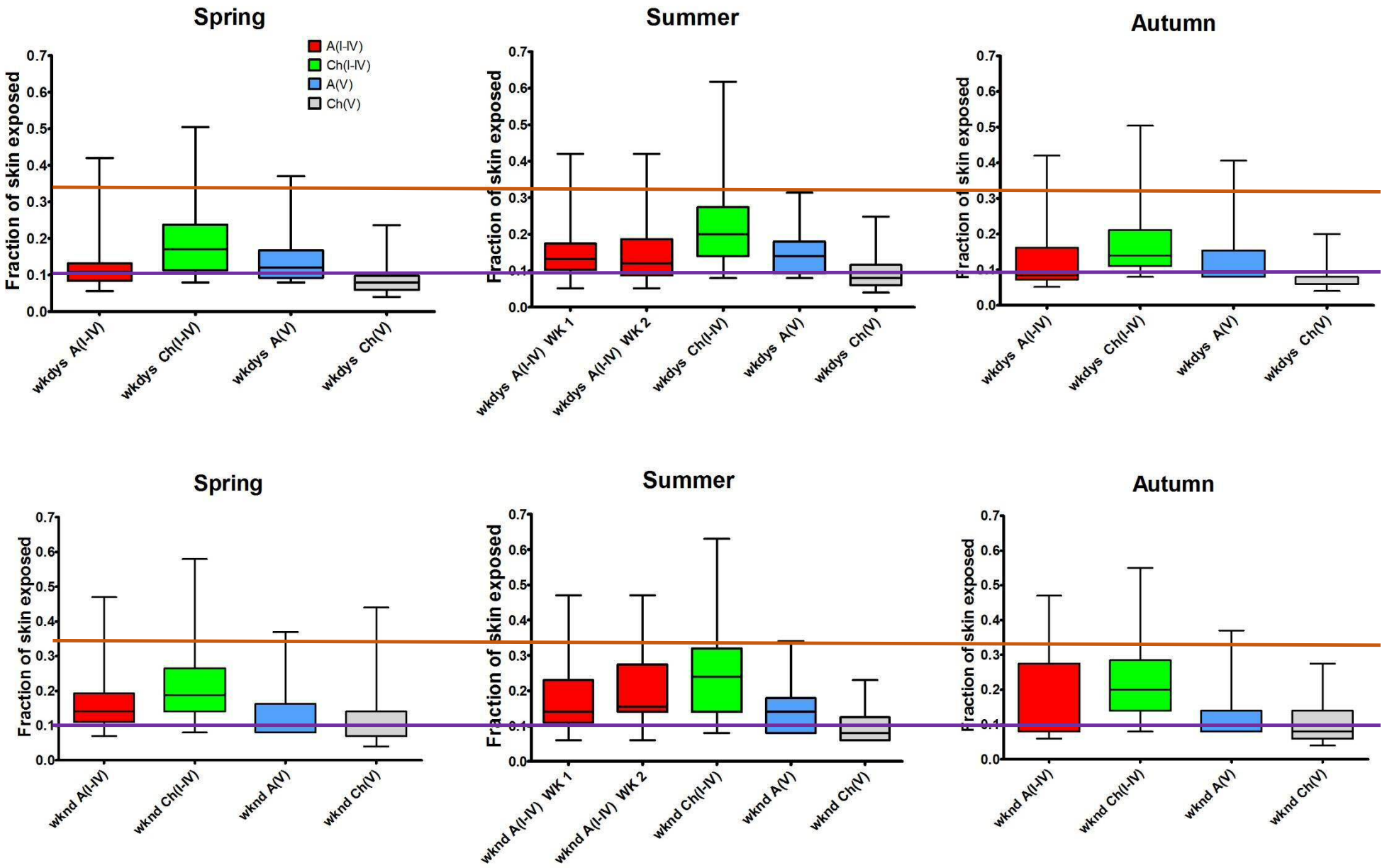
Target exposure for white skin types to remain clear of vitamin D deficiency by end winter is 38 SED acquired in short, daily doses.

Webb, Ann R., Andreas Kazantzidis, Richard C. Kift, Mark D. Farrar, Jack Wilkinson and Lesley E. Rhodes (2018) Colour Counts: Sunlight and Skin Type as Drivers of Vitamin D Deficiency at UK Latitudes. Nutrients 10(4), 457; https://doi.org/10.3390/nu10040457
Webb AR, Kazantzidis A, Kift RC, Farrar MD, Wilkinson J, Rhodes LE (2018) Meeting Vitamin D Requirements in White Caucasians at UK Latitudes: Providing a Choice. Nutrients 10(4), 497; https://doi.org/10.3390/nu10040497

Time outside 12-2pm (BST), Manchester



Skin area exposed in middle of day, Manchester



Conclusion

- Retrospective analysis of unguided sun exposure behaviour shows that many white Caucasians spend sufficient time in the midday sun (and with minimal risk of sunburn), but do not always expose sufficient skin area to meet vitamin D needs (97.5% population with 25(OH)D > 25 nmol/L year-round).
- Across all our studies 10-20% of white Caucasian population had winter vitamin D status < 25 nmol/L.
- Viable – Yes – improve by exposing more skin area
- Skin type V individuals need to spend 25 minutes in the midday sun for equivalent vitamin D synthesis. Median exposure for children on spring and summer weekdays achieved this. Skin area exposed remains insufficient for almost all.
- The great majority of skin type V individuals have 25(OH)D < 25 nmol/L during winter (and year round).
- Viable – No/difficult – alternative source (supplements) recommended

NICE Recommendations:

- 6.6 It is not possible to provide a simple definitive message telling different groups how often and how long they can be exposed to sunlight to ensure minimum risk but maximum benefit. That is because the amount of UV someone gets from sunlight depends on a range of biological, environmental and behavioural factors. But the committee agreed that advice on preventing both skin cancer and low vitamin D status can be combined. It heard (from expert papers 4 and 5) that short (less than the time it takes for skin to redden or burn), frequent periods of sunlight exposure are best for vitamin D synthesis. In addition, this type of exposure is less likely to result in skin cancer.
- 6.19 The risk-benefit ratio of sunlight exposure will vary depending on how dark or light someone's skin is. The committee was particularly concerned about the risks and benefits for darker skinned people because much of the evidence and existing advice is focused on those with lighter skin
- 6.22 The balance of published evidence suggests that skin with darker pigmentation needs longer sunlight exposure than lighter skin to produce equivalent levels of vitamin D. But further research is needed. In the meantime, the committee was clear that people of all skin types should not risk burning their skin.
- 6.30 The recommendations stress the need for tailored individual advice to back up the universal messages. The committee noted that universal interventions could result in adverse effects for some groups and so increase health inequalities. For example, universal messages about protecting the skin from sunlight exposure may inadvertently lead to a reduction in the amount of skin exposed to sunlight among groups at risk of low vitamin D status.

THANKS

- To all our many volunteers over the years

- To the multiple collaborators who have made these studies possible, from clinical staff to school nurses and academic colleagues

- To the funders who have supported the different aspects of the work summarised here: Action Medical Research, British Skin Foundation, BUPA, Cancer Research UK, Dept. Environment Food and Rural Affairs, Dept. of Health, Dunhill Medical Trust

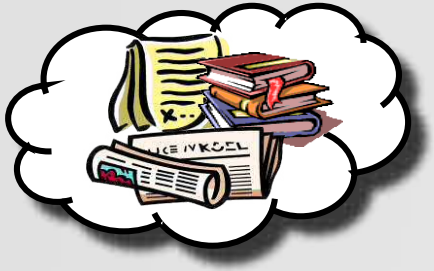
RobotAnalyst automating systematic reviews

SOPHIA ANANIADOU
NATIONAL CENTRE FOR TEXT MINING
COMPUTER SCIENCE

AI (Text Mining & Machine Learning) to support systematic reviews and guideline development and update

- Key databases are manually curated and oriented towards human use
- Concept labels do not always reflect the written language
- The volume of terms in literature, synonyms for the same concepts in different written forms
- Problems of discovery and mapping of new terms found in literature into existing resources have constituted a barrier to ***semantic search***

