Medicine

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Antimicrobial resistance: what role for herbal medicines?

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UKCRC Registered Clinical Trials Units

NHS National Institute for Health Research

What are we using antibiotics for?

- In England, 74% of human antibiotics are prescribed in general practice (ESPAUR report, 2016)
- The majority are prescribed for self limiting conditions

J Antimicrob Chemother 2018; **73** Suppl 2: ii19–ii26
doi:10.1093/jac/dkx502

Journal of Antimicrobial Chemotherapy

Actual versus 'ideal' antibiotic prescribing for common conditions in English primary care

Koen B. Pouwels[1–3]†, F. Christiaan K. Dolk[1,2]†, David R. M. Smith[1], Julie V. Robotham[1]‡ and Timo Smieszek[1,3]*‡

- Data from THIN primary care database, 2013-2015
- Covers 3.7m patients

Table 1. Actual and 'ideal' antibiotic prescribing proportions among patients without comorbidities consulting at a general practice

Condition	Consultations (*n*)	Proportion of consultations with a systemic antibiotic prescription (95% CI)	Ideal proportion of consultations resulting in systemic antibiotic prescriptions (IQR)[16]
Acne	60959	0.43 (0.43–0.44)	0.21 (0.10–0.35)
Acute bronchitis	17084	0.82 (0.82–0.82)	0.13 (0.06–0.22)
Acute cough	573827	0.41 (0.41–0.41)	0.10 (0.06–0.16)
Acute otitis media (age 0–1 year)	14886	0.92 (0.91–0.92)	0.19 (0.09–0.33)
Acute otitis media (age 2–18 years)	39513	0.88 (0.88–0.89)	0.17 (0.08–0.30)
Acute rhinosinusitis	74359	0.88 (0.88–0.88)	0.11 (0.05–0.18)
Acute sore throat	386971	0.59 (0.58–0.59)	0.13 (0.07–0.22)
Asthma exacerbation	23292	0.47 (0.46–0.47)	–[c]
COPD exacerbation	13840	0.73 (0.72–0.74)	0.54 (0.31–0.78)
Gastroenteritis (age >2 years)	114290	0.05 (0.05–0.05)	0.09 (0.04–0.16)
Impetigo	29809	0.53 (0.52–0.53)	0.12 (0.06–0.53)
Influenza-like illness	23787	0.18 (0.18–0.19)	–[c]
Lower respiratory tract infection[a]	161065	0.87 (0.87–0.88)	–[c]
Upper respiratory tract infection[b]	383847	0.25 (0.25–0.25)	–[c]
Urinary tract infection age (>14 years)	128566	0.92 (0.91–0.92)	0.75 (0.61–0.86)

[a]Including non-specific LRTI, COPD exacerbations, acute bronchitis and pneumonia.
[b]Including non-specific URTI, common cold, laryngitis and tracheitis.
[c]Condition for which expert opinion on ideal prescribing proportions was not elicited.

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Do antibiotics help symptoms?
(evidence from RCTs and systematic reviews)

	Average duration before seeing a doctor	Average duration after seeing a doctor	Total duration if untreated	Benefit from antibiotic (hours)	NNT
Otitis media	1-2 days	3-5 days	4 days	8-12 hours	18
Sore throat	3 days	5 days	8 days	12-18 hours	10-20
Sinusitis	5 days	7-10 days	12-15 days	24 hours	13
Bronchitis	10 days	10-12 days	20-22 days	24 hours	10-20

THE LANCET
Infectious Diseases

Lancet Infect Dis 2013;
13: 123–29

Amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected: a 12-country, randomised, placebo-controlled trial

Paul Little, Beth Stuart, Michael Moore, Samuel Coenen, Christopher C Butler, Maciek Godycki-Cwirko, Artur Mierzecki, Slawomir Chlabicz, Antoni Torres, Jordi Almirall, Mel Davies, Tom Schaberg, Sigvard Mölstad, Francesco Blasi, An De Sutter, Janko Kersnik, Helena Hupkova, Pia Touboul, Kerenza Hood, Mark Mullee, Gilly O'Reilly, Curt Brugman, Herman Goossens, Theo Verheij, on behalf of the GRACE consortium

Summary

Background Lower-respiratory-tract infection is one of the most common acute illnesses managed in primary care. Few placebo-controlled studies of antibiotics have been done, and overall effectiveness (particularly in subgroups such as older people) is debated. We aimed to compare the benefits and harms of amoxicillin for acute lower-respiratory-tract infection with those of placebo both overall and in patients aged 60 years or older.

