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Automation technologies for undertaking HTAs and systematic reviews

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James Thomas and Claire Stansfield
Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre)
Social Science Research Unit
UCL Institute of Education
University College London

ePPI CENTRE

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Acknowledgements & declaration of interest

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- I am employed by University College London; receive funding from Cochrane and the funders below for this and related work; co-lead of Project Transform; lead EPPI-Reviewer software development.

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- ('Creative commons' photos used for illustrations)

Aims and objectives

- AIM: outline the potential for using AI/ machine learning to make systematic reviewing HTAs more efficient
- OBJECTIVES:
  - How some of these technologies – especially machine learning - works
  - Demonstrate / discuss some current tools
  - Discuss future directions of travel

Outline

- Introduction to technologies (presentation)
- Practical sessions:
  - Developing search strategies
  - Using citation (and related) networks
  - BREAK
  - Using machine learning classifiers
  - Mapping research activity
- Where's it going (evidence surveillance)??
- Discussion

Context: systematic reviews and HTAs

- Demanding context
- Need to be correct
- Need to be seen to be correct
- Demand very high recall (over precision)
- At odds with much information retrieval work

Why use automation in systematic reviews / HTAs?

- Data deluge
  - E.g. more than 100 publications of trials appear each day (probably)
- Inadequacy of current systems
  - We lose research – systematically – and then spend lots of £ finding it again
    - E.g. in 67 Cochrane reviews in March 2014: >163k citations were screened; 6,599 full text reports were screened; 703 were included
    - That's about 2 million citations screened annually – just for Cochrane reviews
    - Because people make mistakes, recommendation is double citation screening… (££)
  - Even after relevant studies are identified, data extraction consumes more £££
- This means that:
  - only a fraction of available studies are included in systematic reviews / HTAs;
  - systematic reviews do not cover all questions/ domains comprehensively;
  - we don't know when systematic reviews *need* to be updated…

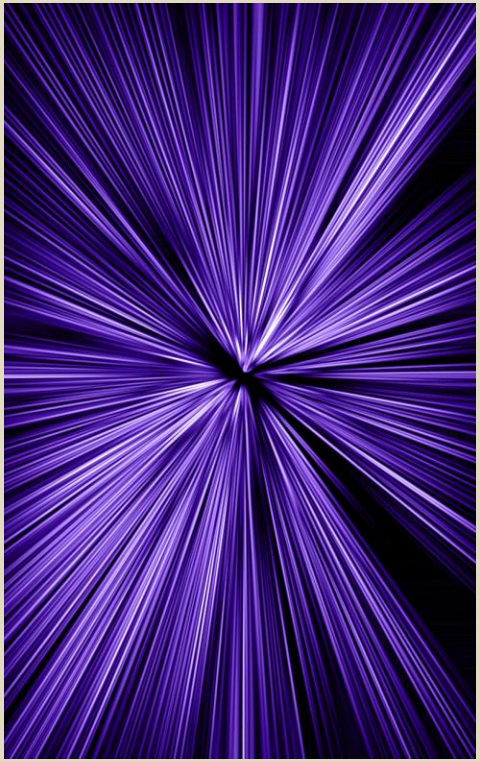
- I could go on… (but won't)
  - There are many other inefficiencies in the systematic review / HTAs process

Why: the current model is unsustainable

- More research is published than ever
- We are better at searching (and finding) more of it
- Reviews / HTAs are getting more complex
- Resources are limited
- *We need new approaches which maximise the use of scarce human resource*

How we will speed up reviewing

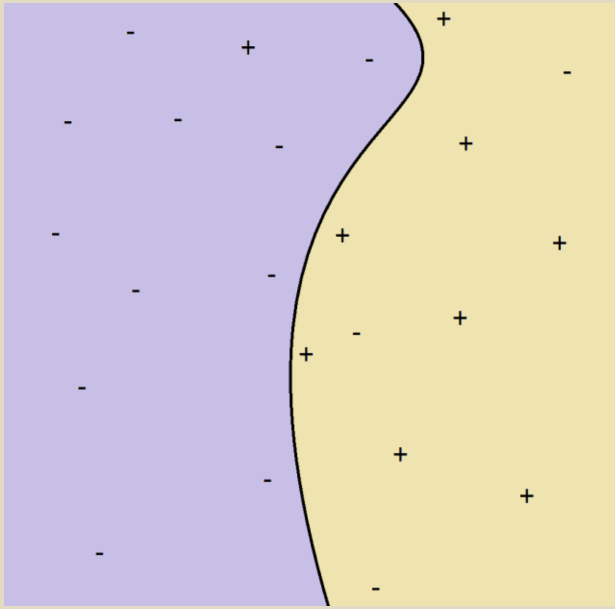
- Through developing – and using – technologies which automate what can be automated; and
- By maximising the use of scarce and valuable human effort

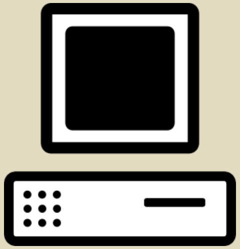


Which technologies are we using?

- Many…
- Automatic ‘clustering’ (unsupervised)
- Machine learning classifiers (supervised)
  - These ‘learn’ to tell the difference between two types of study / document
    - (e.g. “does this citation describe an RCT?”)
  - They learn from classification decisions made by humans.

How does machine learning work?





Building machine classifiers: a very brief de-mystification

1. A dictionary and index are created

- First, the key terms in the studies are listed (ignoring very common words)
- Second, the studies are indexed against the list of terms
  - (the resulting matrix can be quite large)
- Next…

e.g. We have two studies – one is an RCT, and one isn't an RCT

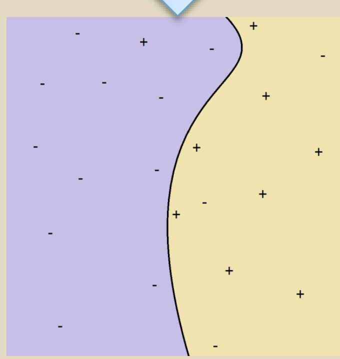
Study 1	Effectiveness of asthma self-care interventions: a **systematic review**	(not an RCT)
Study 2	Effectiveness of a self-monitoring asthma intervention: an **RCT**	(an RCT)

RCT?										
0	1	1	1	1	1	1	1	0	0	0
1	1	1	1	0	0	0	0	1	1	1

2. A statistical model is built

The matrix is used to create a statistical model which is able to distinguish between the two classes of document (e.g. between RCTs and non-RCTs where we have 280,000+ rows of data)

RCT?	Effectiveness	asthma	self	care	interventions	systematic	review	monitoring	intervention	RCT
0	1	1	1	1	1	1	1	0	0	0
1	1	1	1	0	0	0	0	1	1	1

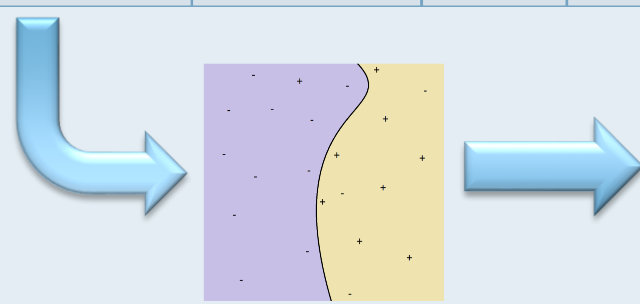


3. The model is applied to new documents

- New citations are indexed against the previously generated list of terms
- The resulting matrix is fed into the previously generated model
- And the model will assign a probability that the new document is, or is not a member of the class in question

e.g. The **effectiveness** of a school-based asthma management programme: an RCT

Effectiveness	asthma	self	care	interventions	systematic	review	monitoring	intervention	RCT
1	1	0	0	0	0	0	0	0	1



93%

Automation in systematic reviews HTAs – what can be done?

– Study identification:
  - Citation screening
  - RCT classifier
– Mapping research activity
– Data extraction
  - Risk of Bias assessment
  - Other study characteristics
  - Extraction of statistical data
– (Synthesis and conclusions)

Assisting search development

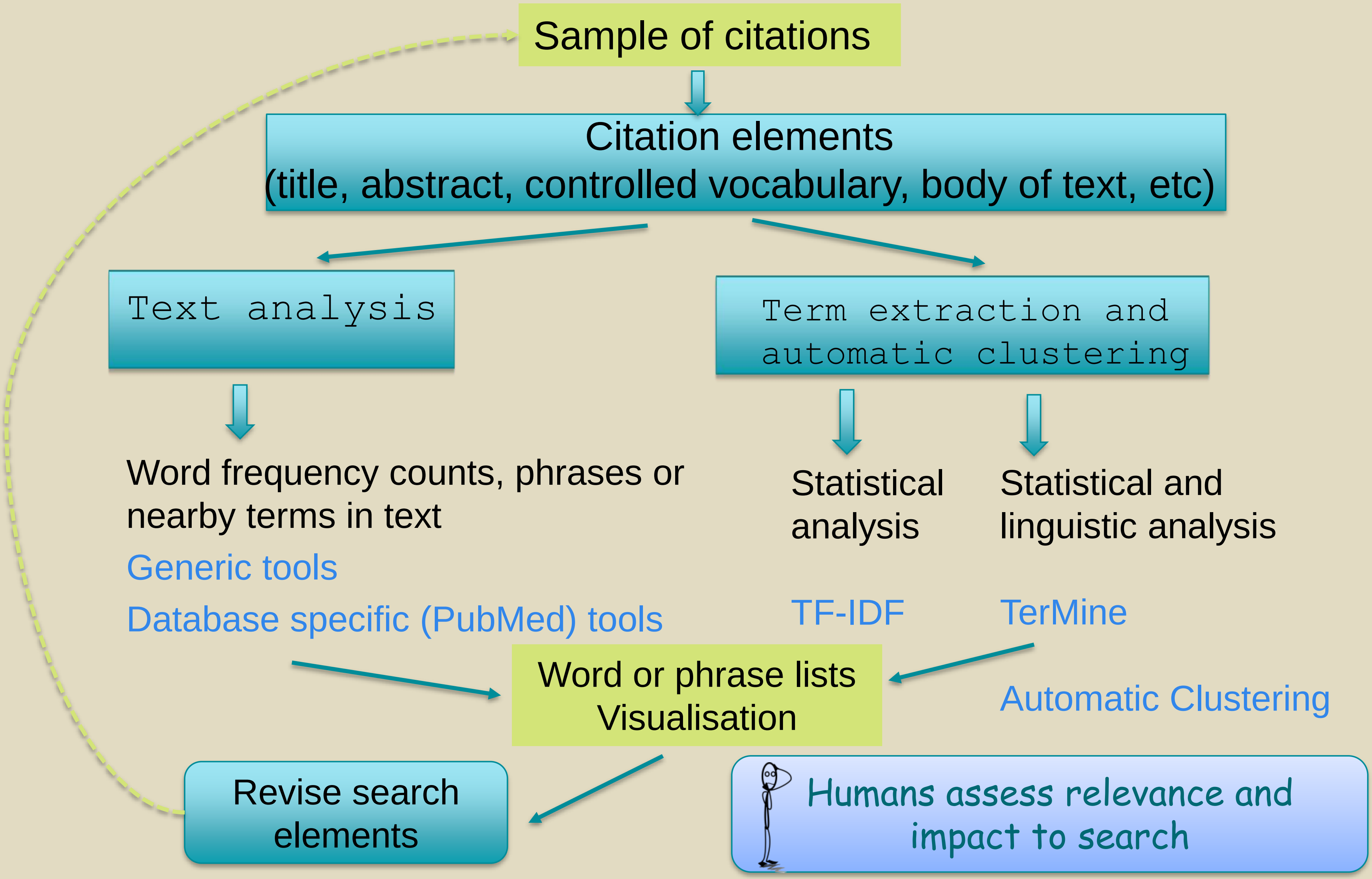
Purpose: to explore linkages or words in text or controlled vocabulary

Applications:

- Increase precision
- Increase sensitivity
- Aid translation across databases
- “Objective” search strategies
- Integrated search and screen systems

Introduction

Discussion


Sample of citations
Citation elements
(title, abstract, controlled vocabulary, body of text, etc)
Text analysis
Term extraction and automatic clustering
Word frequency counts, phrases or nearby terms in text
Generic tools
Database specific (PubMed) tools
Statistical analysis
TF-IDF
Statistical and linguistic analysis
TerMine
Automatic Clustering
Word or phrase lists
Visualisation
Revise search elements
Humans assess relevance and impact to search