Text Mining in a Nutshell



Unstructured Text
(implicit knowledge)

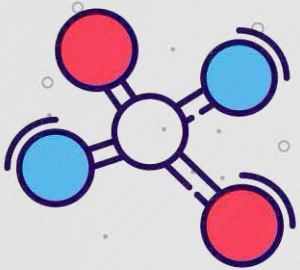
Information Retrieval

Other data

Applications
Semantic search
Data mining

Knowledge Discovery

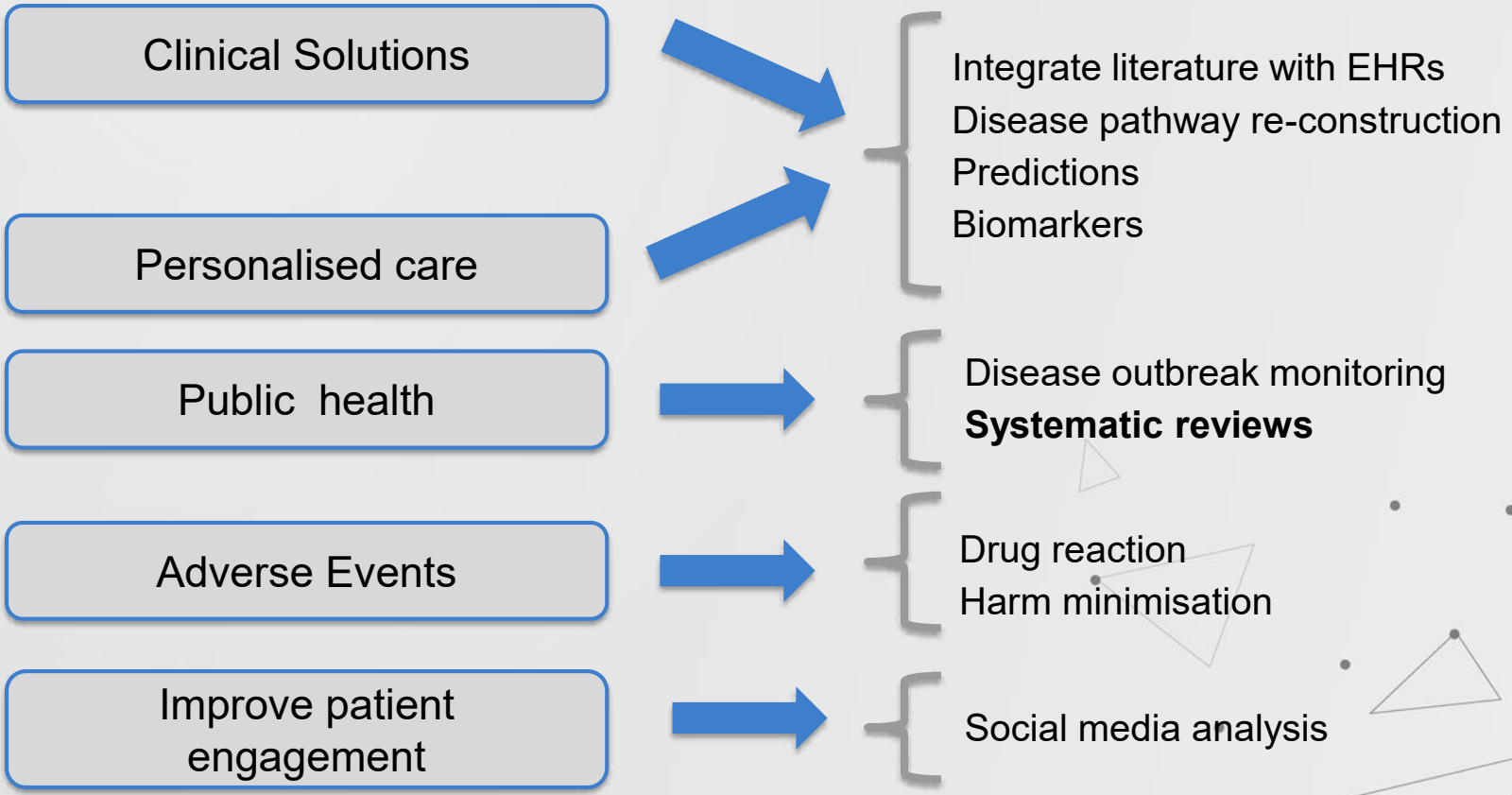
Information Extraction



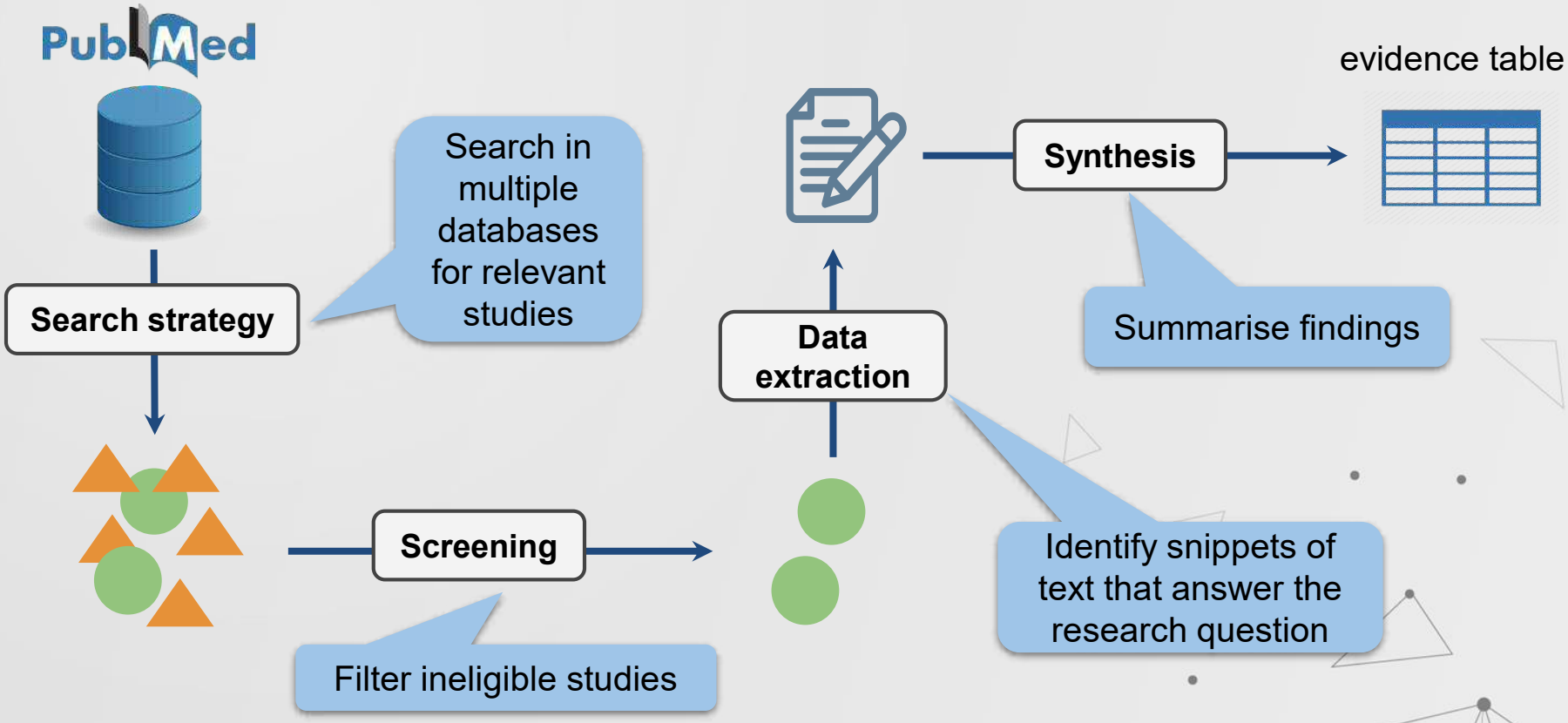
Structured Content
(explicit knowledge)