Methods Patients older than 18 years with acute lower-respiratory-tract infections (cough of ≤28 days' duration) in whom pneumonia was not suspected were randomly assigned (1:1) to either amoxicillin (1 g three times daily for 7 days) or placebo by computer-generated random numbers. Our primary outcome was duration of symptoms rated "moderately bad" or worse. Secondary outcomes were symptom severity in days 2–4 and new or worsening symptoms. Investigators and patients were masked to treatment allocation. This trial is registered with EudraCT (2007-001586-15), UKCRN Portfolio (ID 4175), ISRCTN (52261229), and FWO (G.0274.08N).

Findings 1038 patients were assigned to the amoxicillin group and 1023 to the placebo group. Neither duration of symptoms rated "moderately bad" or worse (hazard ratio 1·06, 95% CI 0·96–1·18; p=0·229) nor mean symptom severity (1·69 with placebo *vs* 1·62 with amoxicillin; difference –0·07 [95% CI –0·15 to 0·007]; p=0·074) differed significantly between groups. New or worsening symptoms were significantly less common in the amoxicillin group than in the placebo group (162 [15·9%] of 1021 patients *vs* 194 [19·3%] of 1006; p=0·043; number needed to treat 30). Cases of nausea, rash, or diarrhoea were significantly more common in the amoxicillin group than in the placebo group (number needed to harm 21, 95% CI 11–174; p=0·025), and one case of anaphylaxis was noted with amoxicillin. Two patients in the placebo group and one in the amoxicillin group needed to be admitted to hospital; no study-related deaths were noted. We noted no evidence of selective benefit in patients aged 60 years or older (n=595).

Interpretation When pneumonia is not suspected clinically, amoxicillin provides little benefit for acute lower-respiratory-tract infection in primary care both overall and in patients aged 60 years or more, and causes slight harms.

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Antibiotic prescribing in primary care: resistance a meta-analysis

	Odds Ratio risk for resistance (95% CI)	
	Antibiotic <2 m	Antibiotic <12 m
UTI (5 studies, 14,348)	2.5 (2.1-2.9)	1.3 (1.2-1.5)
RTI (7 studies, 2,605)	2.4 (1.4-3.9)	2.4 (1.3-4.5)

Longer duration and multiple courses were associated with higher resistance rates

Costelloe et al, *BMJ 2010;340:c2096*

“But doctor, what can I do to feel better?”

- Steam?
  - Steam did not help
- Ibuprofen?
  - did not help when added to paracetamol except in children and in patients with chest infections
  - increased reconsultations

BMJ 2013; 347 doi: https://doi.org/10.1136/bmj.f6041

Ibuprofen, paracetamol, and steam for patients with respiratory tract infections in primary care: pragmatic randomised factorial trial

Paul Little *general practitioner and professor of primary care research*, Michael Moore *general practitioner and reader in primary care*, Joanne Kelly *senior trial manager*, Ian Williamson *general practitioner and senior lecturer in primary care*, Geraldine Leydon *social scientist, principal research fellow*, Lisa McDermott *research fellow*, Mark Mullee *statistician, director research design service*, Beth Stuart *research fellow*, on behalf of the PIPS investigators

University of Southampton, Aldermoor Health Centre, Southampton SO16 5ST, UK

Could alternative medicines help symptoms?