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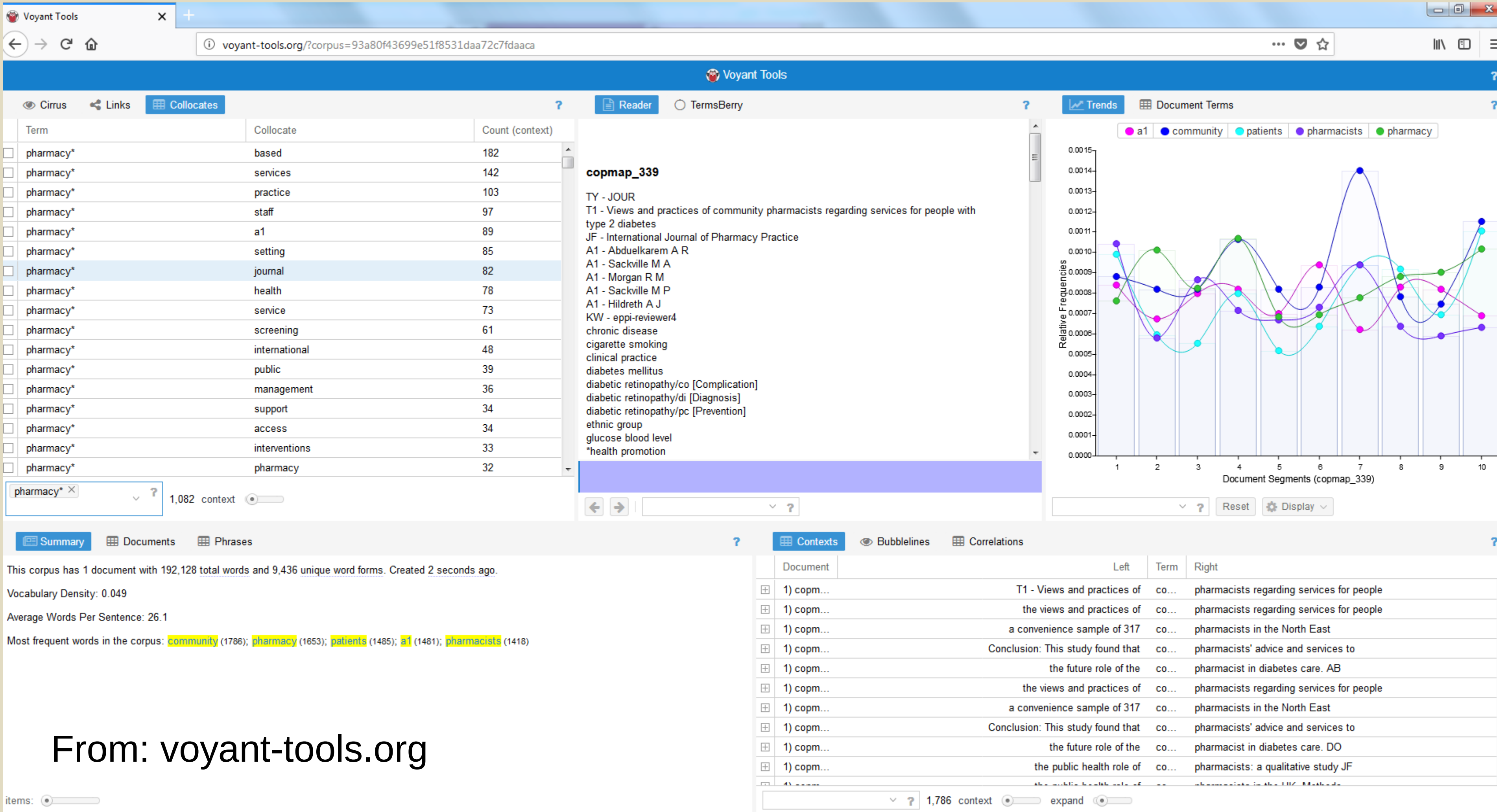

From: voyant-tools.org

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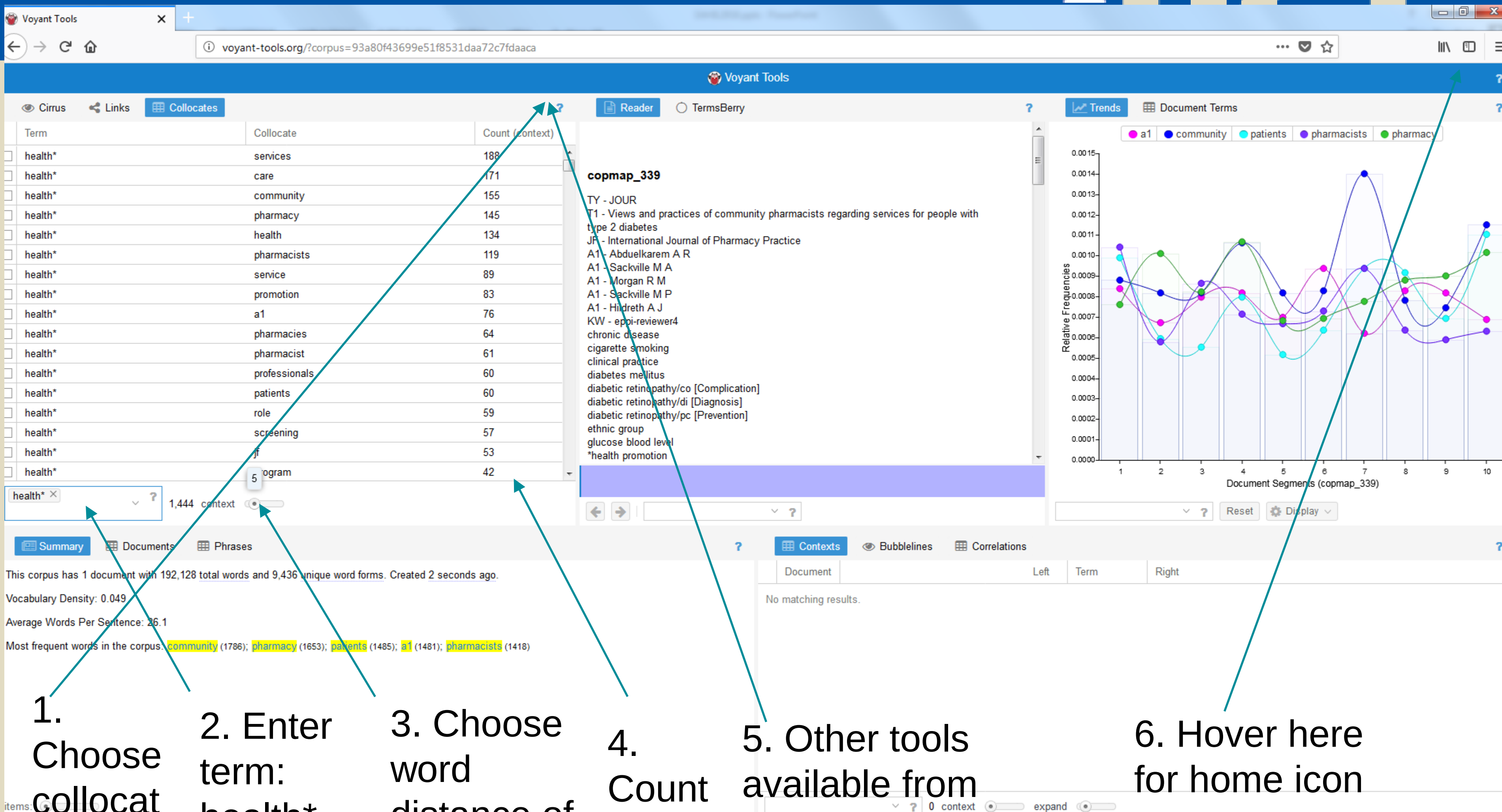


1. Choose collocates tool

2. Enter term: health*

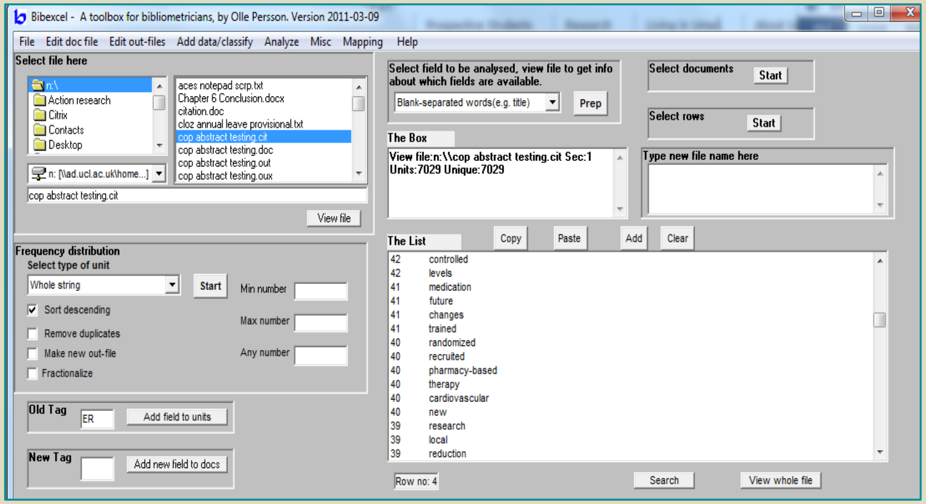
3. Choose word distance of collocates

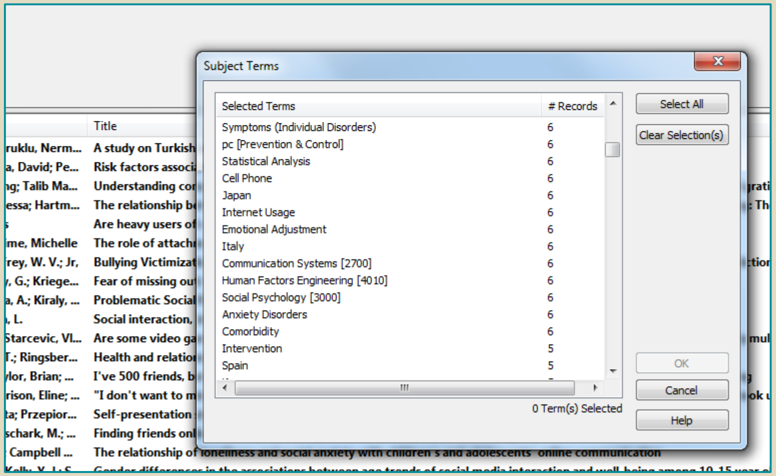
4. Count

5. Other tools available from menu (term grid, Cirrus word clouds etc.

6. Hover here for home icon to start a new analysis

Other tools that have useful functionality include for text analysis…

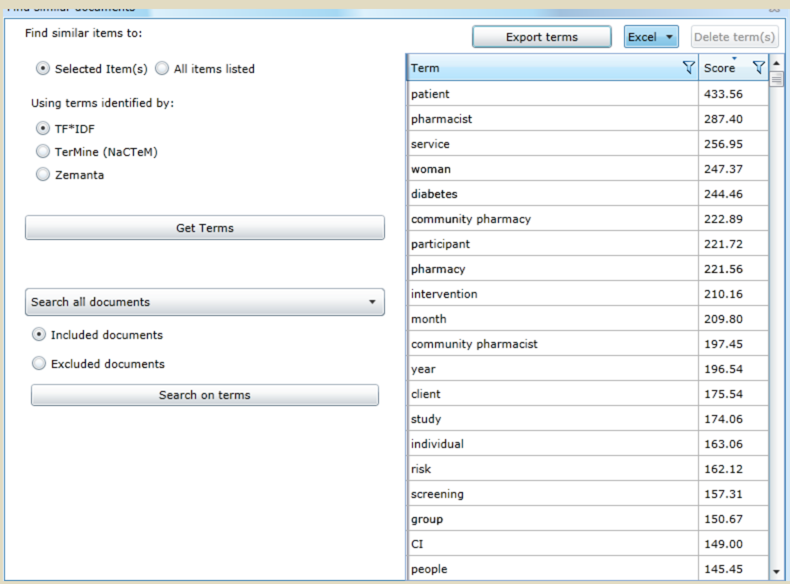




Using Bibexcel to count the number of abstracts a word occurs in

Using Endnote's Subject Bibliography to generate a list of keywords

Applying TD-IDF analysis to 338 studies of public health interventions in community pharmacies (Interface: EPPI-Reviewer 4)



Term	Score
patient	433.56
pharmacist	287.40
service	256.95
woman	247.37
diabetes	244.46
community pharmacy	222.89
participant	221.72
pharmacy	221.56
intervention	210.16
month	209.80
community pharmacist	197.45
year	196.54
client	175.54
study	174.06
individual	163.06
risk	162.12
screening	157.31
group	150.67
CI	149.00
people	145.45