Semantic Metadata Annotations

Applications of text mining in health



Systematic Reviews: steps and challenges



Challenges

- Time consuming and resource-intensive process
  - Low precision of engines (e.g., PubMed); many items to screen
  - Slow process of screening (~2 min/abstract) and extracting data from text (~2hr/abstract)
  - Cannot keep up with rapidly evolving literature (trials published daily)

- TM accelerates the development of Systematic Reviews
  - Improve search
  - Semi-automate citation screening; **workload reduction**

Text Mining for Literature Search

Ideally, a search strategy should maximise:
sensitivity: all relevant studies are included in the review
specificity: minimise screening effort

Increased Sensitivity

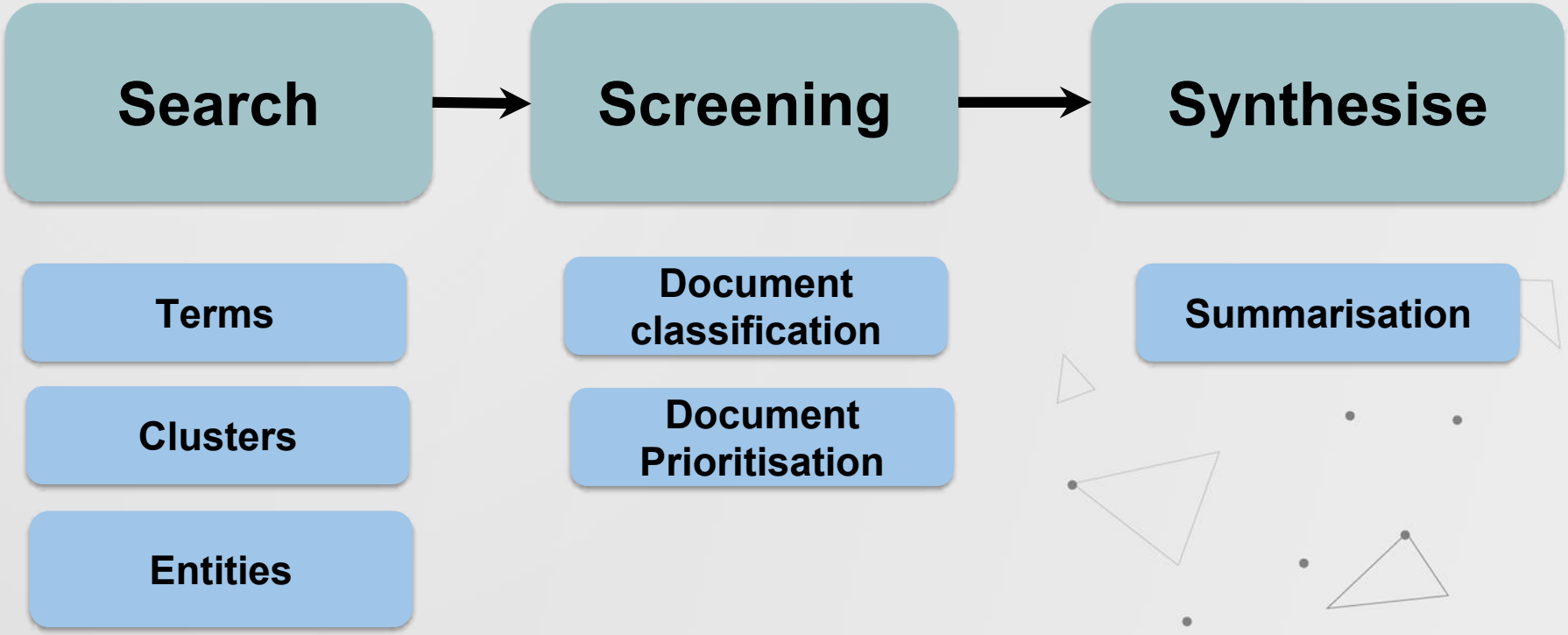
- Augment query with synonyms, orthographic variations, related terms (e.g., extend '*impaired vision*' with '*loss of vision*')
- Include short-forms (e.g., 'GAD') and long-forms of an acronym (e.g., generalised anxiety disorder)
  - An article might contain either the short-form, long-form or both.

Increased specificity

- Disambiguation of query terms (e.g., 'cat' animal or 'cat' protein)
- Disambiguation of acronyms (e.g., '*GAD*' might refer to either '*generalised anxiety disorder*' or '*glutamic acid decarboxylase*')
- Subject-verb-object (SVO) queries instead of keyword-based queries

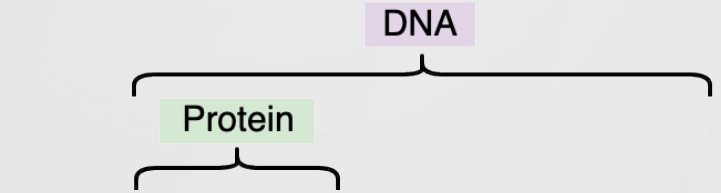
- SVO queries require concepts to have a syntactic relationship thus should increase specificity over keyword-based queries.

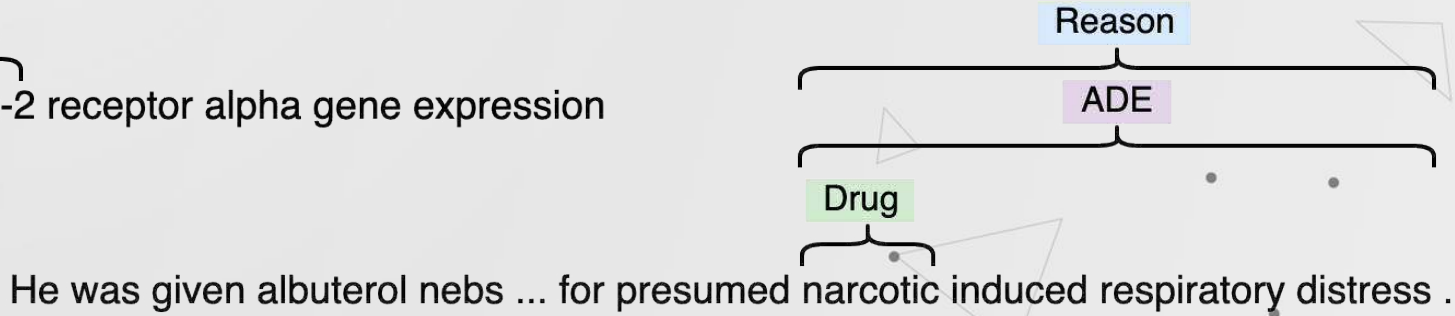
Text Mining Methods for Systematic Reviews



Named Entities

- **Named entities** are typically **embedded in longer entities**
- The embedded entities are known as **nested named entities**

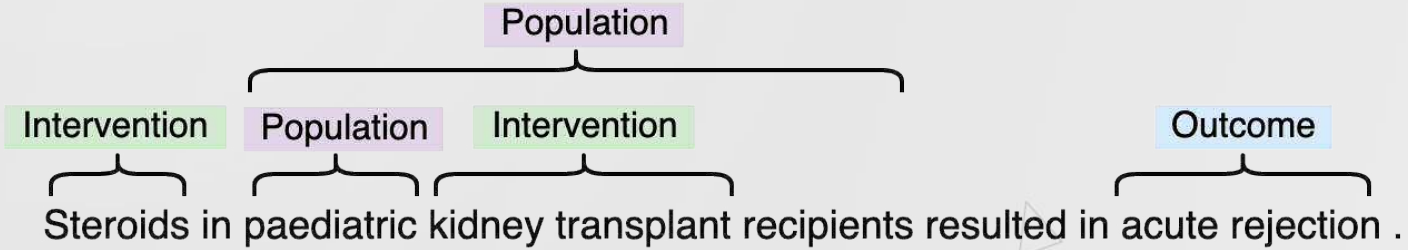




M Ju, M Miwa, S Ananiadou. A Neural Layered Model for Nested Named Entity Recognition. **NAACL-HLT**, 2018