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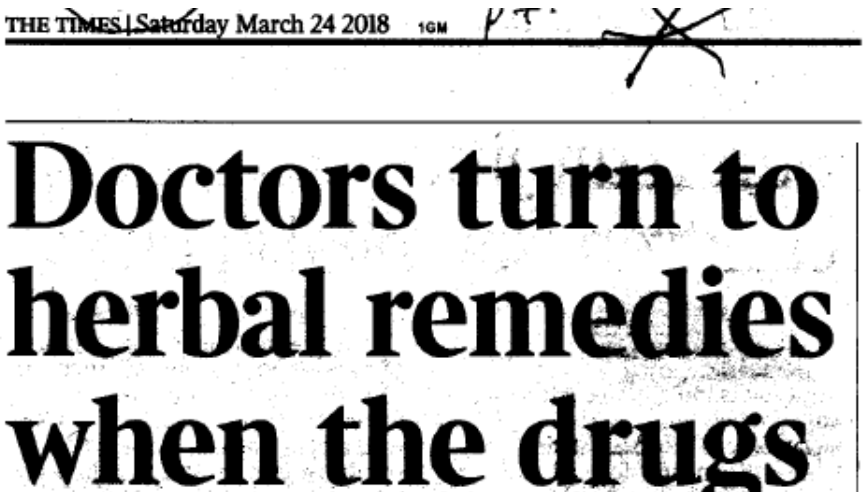

THE TIMES | Saturday March 24 2018 1GM

Doctors turn to herbal remedies when the drugs

Table 4 Median antibiotic prescription rates and RR of prescribing antibiotics in primary care England over 2016

	Any antibiotic/STAR-PU,† median (25th–75th percentile)	RTI antibiotic/STAR-PU,† median (25th –75th percentile)	UTI antibiotic/STAR-PU,† median (25th–75th percentile)
Conventional General Practice (GP) surgeries (n=7274)	1.01 (0.86–1.17)	0.56 (0.46–0.67)	0.22 (0.17–0.26)
IM GP surgeries with IM/CAM-trained GP (n=9)	0.79 (0.73–0.91)*	0.44 (0.37–0.48)*	0.21 (0.19–0.23)
	RR,† (95% CI)	**RR,† (95% CI)**	**RR,† (95% CI)**
Conventional GP surgeries (n=7274)	Ref.	Ref.	Ref.
IM GP surgeries with IM/CAM-trained GP (n=9)	0.78 (0.64 to 0.97)*	0.74 (0.59 to 0.94)*	0.91 (0.72 to 1.17)

*P<0.05.