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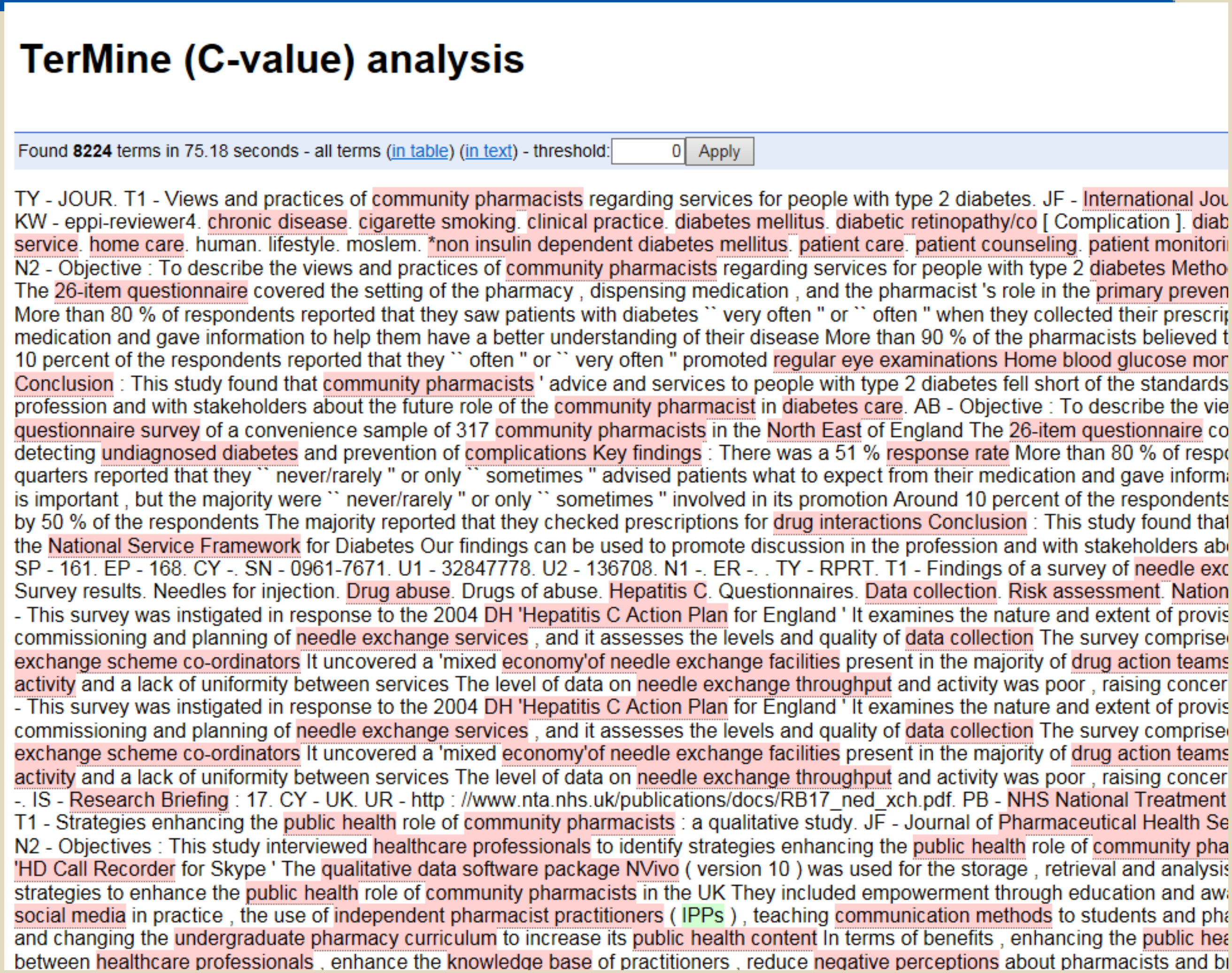
TerMine (C-value) analysis

Found **8224** terms in 75.18 seconds - all terms (in table) (in text) - threshold: 0 Apply

TY - JOUR. T1 - Views and practices of community pharmacists regarding services for people with type 2 diabetes. JF - International Jou
KW - eppi-reviewer4. chronic disease. cigarette smoking. clinical practice. diabetes mellitus. diabetic retinopathy/co [Complication]. diab
service. home care. human. lifestyle. moslem. *non insulin dependent diabetes mellitus. patient care. patient counseling. patient monitori
N2 - Objective : To describe the views and practices of community pharmacists regarding services for people with type 2 diabetes Metho
The 26-item questionnaire covered the setting of the pharmacy , dispensing medication , and the pharmacist 's role in the primary preven
More than 80 % of respondents reported that they saw patients with diabetes `` very often '' or `` often '' when they collected their prescrip
medication and gave information to help them have a better understanding of their disease More than 90 % of the pharmacists believed t
10 percent of the respondents reported that they `` often '' or `` very often '' promoted regular eye examinations Home blood glucose mor
Conclusion : This study found that community pharmacists ' advice and services to people with type 2 diabetes fell short of the standards
profession and with stakeholders about the future role of the community pharmacist in diabetes care. AB - Objective : To describe the vie
questionnaire survey of a convenience sample of 317 community pharmacists in the North East of England The 26-item questionnaire co
detecting undiagnosed diabetes and prevention of complications Key findings : There was a 51 % response rate More than 80 % of respo
quarters reported that they `` never/rarely '' or only `` sometimes '' advised patients what to expect from their medication and gave inform
is important , but the majority were `` never/rarely '' or only `` sometimes '' involved in its promotion Around 10 percent of the respondents
by 50 % of the respondents The majority reported that they checked prescriptions for drug interactions Conclusion : This study found that
the National Service Framework for Diabetes Our findings can be used to promote discussion in the profession and with stakeholders ab
SP - 161. EP - 168. CY -. SN - 0961-7671. U1 - 32847778. U2 - 136708. N1 -. ER -. . TY - RPRT. T1 - Findings of a survey of needle exc
Survey results. Needles for injection. Drug abuse. Drugs of abuse. Hepatitis C. Questionnaires. Data collection. Risk assessment. Nation
- This survey was instigated in response to the 2004 DH 'Hepatitis C Action Plan for England ' It examines the nature and extent of provis
commissioning and planning of needle exchange services , and it assesses the levels and quality of data collection The survey comprise
exchange scheme co-ordinators It uncovered a 'mixed economy'of needle exchange facilities present in the majority of drug action teams
activity and a lack of uniformity between services The level of data on needle exchange throughput and activity was poor , raising concer
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-. IS - Research Briefing : 17. CY - UK. UR - http : //www.nta.nhs.uk/publications/docs/RB17_ned_xch.pdf. PB - NHS National Treatment
T1 - Strategies enhancing the public health role of community pharmacists : a qualitative study. JF - Journal of Pharmaceutical Health Se
N2 - Objectives : This study interviewed healthcare professionals to identify strategies enhancing the public health role of community pha
'HD Call Recorder for Skype ' The qualitative data software package NVivo (version 10) was used for the storage , retrieval and analysis
strategies to enhance the public health role of community pharmacists in the UK They included empowerment through education and awa
social media in practice , the use of independent pharmacist practitioners (IPPs) , teaching communication methods to students and pha
and changing the undergraduate pharmacy curriculum to increase its public health content In terms of benefits , enhancing the public hea
between healthcare professionals , enhance the knowledge base of practitioners , reduce negative perceptions about pharmacists and br

Text view: applying Termine to 338 studies of public health interventions in community pharmacies

From NacTeM http://www.nactem.ac.uk/software/termine/cgi-bin/termine_cvalue.cgi

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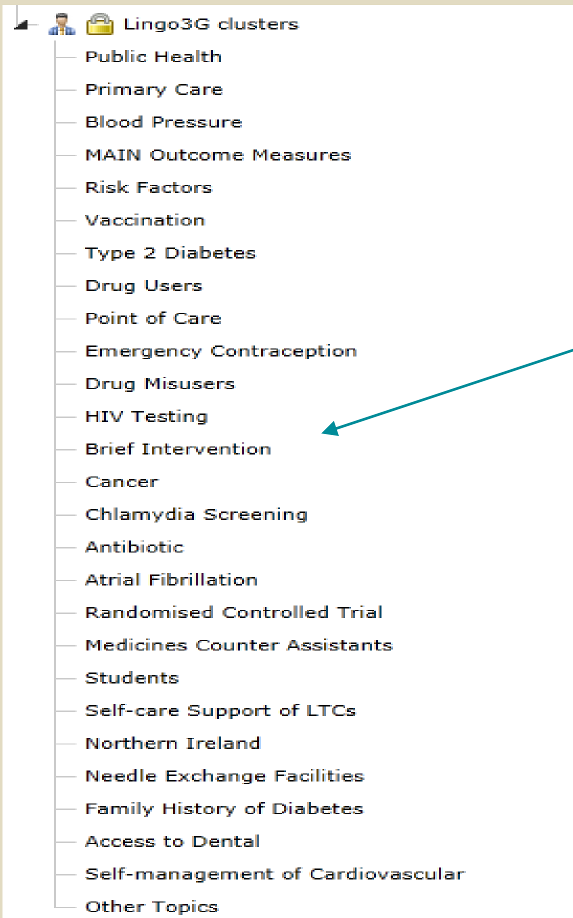
Rank	Term	Score
1	community pharmacy	1033.88501
2	community pharmacist	451.192322
3	public health	232.711411
4	blood pressure	175
5	risk factor	147.822144
6	primary care	138.600006
7	health service	122.838188
8	main outcome	117.029854
9	main outcome measures	113.789383
10	needle exchange	110.720993
11	drug user	100.849159
12	health care	99.918594
13	pharmacy service	96
14	intervention group	89.111115
15	public health service	88.340805
16	cardiovascular disease	82.647057
17	usual care	79.789474
18	health promotion	72.078949
19	control group	71.555557
20	pharmacy practice	71.099998
21	weight management	70.578125
22	body mass index	69.73835
23	cardiovascular risk	66.903847
24	vaccination rate	66.117645
25	international journal	62.5
26	pharmacy staff	62.421051
27	weight loss	61.708332
28	drug therapy	61
29	risk assessment	60.314285
30	hiv testing	57.882355
31	blood glucose	57.468086

Table view: Applying Termine to 338 studies of public health interventions in community pharmacies

From NacTeM http://www.nactem.ac.uk/software/termine/cgi-bin/termine_cvalue.cgi



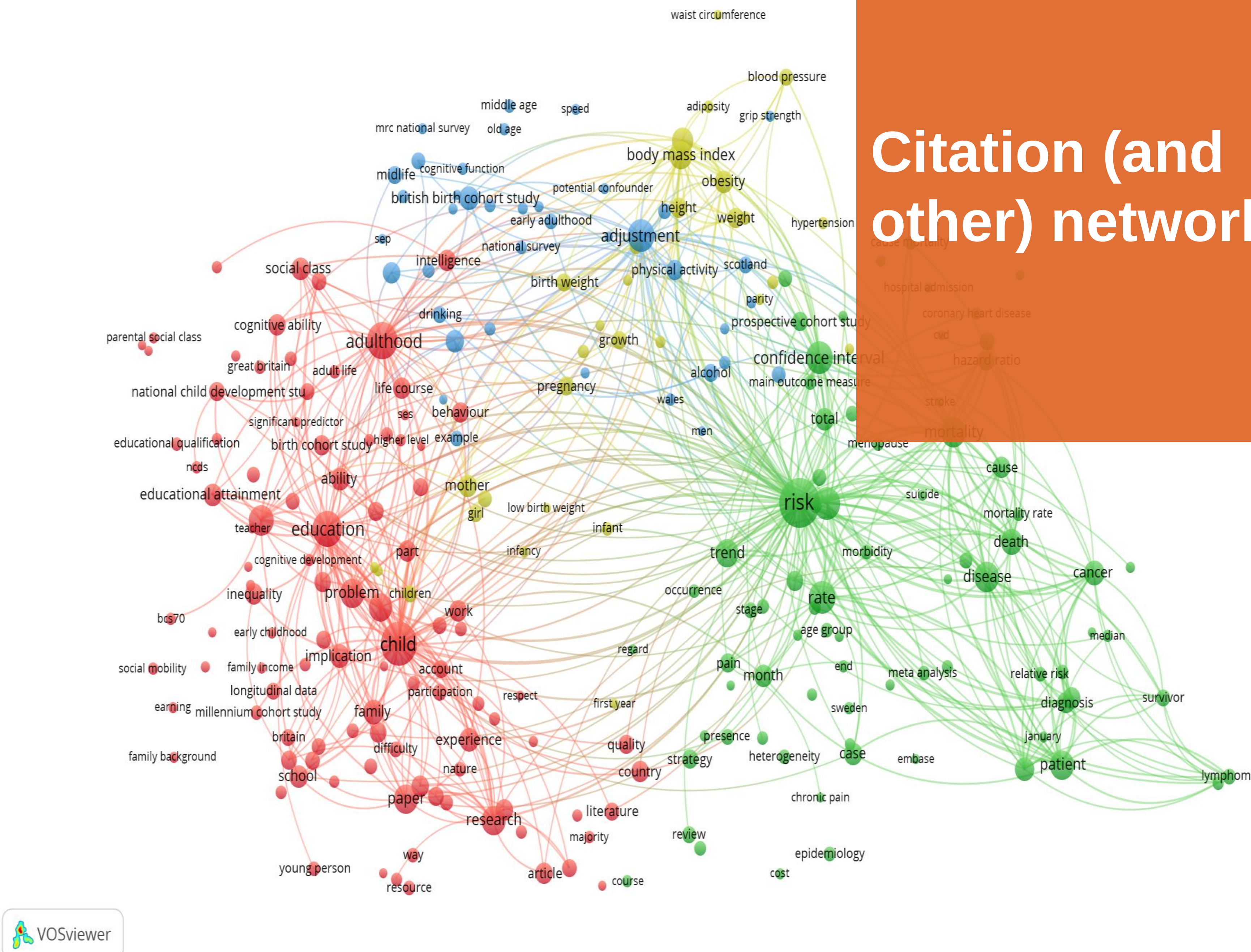
Lingo3G groups sets of citations and assigns labels