PICO Element Extraction

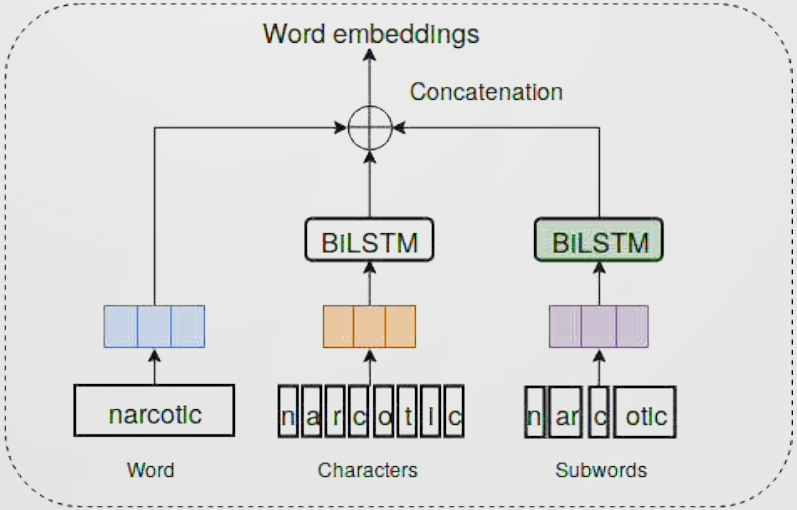
Extract PICO elements of patient/population (P), intervention (I), comparator (C), and outcomes (O) from medical articles

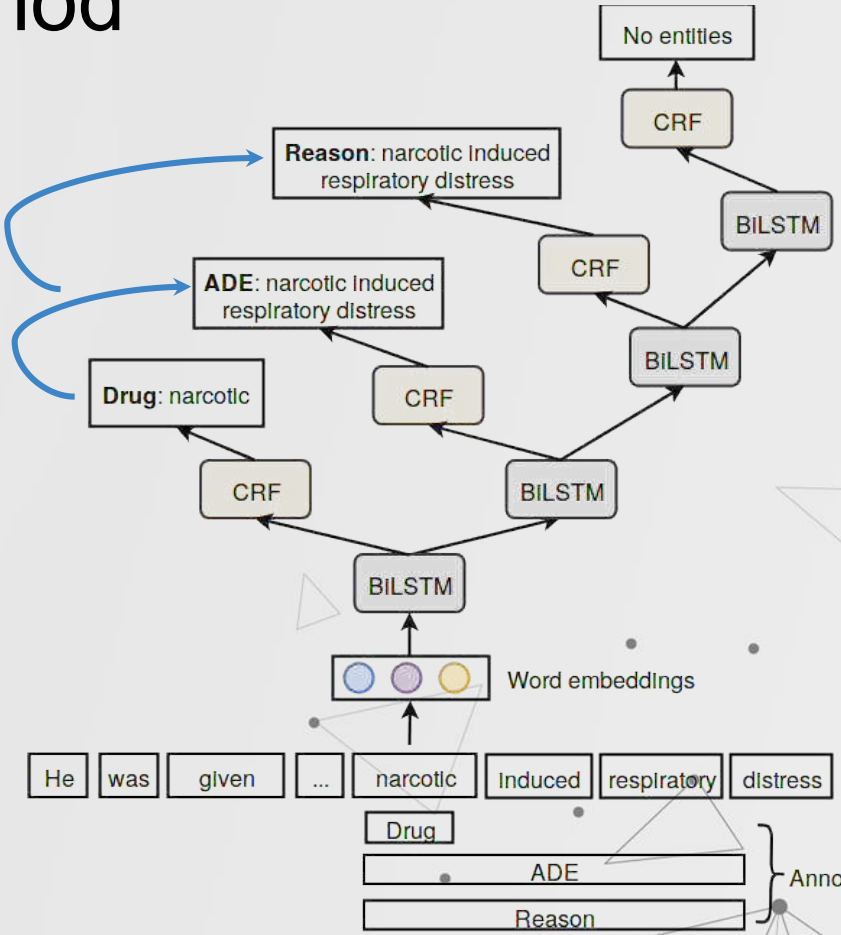


A Brockmeier, M Ju, P Przybyla, S Ananiadou. Improving reference prioritisation with PICO recognition. **BMC Medical Informatics and Decision Making**, 2019

Method

- **Subwords**: combination of the most frequent consecutive characters of words, e.g., subwords of “narcotic”: [n, ar, c, otic]