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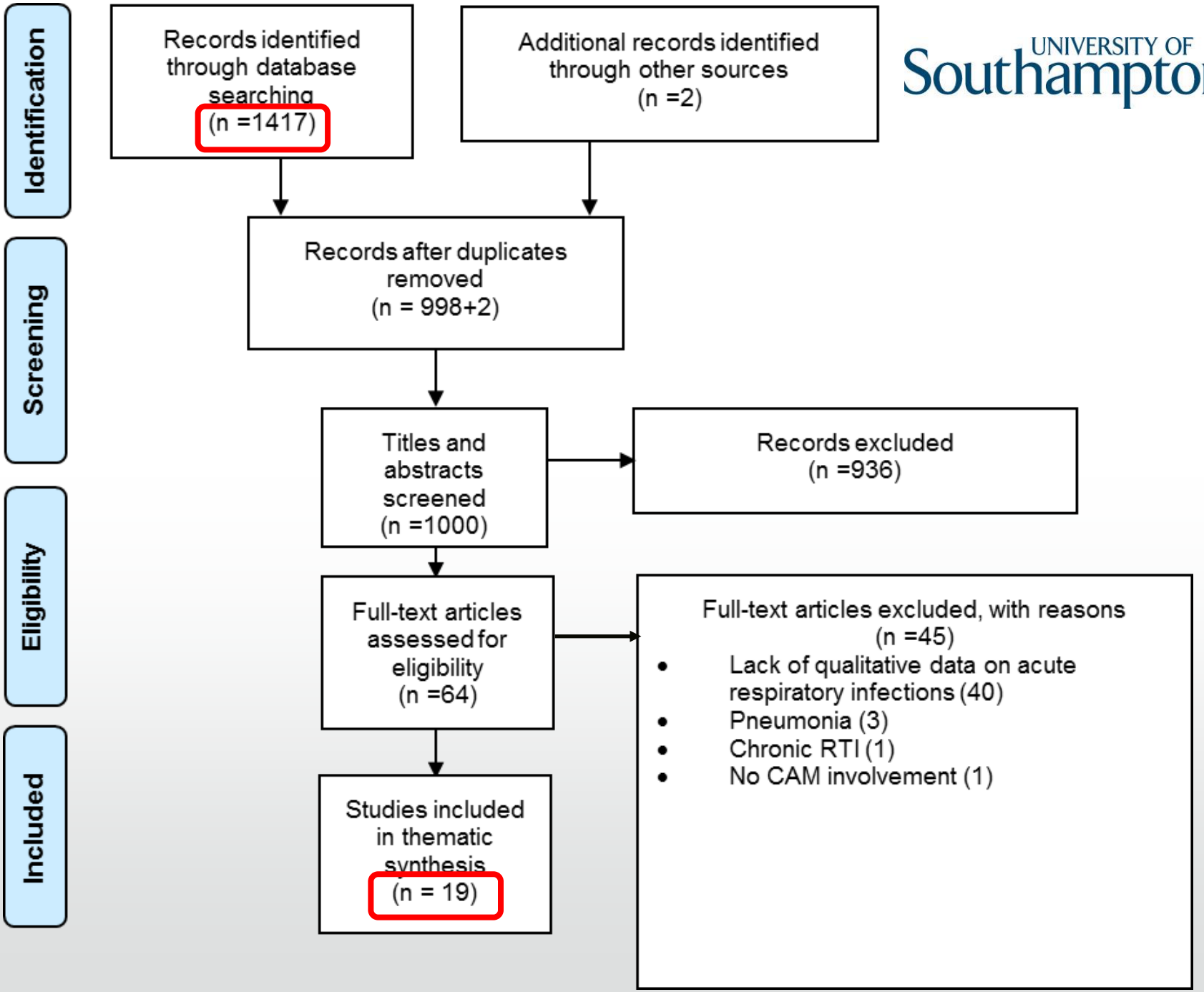
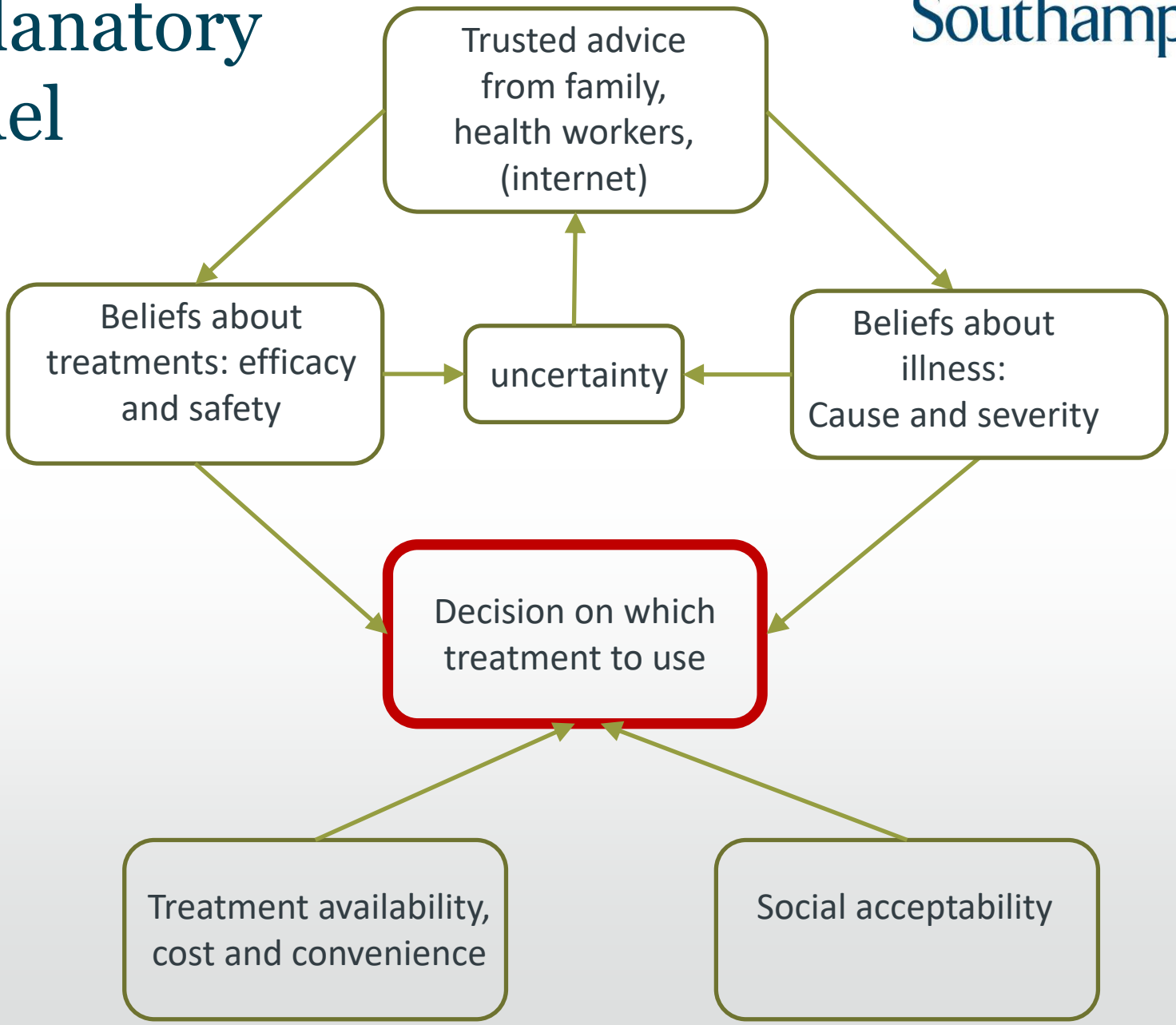
How do people feel about using herbs for treating respiratory infections?