Using Lingo3G to map the same studies of public health interventions in community pharmacies, N=338 (Interface: EPPI-Reviewer 4)

Tools

- Termine
- Voyant tools
- BibExcel

Citation (and other) networks



Citation networks

- Frequently used for supplementary searching
- Rarely the main strategy – concerns re bias and lack of tools with sufficient coverage
- This may be changing

Neural networks

- Currently a very popular machine learning technology
- Can model the interrelationships between huge numbers of words – and concepts
- Underpins Microsoft Academic ‘recommended papers’ (combined with citation relationships)

Tools

- Sources of data
  - Traditional – e.g. Web of Science / Scopus
  - Newer – CrossRef / Microsoft Academic
- Tools
  - Web browser
  - Publish or Perish (now at v.6)
  - VosViewer / + related

BREAK

Using machine classifiers

What does a classifier do?

- It takes as its input the title and abstract describing a publication
- It outputs a ‘probability’ score – between 0 and 1 which indicates how likely the publication is to being the ‘positive class’ (e.g. is an RCT)
- Classification is an integral part of the ‘evidence pipeline’

Pre-built or 'build your own'

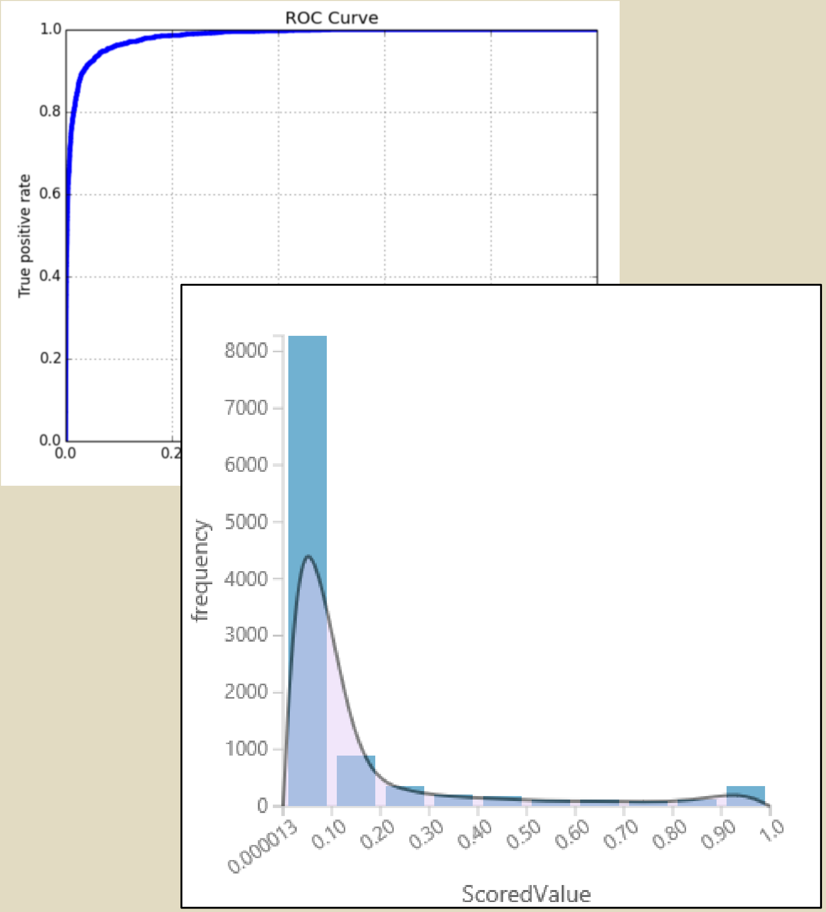
- Pre-built in EPPI-Reviewer
  - Developed from established datasets
  - RCT model
  - Human studies model
  - Systematic review model
  - Economic evaluation
- Build your own
  - Within individual reviews (e.g for iterative citation screening)
  - Across reviews (similar to above)

Building classification tools: no easy task

- Quality of data
- Generalisability
- Stages
  - Build the classifier
  - Calibrate for desired precision / recall
  - Validate

Pre-built classifier

- An RCT classifier was built using more than 280,000 records from Cochrane Crowd
- 60% of the studies have scores < 0.1
- If we trust the machine, and automatically exclude these citations, we're left with 99.897% of the RCTs (i.e. we lose 0.1%)
- Is that good enough?
- Systematic review community needs to discuss appropriate uses of automation

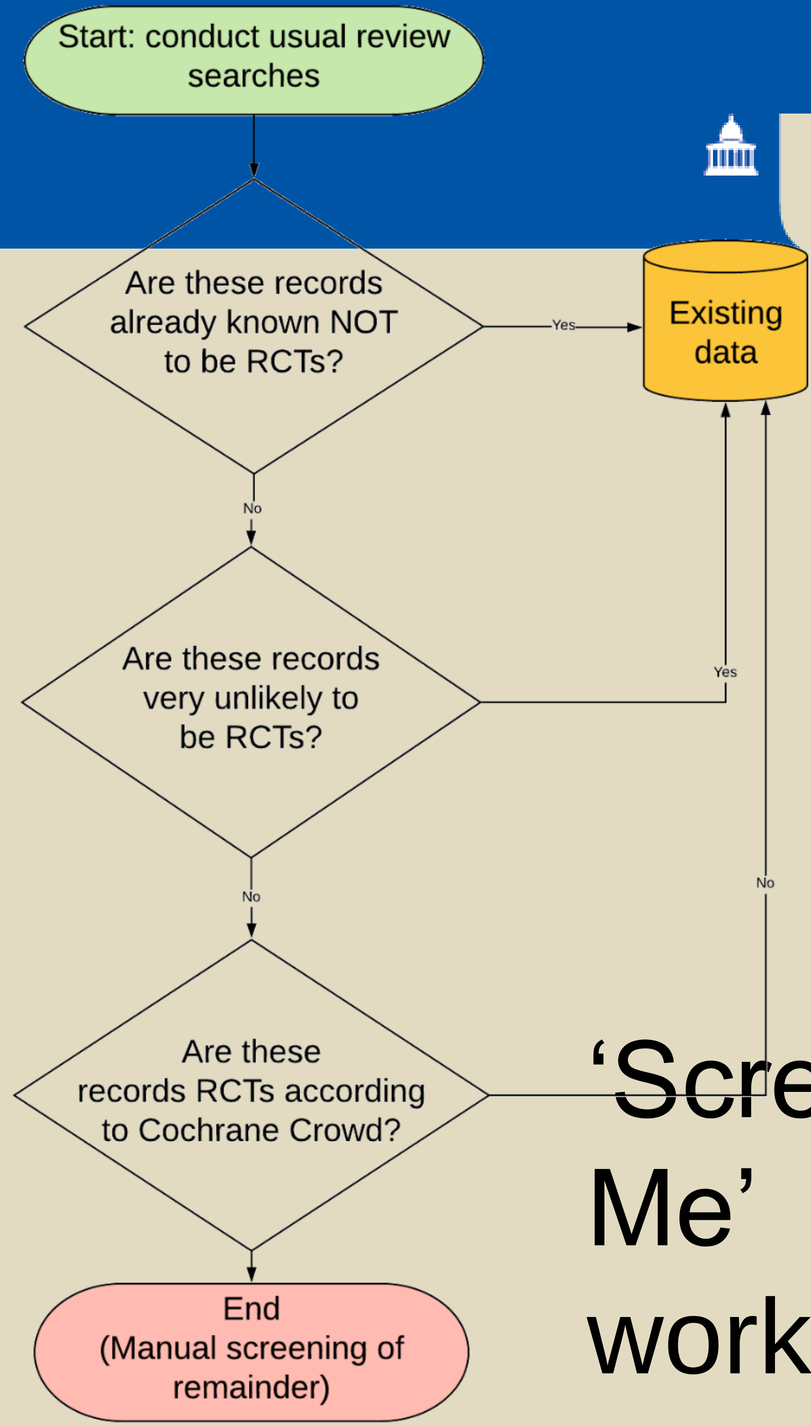


The 'Screen 4 Me' workflow

- A new service which is currently being rolled out for Cochrane authors

1. Upload search results
2. Non-RCTs removed using:
   a) Data reuse
   b) Machine learning
   c) Crowdsourcing
3. Remaining records returned to authors

Offers huge efficiencies for these reviews



‘Screen 4 Me’ workflow

‘Build your own’

- Citation screening for individual reviews
- For use across reviews (dependent on data)

O'Mara-Eves *et al. Systematic Reviews* 2015, **4**:5
http://www.systematicreviewsjournal.com/content/4/1/5

SYSTEMATIC REVIEWS

RESEARCH Open Access

Using text mining for study identification in systematic reviews: a systematic review of current approaches

Alison O'Mara-Eves[1], James Thomas[1*], John McNaught[2], Makoto Miwa[3] and Sophia Ananiadou[2]

Abstract

Background: The large and growing number of published studies, and their increasing rate of publication, makes the task of identifying relevant studies in an unbiased way for inclusion in systematic reviews both complex and time consuming. Text mining has been offered as a potential solution: through automating some of the screening process, reviewer time can be saved. The evidence base around the use of text mining for screening has not yet been pulled together systematically; this systematic review fills that research gap. Focusing mainly on non-technical issues, the review aims to increase awareness of the potential of these technologies and promote further collaborative research between the computer science and systematic review communities.

Methods: Five research questions led our review: what is the state of the evidence base; how has workload reduction been evaluated; what are the purposes of semi-automation and how effective are they; how have key contextual problems of applying text mining to the systematic review field been addressed; and what challenges to

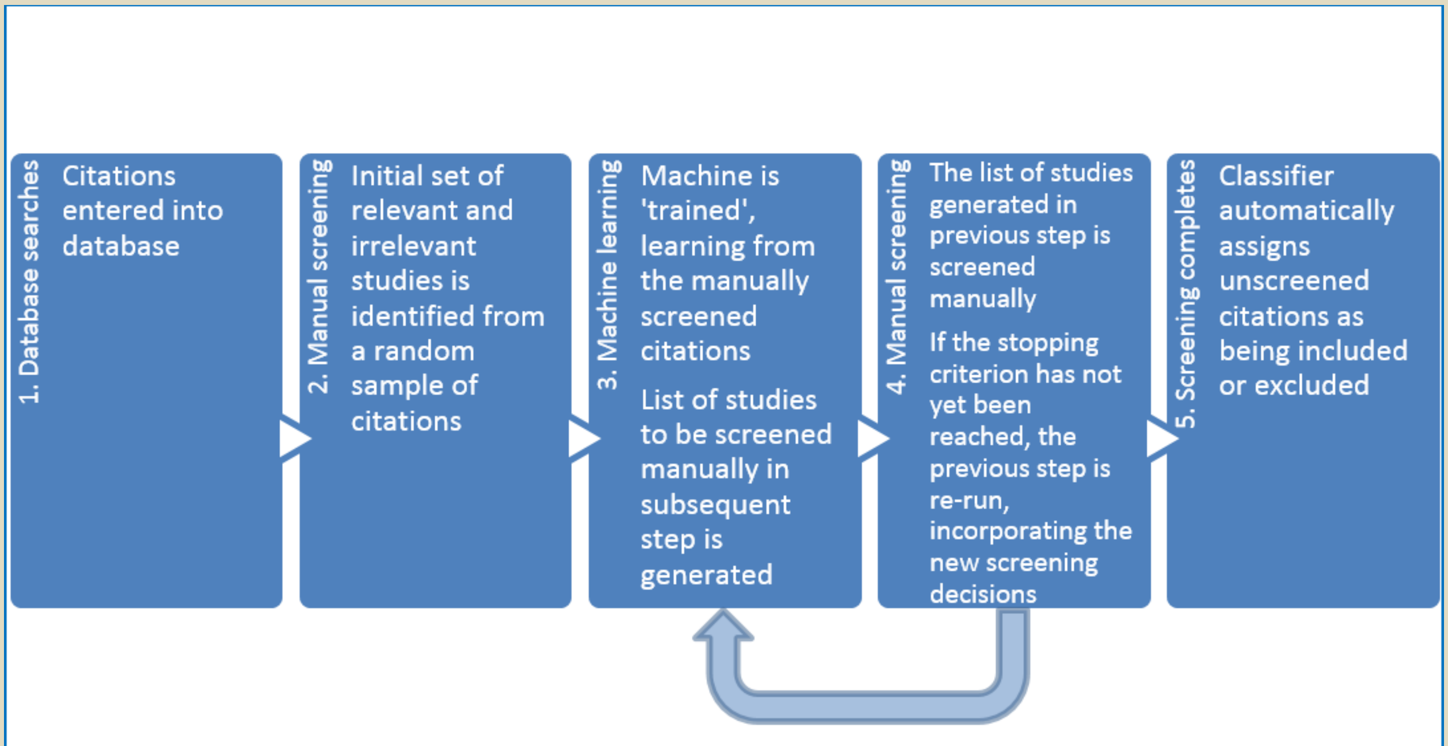
Citation screening

- Has received most R&D attention
- Diverse evidence base; difficult to compare evaluations
- 'semi-automated' approaches are the most common
- Possible reductions in workload in excess of 30% (and up to 97%)