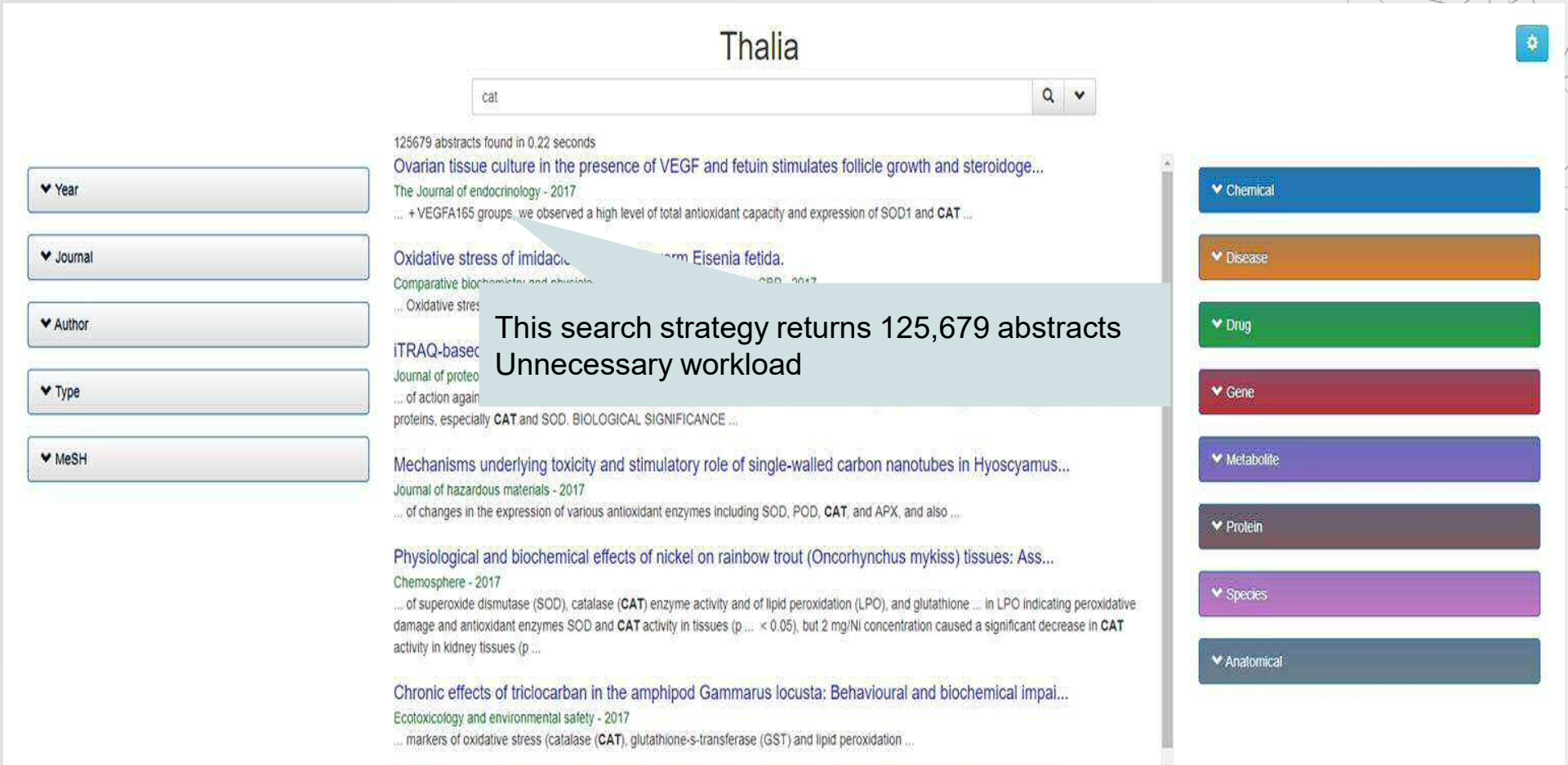




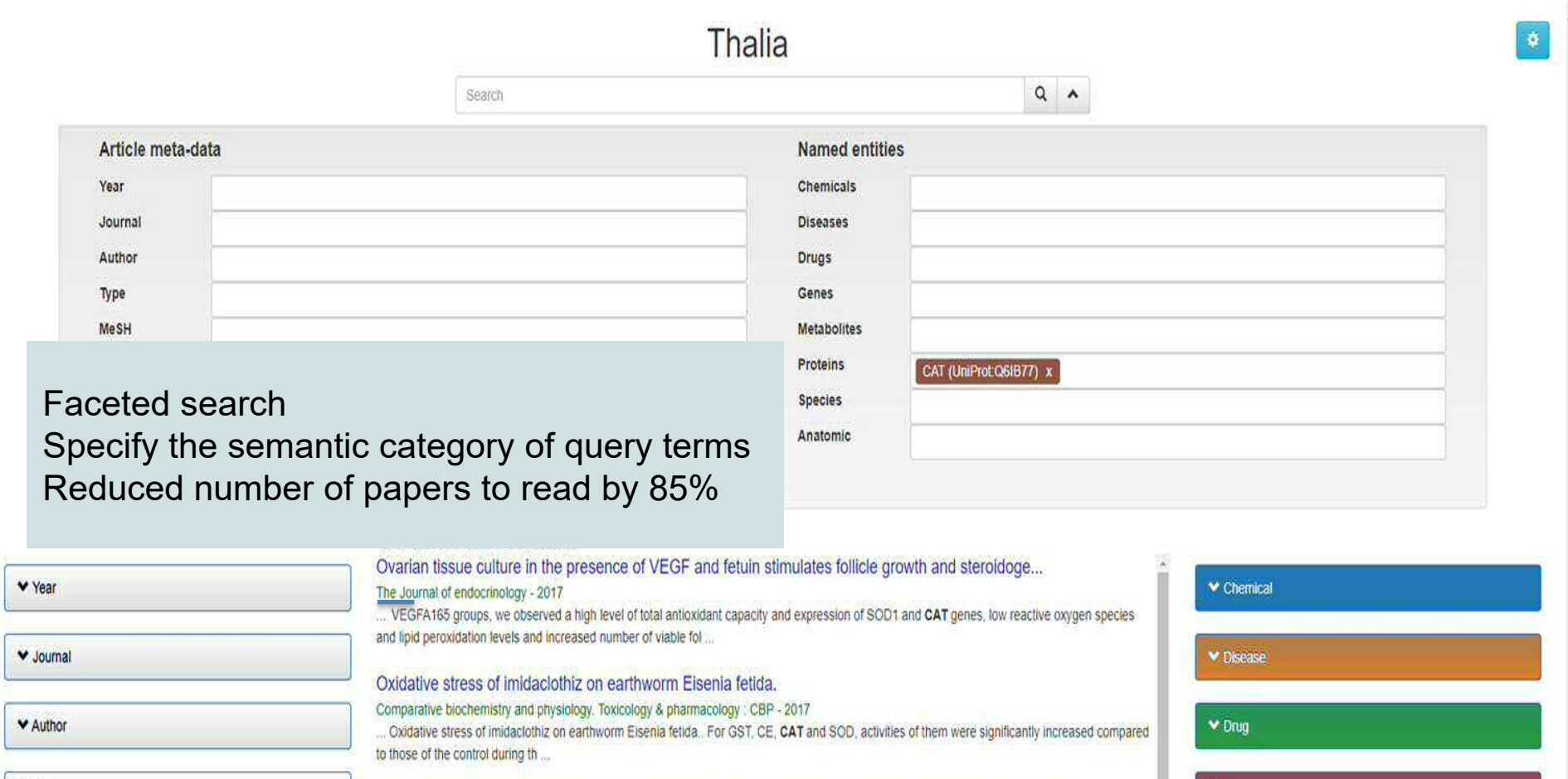
Uses inner entities to detect outer entities