- Systematic review of qualitative studies
- Research questions:
  - What do patients, health workers and the public think about the use of Complementary and Alternative Medicines (CAM) for the treatment of acute respiratory infections (ARIs)?
  - What are the barriers and facilitators to the use of CAM for reducing the over-use of antibiotics for ARIs?


Identification
Screening
Eligibility
Included
Records identified through database searching (n =1417)
Additional records identified through other sources (n =2)
Records after duplicates removed (n = 998+2)
Titles and abstracts screened (n =1000)
Records excluded (n =936)
Full-text articles assessed for eligibility (n =64)
Full-text articles excluded, with reasons (n =45)
Lack of qualitative data on acute respiratory infections (40)
Pneumonia (3)
Chronic RTI (1)
No CAM involvement (1)
Studies included in thematic synthesis (n = 19)

Explanatory model



Could herbal medicines help to reduce antibiotic use?

- Respiratory tract infections:
  - *Andrographis paniculata*: systematic review, qualitative study, pilot trial
  - *Pelargonium sidoides*: HATRIC trial
- Urine infections:
  - *Arctostaphylos uva-ursi*: ATAFUTI trial
  - TCM: RUTI trial
- Future studies

PLOS ONE

RESEARCH ARTICLE

Andrographis paniculata (Chuān Xīn Lián) for symptomatic relief of acute respiratory tract infections in adults and children: A systematic review and meta-analysis

Xiao-Yang Hu[1]*, Ruo-Han Wu[2], Martin Logue[1], Clara Blondel[3], Lily Yuen Wan Lai[1], Beth Stuart[1], Andrew Flower[1], Yu-Tong Fei[2], Michael Moore[1], Jonathan Shepherd[4], Jian-Ping Liu[2], George Lewith[1†]