Summary of conclusions

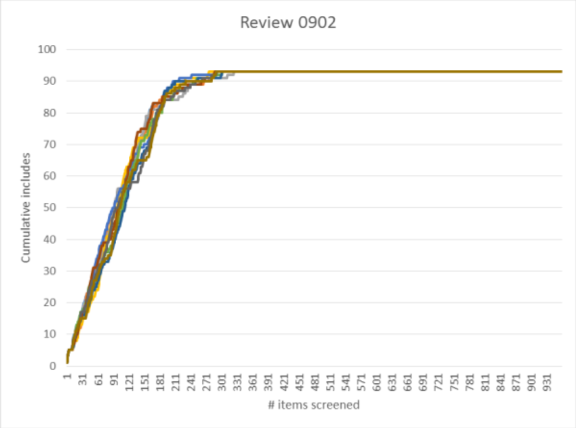
- Screening prioritisation
  - 'safe to use'
- Machine as a 'second screener'
  - Use with care
- Automatic study exclusion
  - Highly promising in many areas, but performance varies significantly depending on the domain of literature being screened

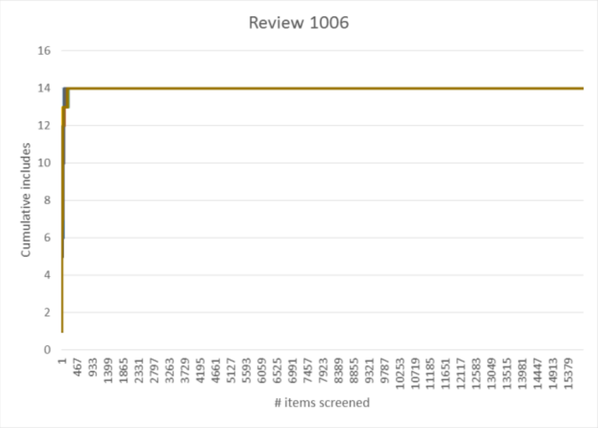
How the machine learns…

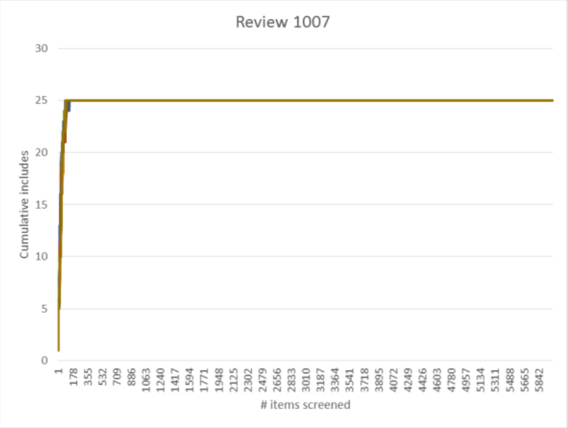


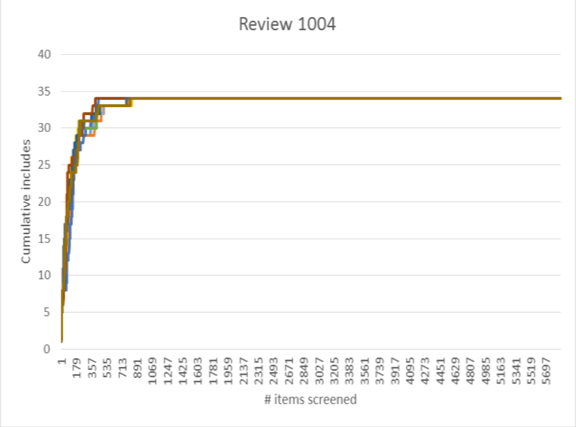
And it can work quite well…

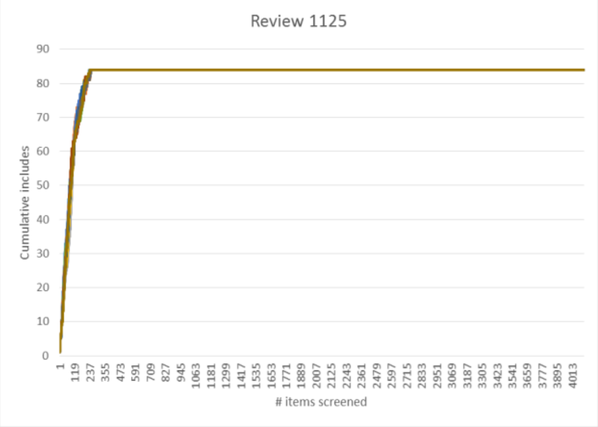
Does it work? e.g. reviews from Cochrane Heart Group

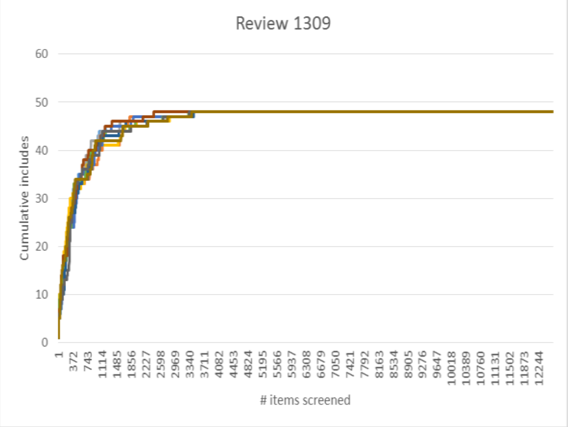












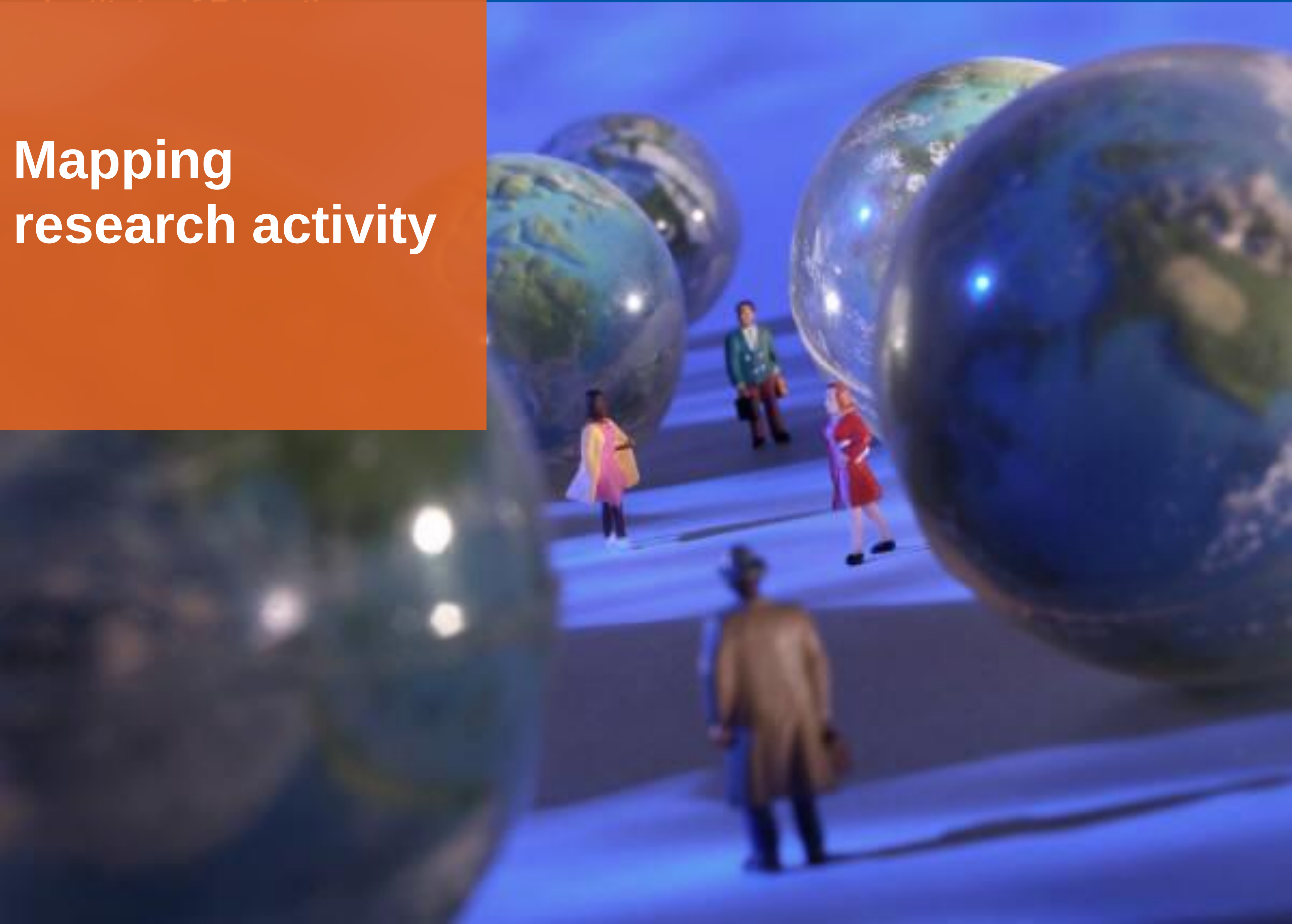
Testing models for TRoPHI register of health promotion controlled trials

N=9,431 records	Pre-built RCT classifier		Build your own classifier			
			Best		Second best	
Items scored 11-99:	RCTs	NonRCTs	RCTs	NonRCTs	RCTs	NonRCTs
Precision	12%	3%	17%	5%	12%	4%
Recall	99%	86%	99%	99%	99%	100%
Screening reduction	43%		**58%**		41%	

Tools

- Klasifiki [https://er5-alpha.ucl.ac.uk/klasifiki] (across reviews)
  - Very new: a version put online especially for today!
- Citation screening (within reviews)
  - Abstrakr
  - EPPI-Reviewer
  - Rayyan
  - Swift ActiveScreener

Mapping research activity



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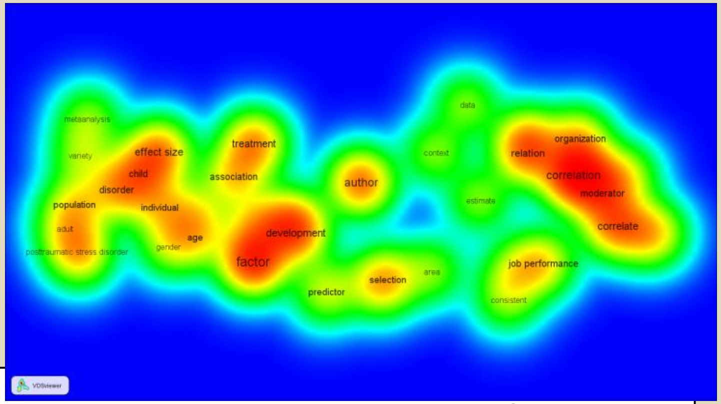
Mapping research activity

- It is possible to apply ‘keywords’ to text automatically, without needing to ‘teach’ the machine beforehand
- This relies on ‘clustering’ technology – which groups studies which use similar combinations of words
- Very few evaluations
  - Can be promising, especially when time is short
  - But users have no control on the terms actually used