Dynamically stacks BiLSTM-CRF blocks

Application: Faceted Semantic Search

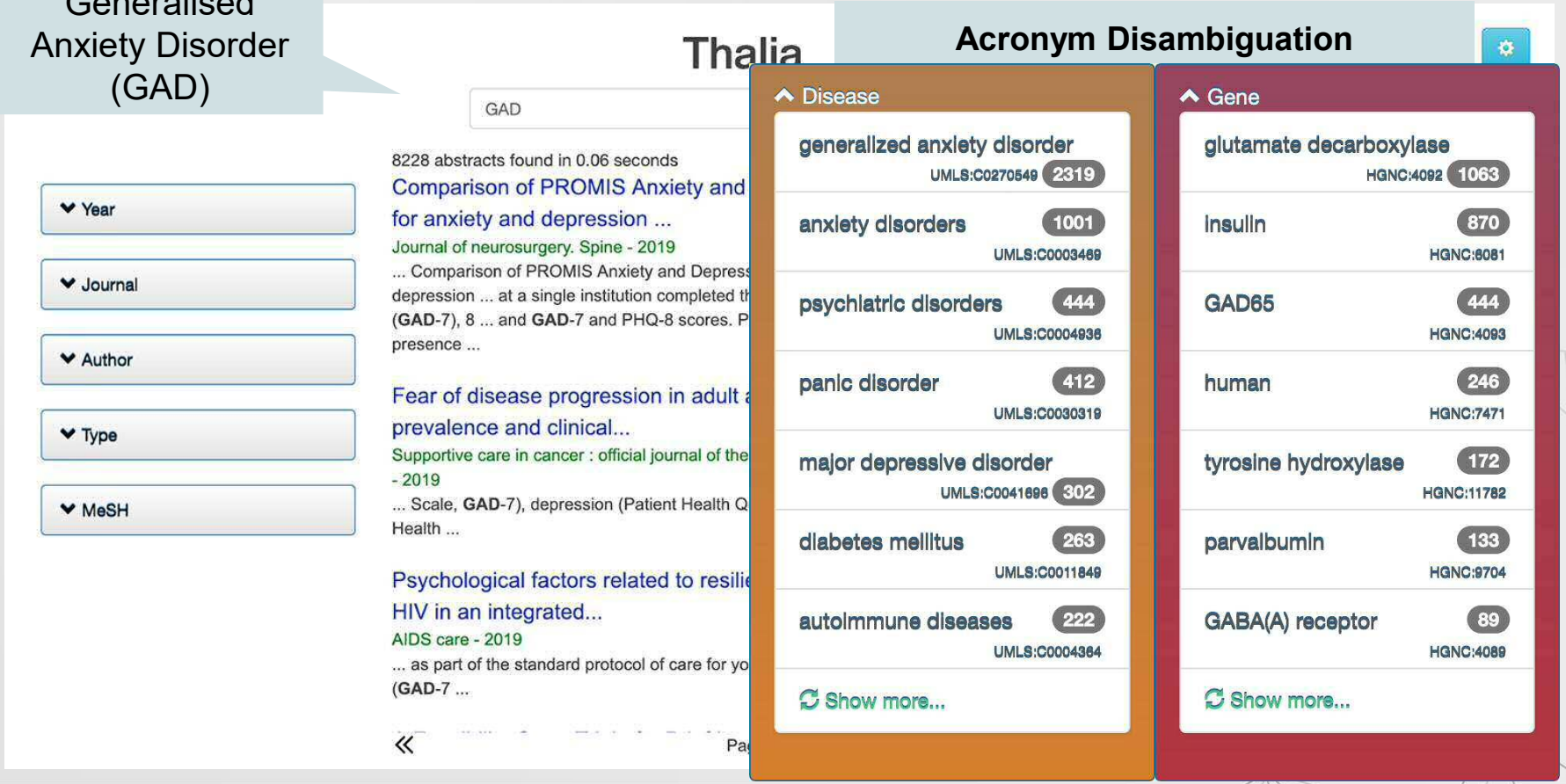


Application: Faceted Semantic Search

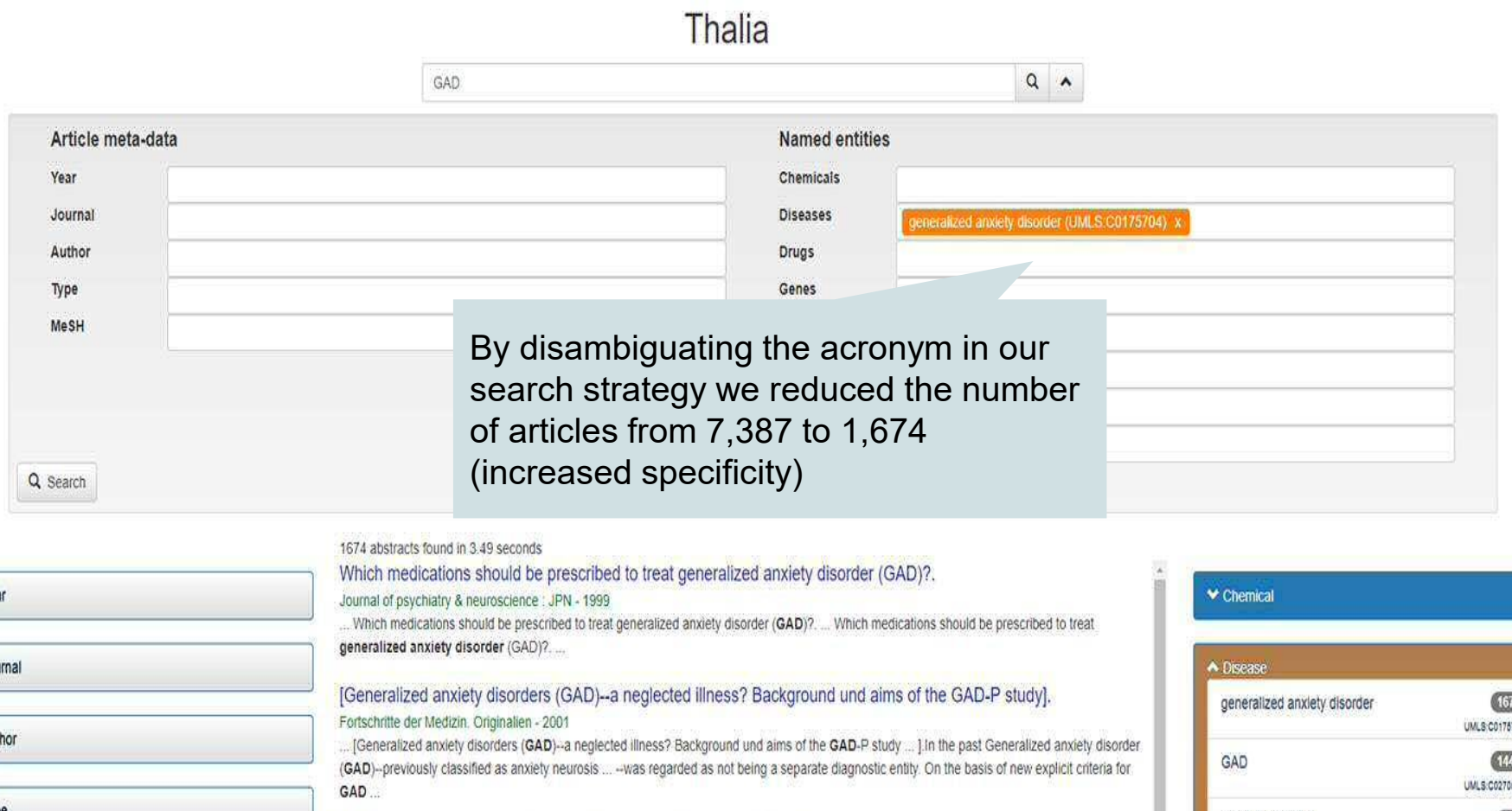


Application: Faceted Semantic Search

Generalised Anxiety Disorder (GAD)

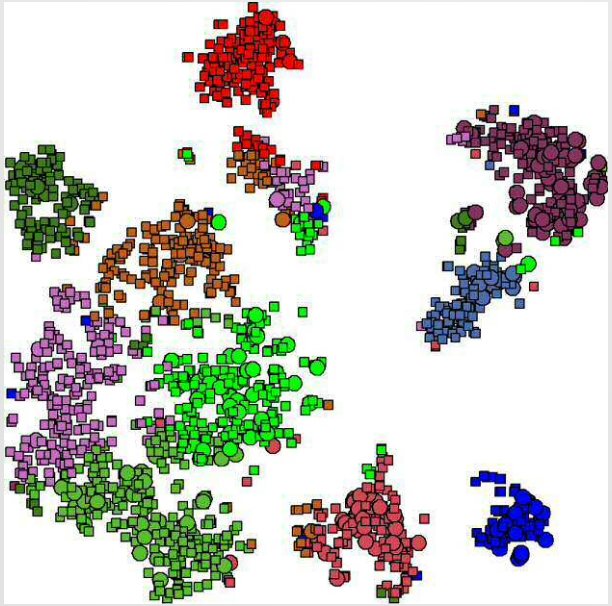


Application: Faceted Semantic Search



Descriptive Clustering for Search

- Organise large collections into non-overlapping clusters
  - Each cluster is a group of *similar* documents
- Describe each cluster using a set of keywords or phrase
  - Prevalent within the cluster - Localised to the cluster



Behaviour change (10 clusters from 1667 references)

- physical, pain, activity, trial, diabetes (250)
- physician, dietitian, contraception, care (224)
- woman, fat, food, weight, intake, dietary (222)
- sexual, work, young people, child (194)
- smoking cessation, abstinence, nicotine (174)
- hiv, condom, testing, sex, prevention, hiv/aids (147)
- alcohol, drinking, screening, brief intervention (144)
- student, school, nursing, teach, performance (134)
- cancer, dental, tobacco, dentist, tobacco use (91)

Descriptive Clustering for Search

physician, dietitian, lifestyle, care, patient, practice, contraception, heart, improve, consultation, medicine, nurse, cite, pharmacist, management (236)

physical, pain, self-management, chronic, trial, exercise, review, type, activity, diabete, randomise, improvement, quality, cognitive, outcome (233)

weight, dietary, fat, food, intake, woman, healthy, nutrition, participant, vegetable, lifestyle, behavior, overweight, physical_activity, african (224)

sexual, work, child, young_people, mental, lesbian, issue, counsellor, experience, multicultural, article, client, justice, argue, therapeutic (197)

smoking, smoker, quit, smoke, cessation, smoking_cessation, nicotine, abstinence, smoking_cessation_intervention, smoking_status (175)

physician, dietitian, lifestyle, care, patient, practice, contraception, heart, improve, consultation, medicine, nurse, cite, pharmacist, management (236)

physical, pain, self-management, chronic, trial, exercise, review, type, activity, diabete, randomise, improvement, quality, cognitive, outcome (233)

weight, dietary, fat, food, intake, woman, healthy, nutrition, participant, vegetable, lifestyle, behavior, overweight, physical_activity, african (224)

sexual, work, child, young_people, mental, lesbian, issue, counsellor, experience, multicultural, article, client, justice, argue, therapeutic (197)

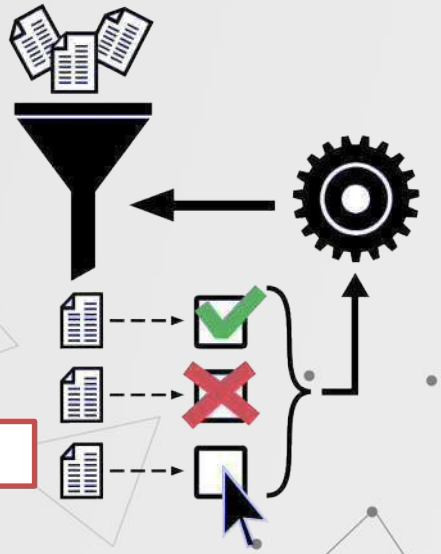
smoking, smoker, quit, smoke, cessation, smoking_cessation, nicotine, abstinence, smoking_cessation_intervention,