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2 Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China,
3 AgroParisTech, Paris Institute of Technology for Life, Food and Environmental Sciences, Paris, France,
4 Southampton Health Technology Assessments Centre (SHTAC), Faculty of Medicine, University of Southampton, Southampton, United Kingdom

Andrographis paniculata for symptomatic relief of acute respiratory tract infections

- 33 trials, comprising 7175 patients

Outcome	Measure (95% CI)
Mean severity of cough (Standardised mean difference)	-0.39 (-0.67 to -0.10)
Time to symptom resolution (days) – Andrographis alone compared to usual care	-3.55 days (-5.5 to -1.5)
Time to symptom resolution (days) – Andrographis PLUS usual care compared to usual care alone	-1.27 days (-1.58 to -0.97)

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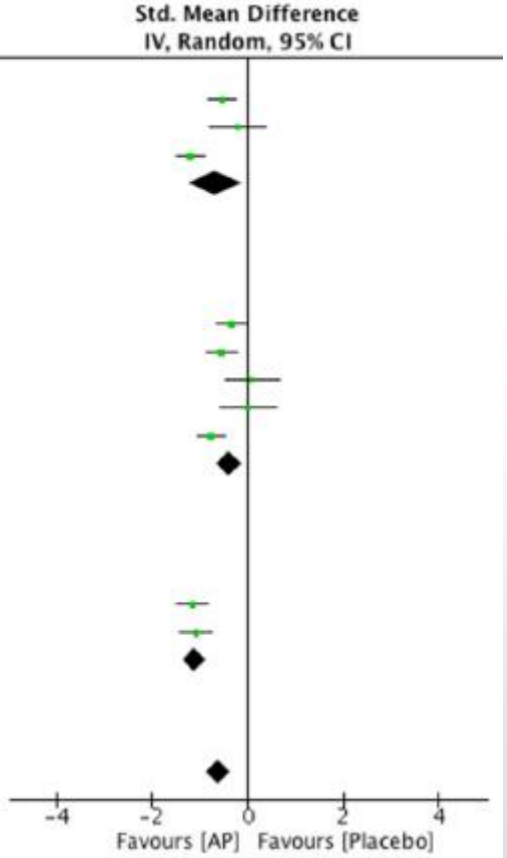
Andrographis vs Placebo
Symptom severity improvement