Original Article

Research Synthesis Methods

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(wileyonlinelibrary.com) DOI: 10.1002/jrsm.1082

‘Clustering’ documents automatically to support scoping reviews of research: a case study

Claire Stansfield,*† James Thomas† and Josephine Kavanagh†

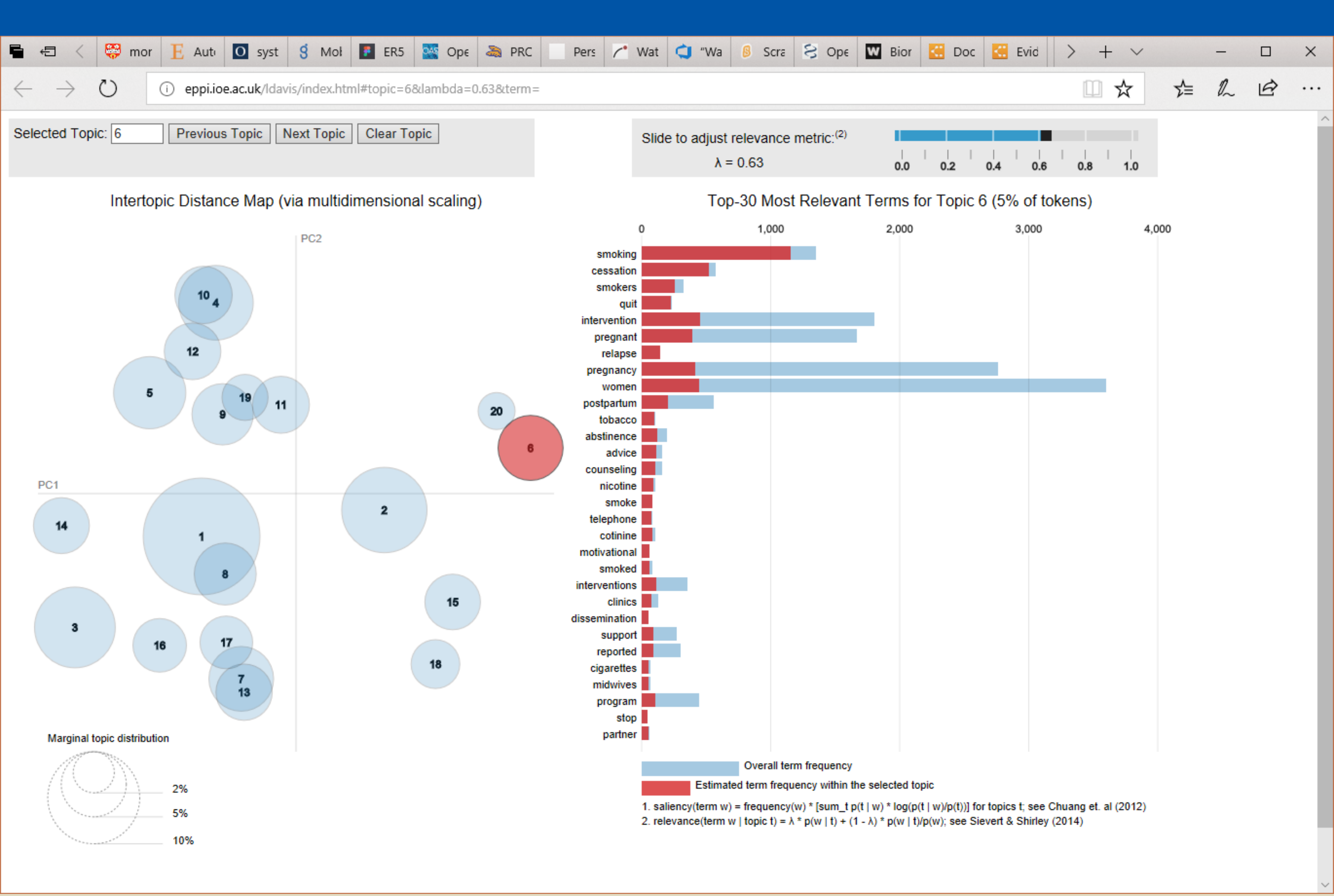
Background: Scoping reviews of research help determine the feasibility and the resource requirements of conducting a systematic review, and the potential to generate a description of the literature quickly is attractive.

Aims: To test the utility and applicability of an automated clustering tool to describe and group research studies to improve the efficiency of scoping reviews.

Methods: A retrospective study of two completed scoping reviews was conducted. This compared the

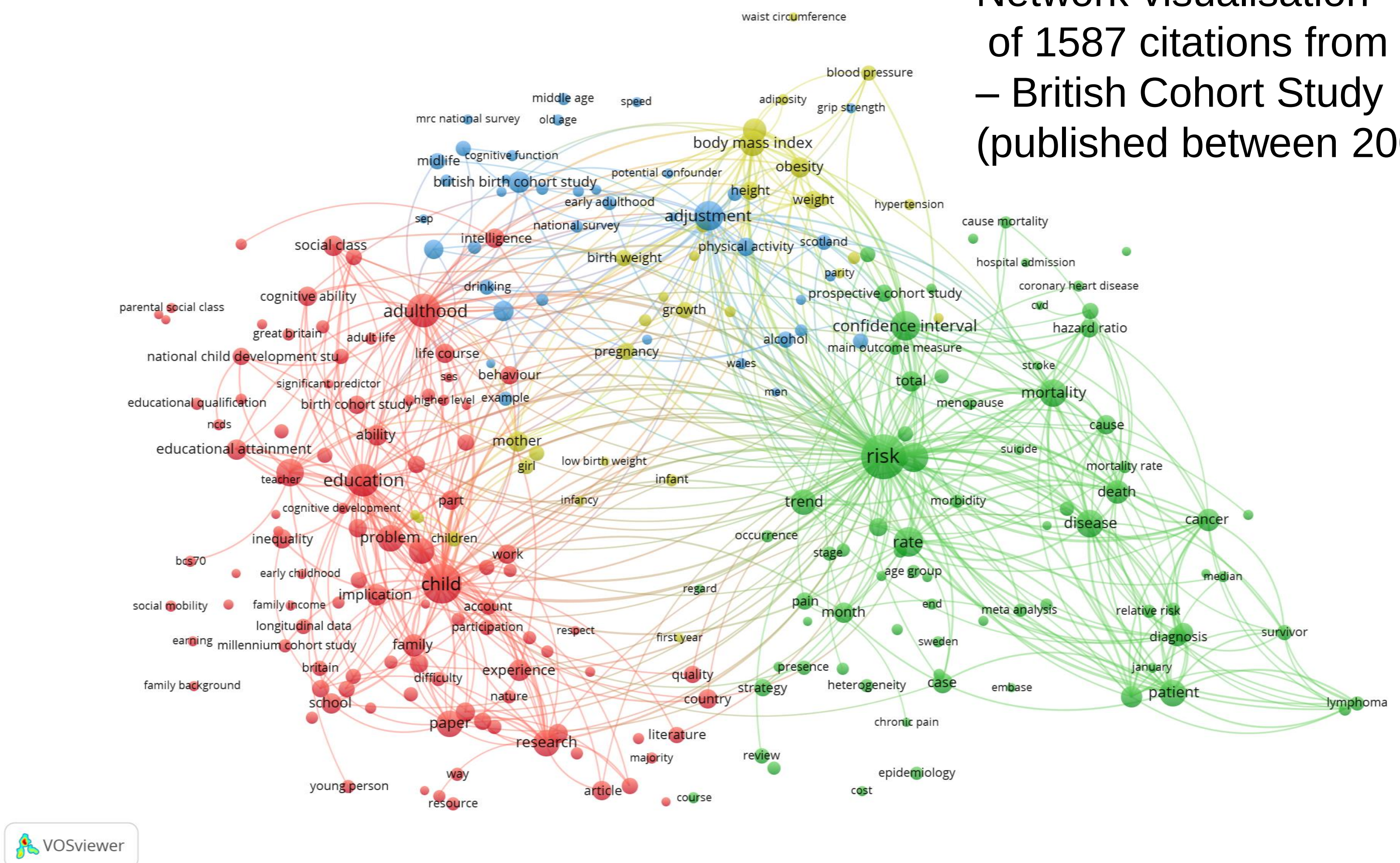
Technologies for identifying sub-sets of citations

- Different families of techniques
  - Fairly simple approaches which examine term frequencies to group similar citations
  - More complex approaches, such as Latent Dirichlet Allocation (LDA)
- The difficult part is finding good labels to describe the clusters
  - But are labels always needed?
- Visualisations are often incorporated into tools

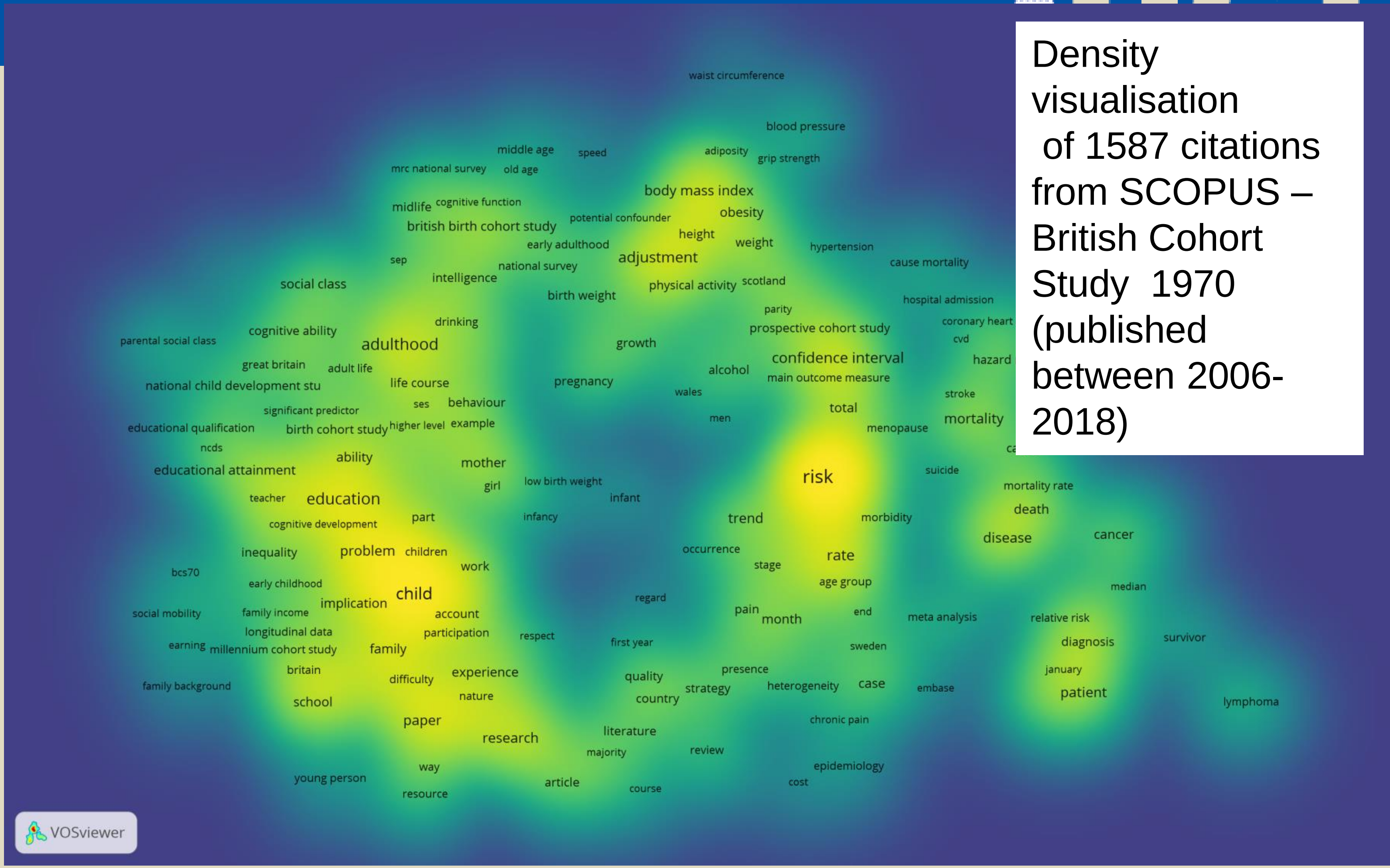


http://eppi.ioe.ac.uk/ldavis/index.html#topic=6&lambda=0.63&term=

Network visualisation
of 1587 citations from SCOPUS
– British Cohort Study 1970
(published between 2006-2018)