Systematic Reviews: RobotAnalyst

- Web-based screening system
- Text mining & **active learning** to prioritise reviews

  based on **relevancy-feedback**
  - Harness human decisions to **prioritise unseen references**
- Unsupervised exploration of references using topic modelling and descriptive clustering

RobotAnalyst



http://www.nactem.ac.uk/robotanalyst/

Link to demo:
https://www.youtube.com/watch?v=et1DEZnbgao&feature=youtu.be

P Przybyla, A Brockmeier, G Kontonatsios, MA Le Pogam, J McNaught, E Von Elm Bjorn, K Nolan, S Ananiadou. Prioritising references for systematic reviews with RobotAnalyst: a user study. **Research Synthesis**, 2018

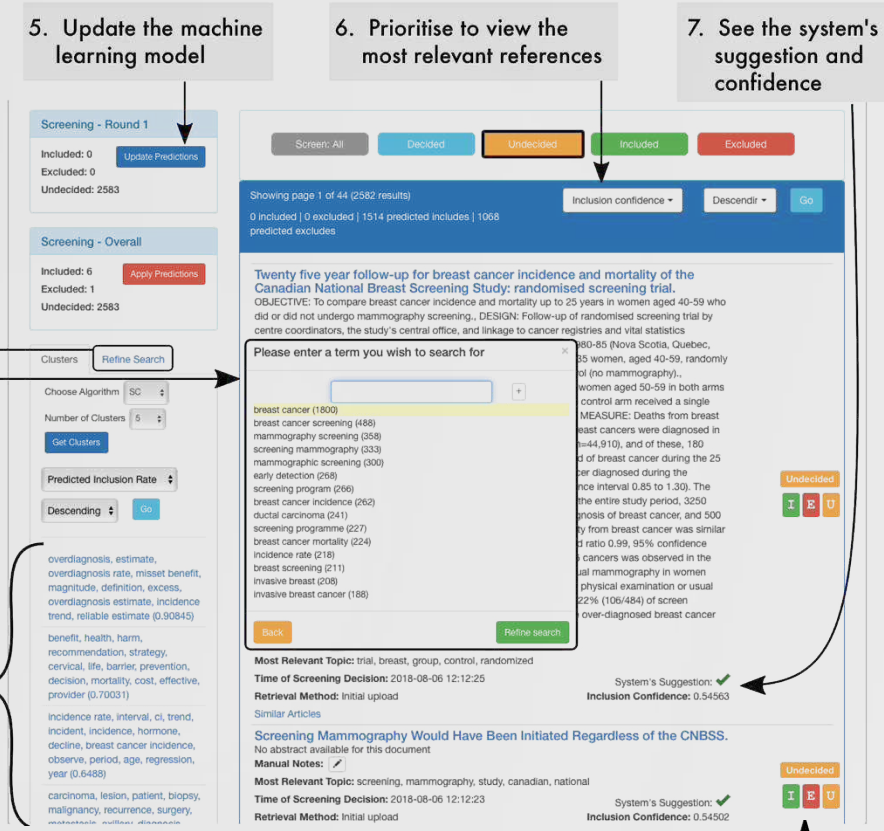
Web-based platform for searching and screening

1. Import references as RIS files from online databases, EndNote, etc.

2. Search collection to pinpoint initial inclusions

3. Explore the collection's clusters, each described by a set of (multiword) keywords

Order citations per cluster relevance



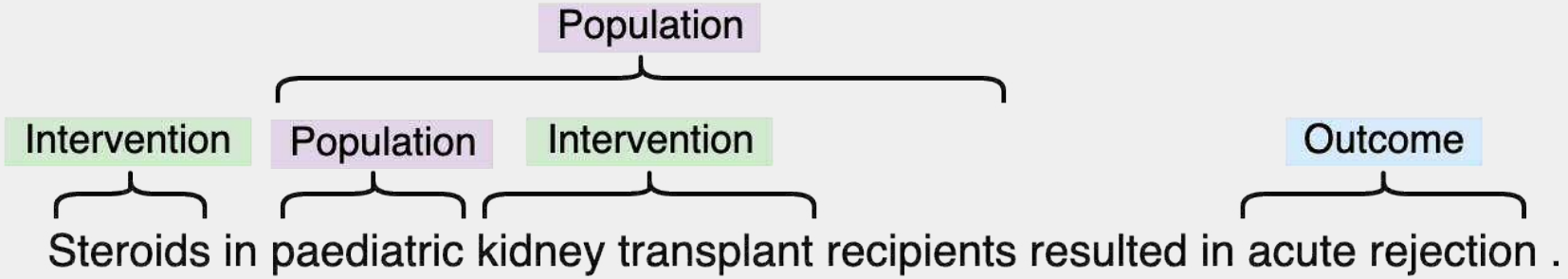
Performance Measures

- Prioritise the most relevant references
- Work saved over sampling at 95% (WSS@95%) and area under the recall curve (AUC)
    - WSS@95% measures the % of documents that do not need to be screened if the analyst were to stop screening upon reaching a recall of 95%, compared to random order screening
    - AUC averages workload across all recall levels

Reference Prioritisation with PICO

Task Screen relevant documents by incorporating PICO elements within biomedical and medical document collections

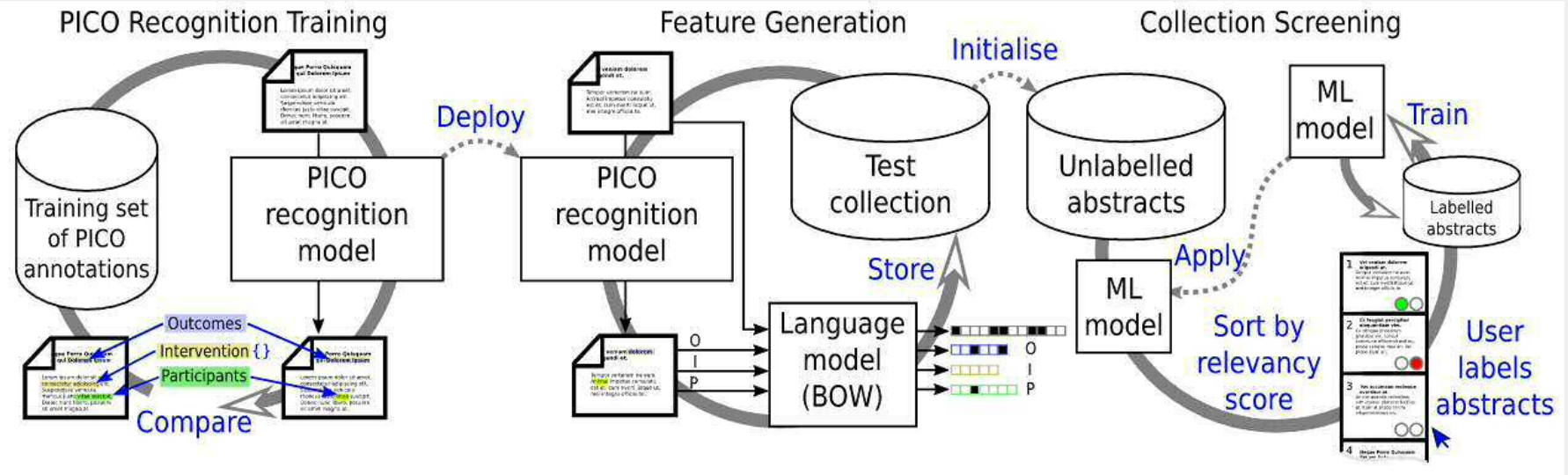
PICO Elements: patient/population (P), intervention (I), comparator (C), and outcomes (O)



A Brockmeier, M Ju, P Przybyla, S Ananiadou. Improving reference prioritisation with PICO recognition. **BMC Medical Informatics and Decision Making**, 2019