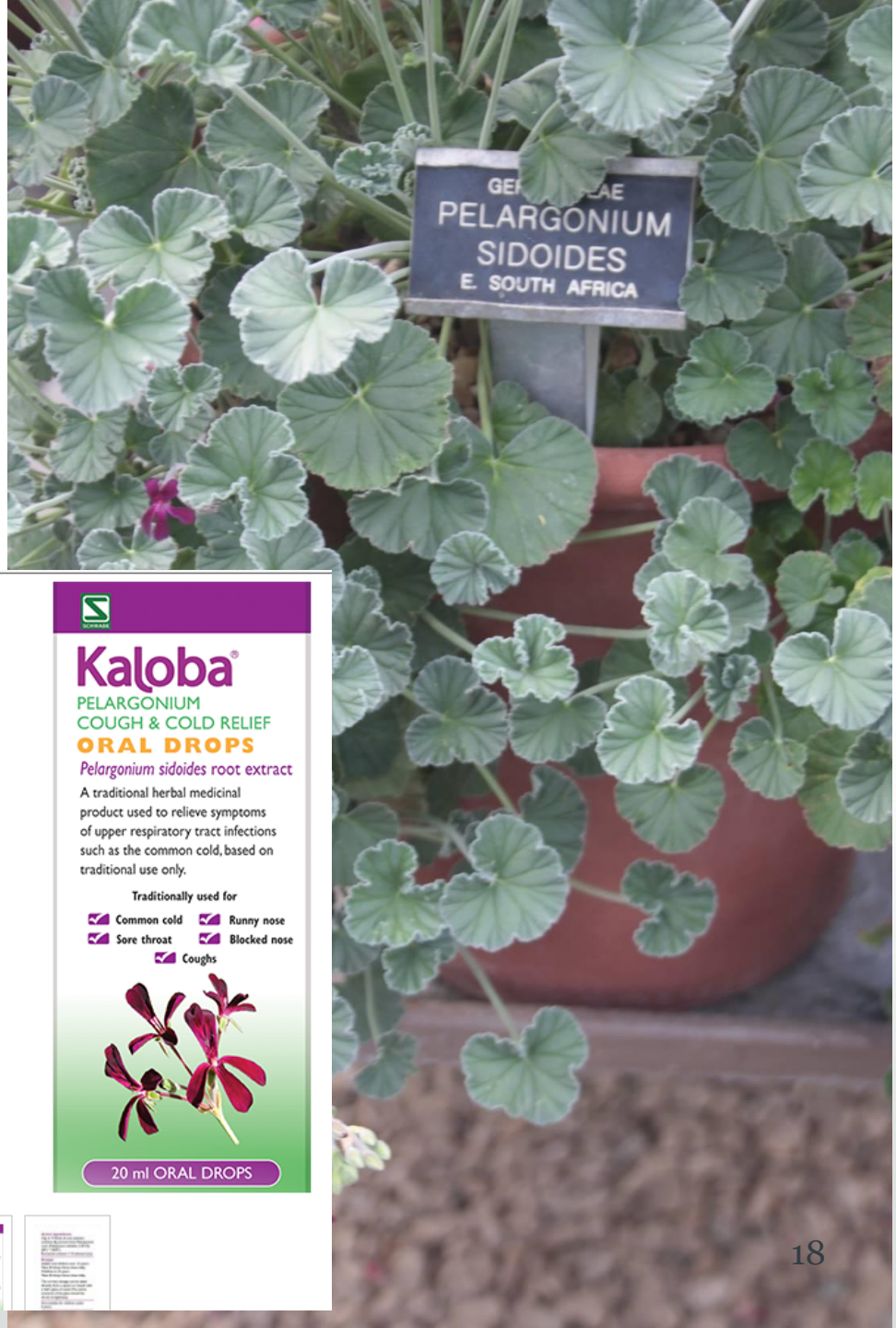
Study or Subgroup	A. paniculata mono Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
4.1.1 Overall symptom								
Melchior, 2000	2.97	3.47	89	5.16	4.54	90	11.0%	-0.54 [-0.84, -0.24]
Melchior, 2000 (pilot)	3.13	2.69	23	3.87	3.96	23	7.9%	-0.21 [-0.79, 0.36]
Saxena, 2010	66.65	59.26	112	142.69	65.89	108	11.2%	-1.21 [-1.50, -0.92]
Subtotal (95% CI)			**224**			**221**	**30.1%**	**-0.69 [-1.26, -0.12]**
Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 14.64$, df = 2 (P = 0.0007); $I^2 = 86\%$								
Test for overall effect: Z = 2.38 (P = 0.02)								
4.1.2 Cough								
Caceres, 1999	2.02	1.62	79	2.67	2.14	79	10.9%	-0.34 [-0.66, -0.03]
Caceres, 1999	1.71	1.24	79	2.52	1.64	79	10.8%	-0.55 [-0.87, -0.24]
Melchior, 2000 (pilot)	0.26	0.45	23	0.22	0.42	23	7.9%	0.09 [-0.49, 0.67]
Melchior, 2000 (pilot)	0.17	0.39	23	0.17	0.39	23	7.9%	0.00 [-0.58, 0.58]
Saxena, 2010	23.26	17.08	89	35.91	15.92	99	11.1%	-0.76 [-1.06, -0.47]
Subtotal (95% CI)			**293**			**303**	**48.6%**	**-0.39 [-0.67, -0.10]**
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 10.85$, df = 4 (P = 0.03); $I^2 = 63\%$								
Test for overall effect: Z = 2.65 (P = 0.008)								
4.1.3 Sore throat								
Caceres, 1999	1.63	1.11	79	3.1	1.38	79	10.6%	-1.17 [-1.51, -0.83]
Saxena, 2010	15	17.02	82	33.99	17.55	74	10.6%	-1.09 [-1.43, -0.76]
Subtotal (95% CI)			**161**			**153**	**21.2%**	**-1.13 [-1.37, -0.89]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.09$, df = 1 (P = 0.76); $I^2 = 0\%$								
Test for overall effect: Z = 9.28 (P < 0.00001)								
Total (95% CI)			**678**			**677**	**100.0%**	**-0.63 [-0.89, -0.36]**
Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 47.17$, df = 9 (P < 0.00001); $I^2 = 81\%$								
Test for overall effect: Z = 4.68 (P < 0.00001)								
Test for subgroup differences: $Chi^2 = 15.58$, df = 2 (P = 0.0004), $I^2 = 87.2\%$								