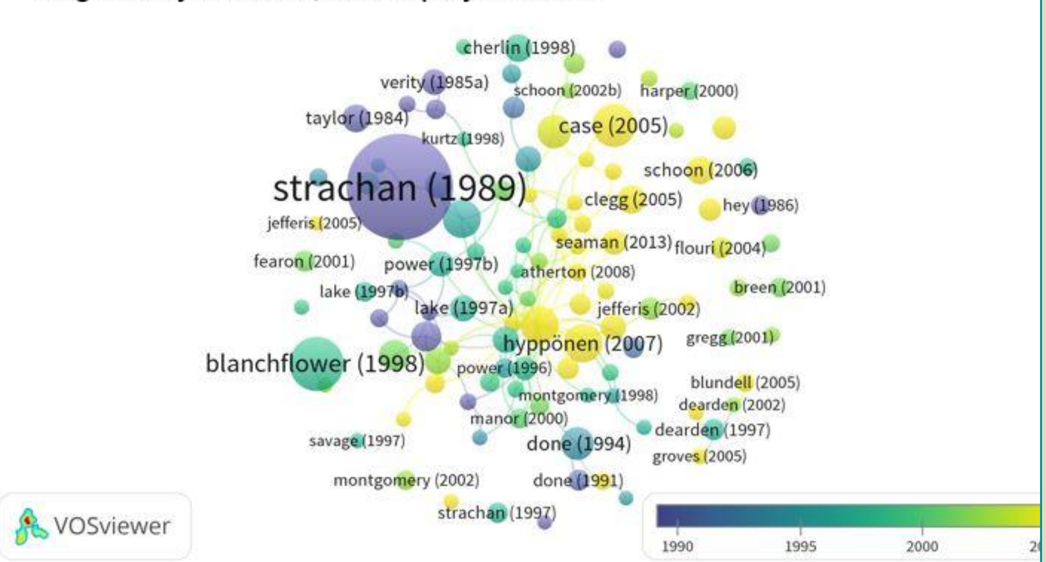


Density visualisation of 1587 citations from SCOPUS – British Cohort Study 1970 (published between 2006-2018)

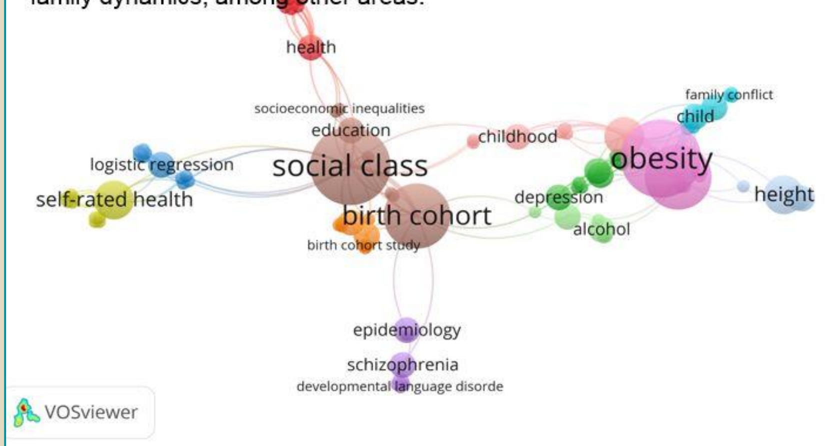


Citation Analysis Example

Highly cited studies: Highly cited papers discovered in Scopus, weighted by citations, are displayed below

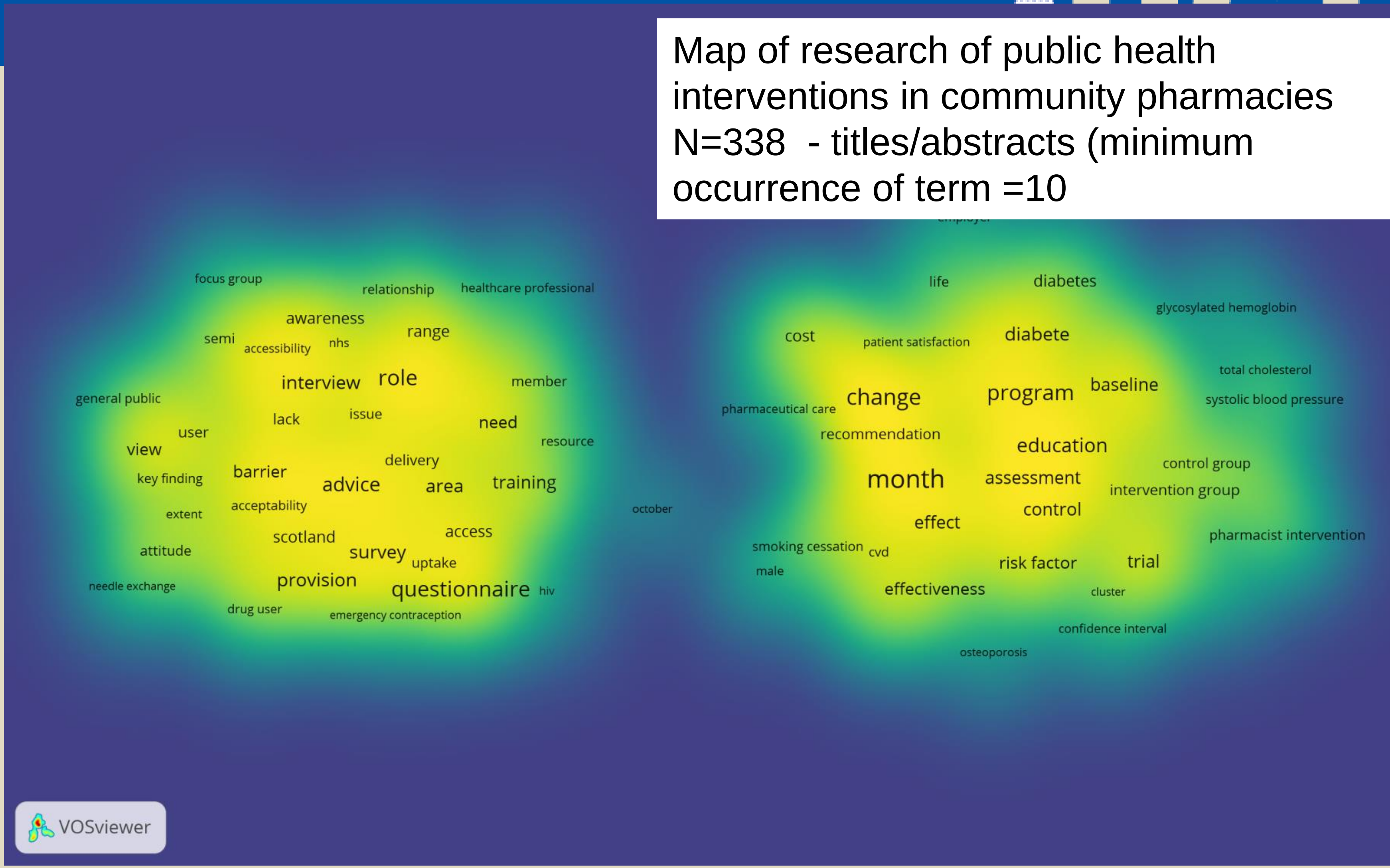


Subject areas of highly cited studies Among the sample of highly cited papers from Scopus, twelve distinct clusters are observed, weighted below in terms of occurrence. The clusters clearly show the contribution of the NCDS in understanding patterns of social class, obesity/BMI, and family dynamics, among other areas.



From: Kneale et al. (2018) Taking stock: Exploring the contribution of the NCDS using systematic review techniques. Protocol and preliminary results. Poster presentation: NCDS 60 years of our lives, UCL Institute of Education, 8-9 March.

Map of research of public health interventions in community pharmacies N=338 - titles/abstracts (minimum occurrence of term =10



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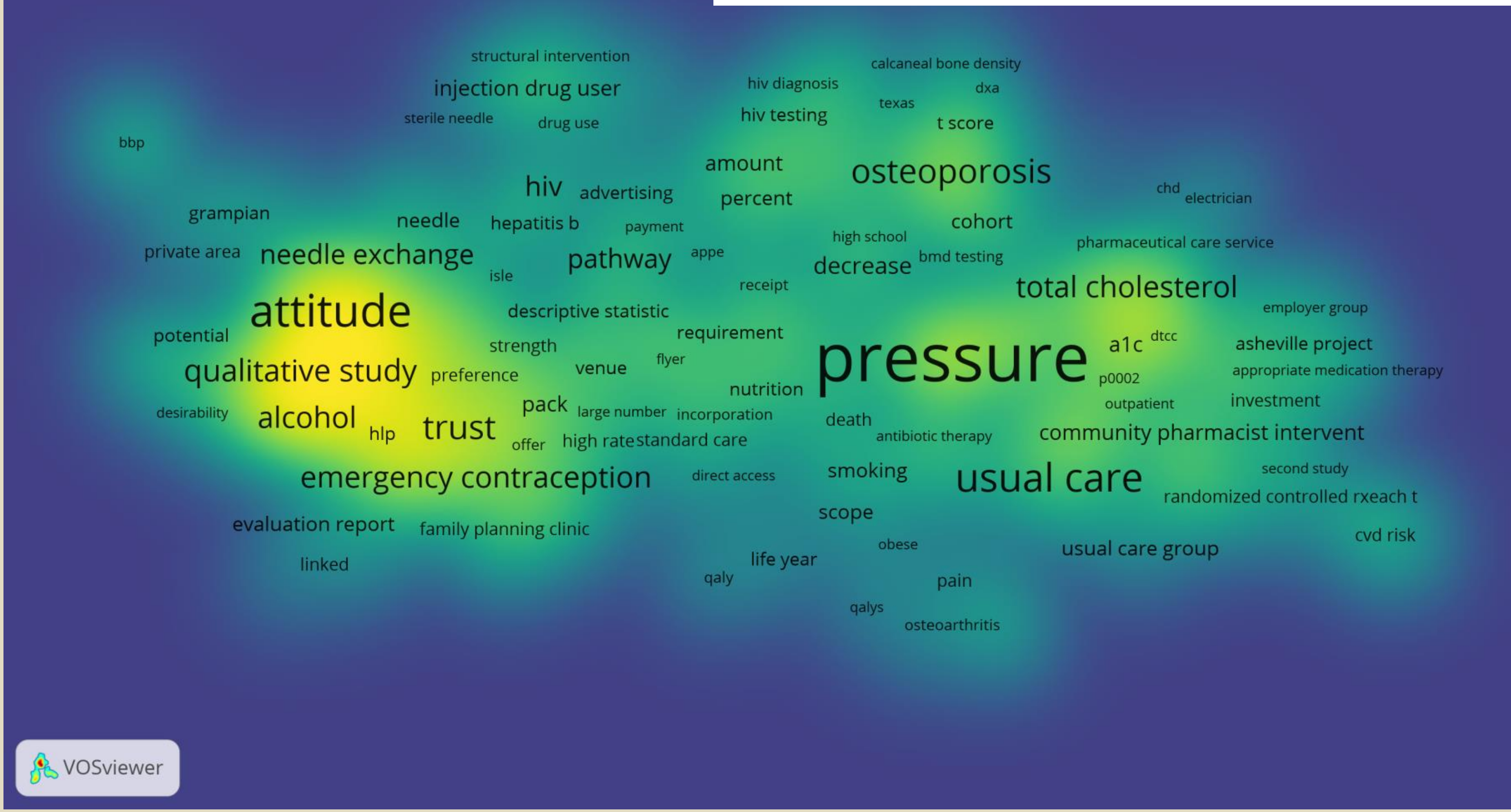
Data as previous slide, N=338: minimum occurrence of term = 2 (instead of 10)



RobotAnalyst

- Systematic review software designed by National Centre for Text Mining at the University of Manchester:
  - Topic modelling, term extraction, search in text and metadata,
  - Automatic classification based on user's decisions
- Currently being evaluated (users welcome! – contact NaCeTM); to be released soon