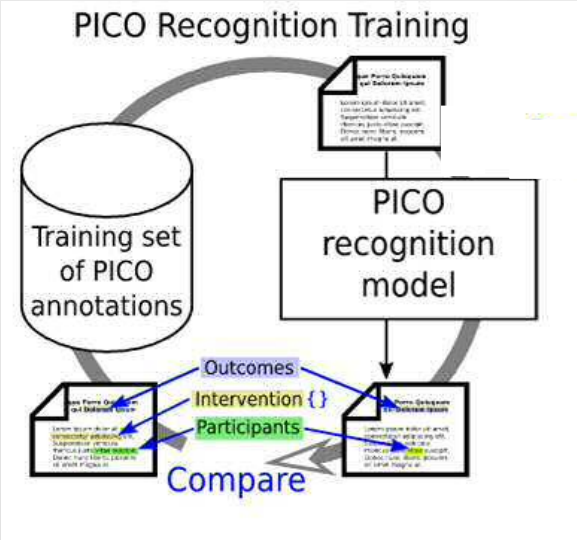
Workflow of Reference Prioritisation

Phrase 1 → **Phrase 2** → **Phrase 3**

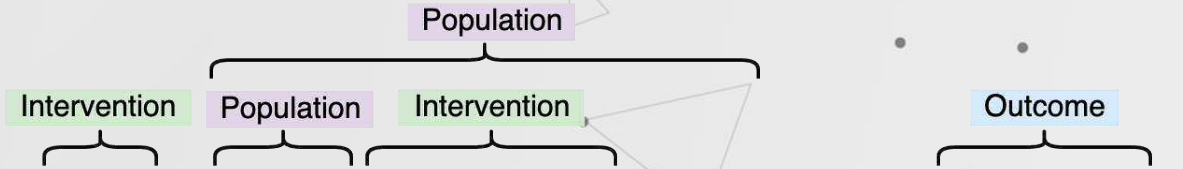


Phrase 1

Phrase 1



- Task: extraction of PICO elements from medical articles
- PICO Recognition: Nested named entity recognition
- Model: layered BiLSTM-CRF model (Ju et al. 2018)



Experimental Evaluation - PICO Extraction

PICO Corpus: 5,000 abstracts of medical articles describing clinical randomized controlled trials

Top-level	Patient-population-problem	Intervention/ Comparator	Outcome
Fine-grained	Age	Control	Adverse effect
	Condition	Educational	Mental
	Sample size	Pharmacological	Mortality
	Sex	Physical	Pain
		Psychological	Physical
		Surgical	Other
		Other	

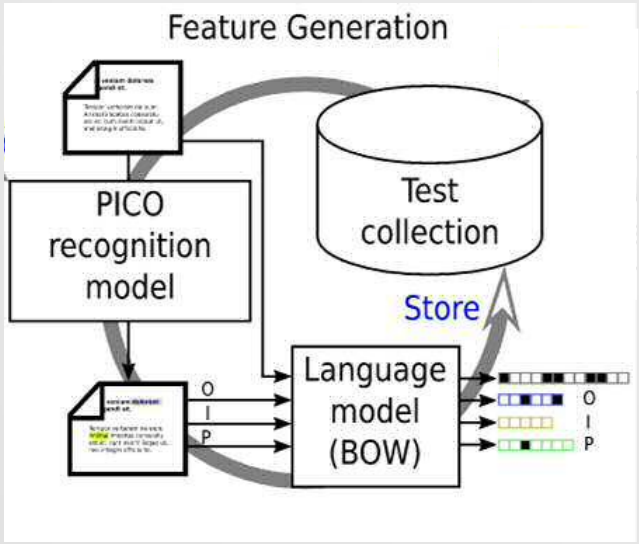
The top-level and fine-grained PICO elements

	Token-wise			Document-level BOW		
	Precision	Recall	F-1	Precision	Recall	F-1
Participants	0.81	0.62	0.70	0.86	0.71	0.78
Interventions	0.69	0.47	0.56	0.83	0.52	0.64
Outcomes	0.66	0.75	0.70	0.73	0.81	0.77

Performance on the test set per input representation

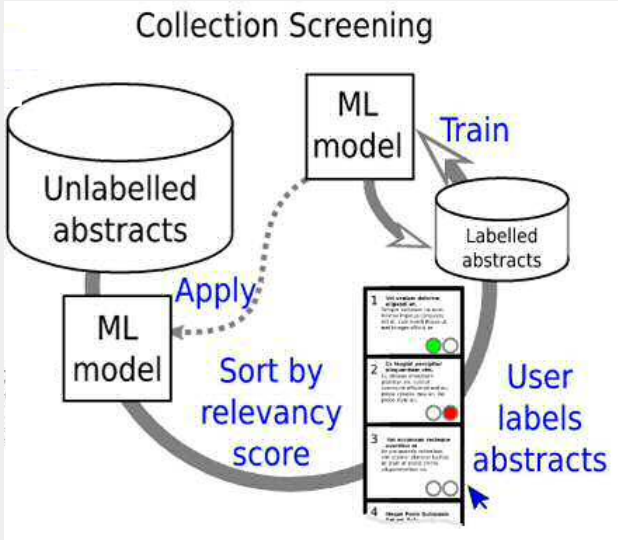
B Nye, J J Li, R Patal, et al. A Corpus with Multi-Level Annotations of Patients, Interventions and Outcomes to Support Language Processing for Medical Literature. **ACL**, 2018

Phrase 2



- Task: convert each abstract to a vector
- PICO recognition model: **Phrase 1**
- Vector = $BOW_{abstract}$ + BOW_{title} + BOW_{PICO}
- Bag-of-word (BOW): if the word is in the given context or not

Phrase 3



Task: screen collections

ML model: classifies each document is relevant or not

Steps:

1. User labels abstracts relevant or not
2. Labeled abstracts are used to train our model
3. Apply the model to the remaining unlabeled abstracts
4. User labels top ranked abstracts
5. Repeat the above process: 1 - 4

- Inclusion of PICO features improves performance with substantial gains
- PICO tagged segments in text are predictive features for inclusion
- Combine relevancy classification pipeline with PICO
- PICO tagging an interpretable process emulating human annotation
- Annotations can be used on the own to improve search

Data

- DERP (Drug Effectiveness Review Project) (Cohen AM 2006), 17890 documents from PubMed
- OHAT and CAMARADES (Howard BE, et al. 2016), 90322 documents from PubMed and other databases

.

Work	OHAT and CAMARADES	DERP
Matwin S, et al. (2010)	-	33.5
Cohen AM (2011)	-	40.8
Howard BE, et al. (2016)	76.6	48.8*
Ours (without PICO)	77.9	43.2
Ours (with PICO)	**78.2**	**44.8**

Evaluation Metric: WSS@95%, measures manual screening effort saved by a reviewer that would stop the process after finding 95% of the relevant documents.

Other NaCTeM search-based systems

- **ASCOT** (Assisting Search and Creation Of clinical Trials)
  - http://www.nactem.ac.uk/ClinicalTrialProtocols/
  - Enrich clinical trial collections with metadata
  - Document clustering
- **EUPMC** Evidence Finder
  - Query-based search in full text articles
  - Search by meta-knowledge dimension
- **FACTA+**
  - http://www.nactem.ac.uk/facta/
  - Generating hypotheses based on indirect associations across documents
- **HoM** (History of Medicine)
  - http://nactem.ac.uk/hom/
  - Semantic search system over historical medical archives
  - Historical tracking of query terms and their evolution
- **MEDIE**
  - Biomedical event retrieval from Medline
  - Event based faceted search

Conclusions

- SR development challenging, due to size and inconsistency of literature
- Majority of clinicians/analysts do not possess expert literature search skills
- Difficult to develop complex search strategies
- Production of SRs is time consuming, update cycles often of years
- Systems like RobotAnalyst cut screening time by at least 50% by ranking the most relevant reference

National Centre for Text Mining

- 1st publicly funded national text mining centre
- Location: Manchester Institute of Biotechnology
- Phase I - Biology (2005-2008)
- Phase II - Biology, Medicine, Social Sciences (2008-2011)
- Phase III – Biology, Medicine, Humanities, Social Sciences; Fully sustainable centre (2011-)

www.nactem.ac.uk

NaCTeM People

Research Staff











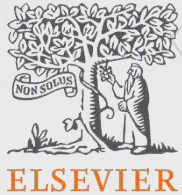

Visitors


Students






Funding sources



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THANK YOU!