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

Tools

- LDAVis
- Carrot2 Search
- VosViewer
- RobotAnalyst

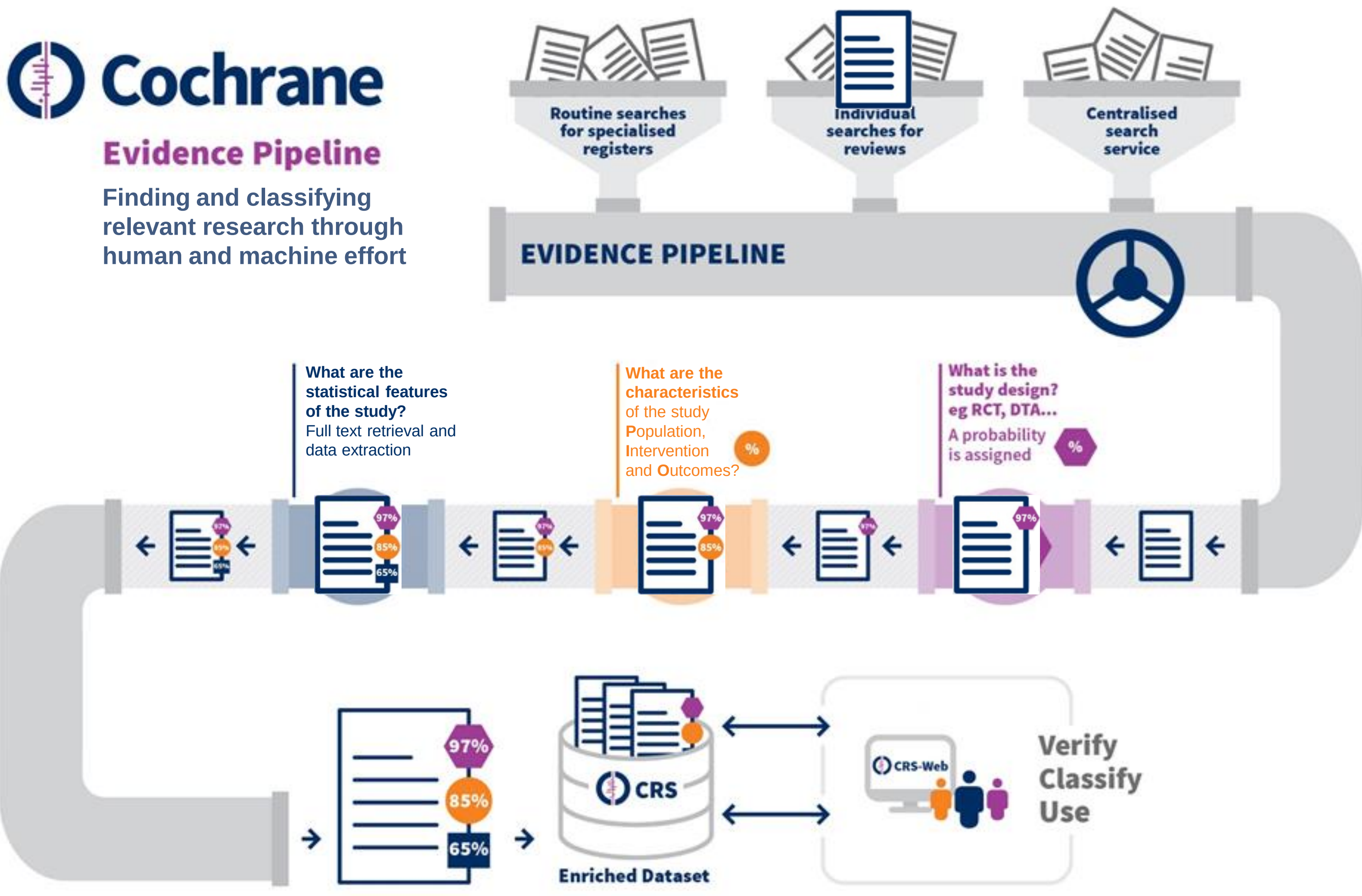
Changing the process: systems for research surveillance

Where might we be headed??

- Evidence ‘surveillance’
- Living systematic reviews and guidelines
- Automated updates??

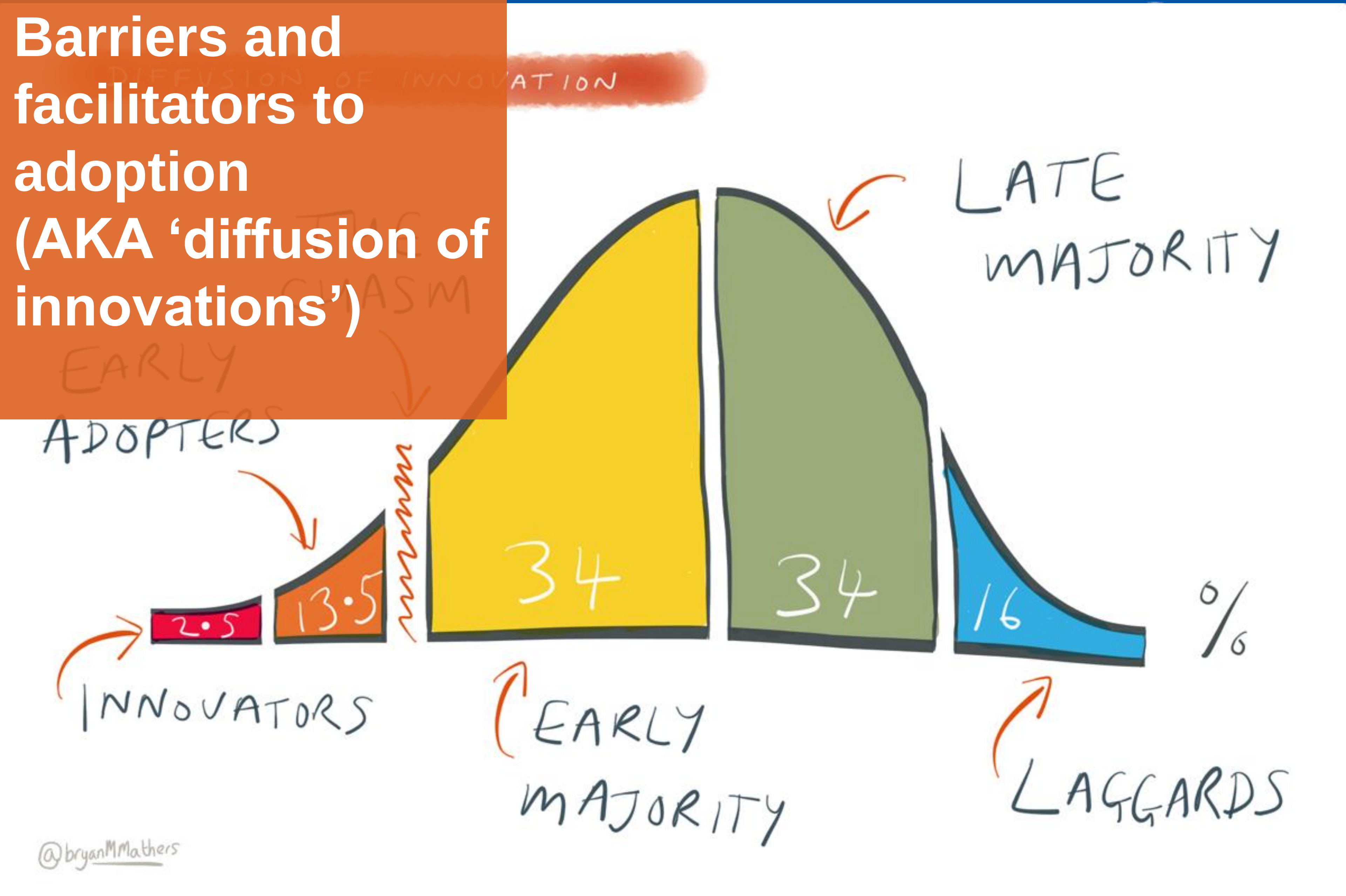
Surveillance work flow

1. Federated search
2. Deduplication
3. Classification (eligibility assessment)
4. Full text retrieval
5. Full text parsing
6. Identification of segments of text
7. Classification (e.g. PICO)
8. Key information extraction (e.g. # participants)
9. Structured data extraction (e.g. tables)
10. Synthesis
11. Alert: this review / guideline may need updating



http://community.cochrane.org/tools/project-coordination-and-support/transform

Barriers and facilitators to adoption (AKA 'diffusion of innovations')



oreilly.com/learning/how-to-build-and-run-your-first-deep-learning-network

```
sudo apt-get install -y libprotobuf-dev libleveldb-dev libsnappy-dev libopencv-dev libboost-all-dev libhdf5-serial-dev protobuf-compiler gcc-4.6 g++-4.6 gcc-4.6-multilib g++-4.6-multilib gfortran libjpeg62 libfreeimage-dev libatlas-base-dev git python-dev python-pip
```

Google's logging framework isn't available through a repository, so you have to build that from source:

```
wget https://google-glog.googlecode.com/files/glog-0.3.3.tar.gz
tar zxvf glog-0.3.3.tar.gz
cd glog-0.3.3
./configure
make
sudo make install
cd ..
```

You should be ready to pull down the Caffe source code:

git clone https://github.com/BVLC/caffe.git
cd caffe

CUDA has problems with the default gcc 4.8 compiler, so you'll need to switch to 4.6:

```
sudo update-alternatives --install /usr/bin/cc cc /usr/bin/gcc-4.6 30
sudo update-alternatives --install /usr/bin/c++ c++ /usr/bin/g++-4.6 30
```

There's a list of Python module dependencies inside the Caffe project, so you'll use PIP to install those, which can take a while:

sudo pip install -r python/requirements.txt

Trialability??

Five characteristics

- **Greater relative advantage**
  - the degree to which an innovation is perceived as better than the idea it supersedes
- **Compatibility**
  - infrastructural and conceptual
- **Trialability**
  - the degree to which an innovation may be experimented with on a limited basis
- **Observability**
  - the degree to which the results of an innovation are visible to others
- **Less complexity**
  - the degree to which an innovation is perceived as difficult to understand and use

Rogers E. Diffusion of innovations. 5th ed. New York, NY: Free Press; 2003.

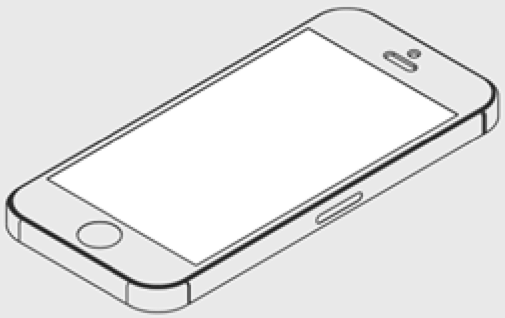
Discussion

https://www.mentimeter.com/app

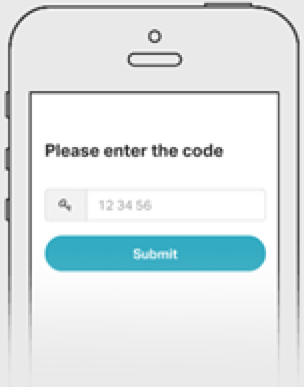
Go to **www.menti.com** and use the code 57 09 13

What methods and processes will need to be developed to use these tools?

Mentimeter



www.menti.com



1 Grab your phone

2 Go to www.menti.com

3 Enter the code 80 60 84 and vote!

Which new approach(es) are you most likely to try out for yourself?

What are your concerns?

What do you think are the potential benefits?

What methods and processes will need to be developed to use these tools?

Research registers

Review types

Efficiency

Topic modelling and mapping

Skills

Reduce recall

Software

Information Literacy

Availability

Risk

Processes

Transparency

Acceptability

Opportunities

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Selected bibliography

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- O'Mara-Eves A, et al. (2015). Using text mining for study identification in systematic reviews: a systematic review of current approaches. *Syst Rev* 4: 5.
- Thomas J, et al. (2011). Applications of text mining within systematic reviews. *Res Synth Meth* 2(1): 1-14.
- Stansfield C, et al. (in press) Text mining for search term development in systematic reviewing: a discussion of some methods and challenges. *Res Synth Meth*.

- https://blogs.technet.microsoft.com/machinelearning/2017/04/20/textmining-to-improve-the-health-of-millions-of-citizens/

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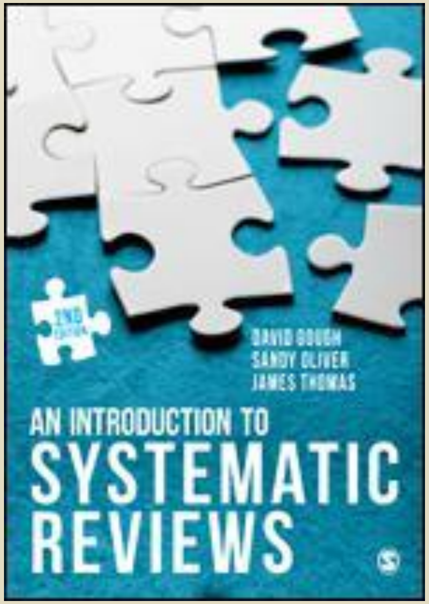
Thank you

EPPI-Centre website: http://eppi.ioe.ac.uk

Email
j.thomas@ucl.ac.uk
c.stansfield@ucl.ac.uk



The EPPI-Centre is part of the Social Science Research Unit at the UCL Institute of Education, University College London

EPPI-Centre
Social Science Research Unit
Institute of Education
University of London
18 Woburn Square
London WC1H 0NR

Tel +44 (0)20 7612 6397
Fax +44 (0)20 7612 6400
Email eppi@ioe.ac.uk
Web eppi.ioe.ac.uk/