GRAPHALO study

- *AndroGRAPHis pAnicuLata* in the treatment Of adults with Acute Respiratory Tract Infections (ARTIs): a double blind randomised placebo controlled feasibility study
  - 2 groups of 30 patients
  - Capsule andrographis (whole plant), 300 mg, 3 capsules 4 times daily versus matching placebo
  - Outcomes: recruitment feasibility; primary outcome: proportion of symptom improvement, side effects, antibiotic prescription, symptom diary for 14d; EQ-5D
- Interviews with GPs regarding their views on herbal medicine for acute RTI in primary care

Pelargonium sidoides



Relieves symptoms of the common cold

THR Kaloba Pelargonium Cough & Cold Relief Oral Drops

Pelargonium sidoides root extract oral drops

20ml

Traditionally used for:

- Common cold
- Sore throat
- Cough
- Runny nose
- Blocked nose

★★★★★ Rated 5.00 stars

Pelargonium sidoides extract for treating acute respiratory tract infections

New search | Review | Intervention

Antje Timmer, Judith Günther, Edith Motschall, Gerta Rücker, Gerd Antes, Winfried V Kern

First published: 22 October 2013

Editorial Group: Cochrane Acute Respiratory Infections Group

DOI: 10.1002/14651858.CD006323.pub3 View/save citation

- trials of efficacy for acute bronchitis
  - 3 in adults (n= 341)
  - 2 in children (n=420)
  - Liquid preparation was effective, tablets were not
- 2 trials of efficacy in acute sinusitis
  - Liquid preparation was effective, tablets were not

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Pelargonium sidoides liquid extract for acute bronchitis

Outcome	Placebo Group	Pelargonium Group	Difference	Number needed to treat
Recovery by day 7 (in adults)	4.7%	37.1%	32.4%	3
Recovery by day 7 (in children)	7.4%	19.0%	11.2%	8.6
Adverse events (in children)	13.0%	16.3%		No significant difference

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HATRIC trial

- **H**erbal **A**lternative **T**reatment for lower **R**espiratory tract **I**nfections with **C**ough in adults
- Double blind, randomised, placebo controlled feasibility trial
- 4 groups of 40 patients:
  - Liquid *Pelargonium sidoides* root extract, 30 drops 3x daily versus matching placebo
  - Tablets of *Pelargonium sidoides* root extract, 20mg 3x daily, versus placebo
- Outcomes: recruitment feasibility; primary outcome (antibiotic prescription, symptom diary for 28d); EQ-5D
- Interviews with participants and GPs regarding their views on herbal medicine for RTI in primary care

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HATRIC trial

- Participants were identified in primary care when presenting with acute cough illness (20 health centres)
- We encouraged delayed or no antibiotics
- 134 patients were recruited in March – December 2018
- Diaries containing all key information were obtained from 107 (80%) participants.
- Nested qualitative study: patients and GPs were broadly supportive
- Funding: NIHR, Industrial sponsorship (Schwabe)

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Urinary Tract Infections (UTIs)

- UTIs are common: 40-50% of women experience a UTI
- 20-30% will have a second infection
  - 25% of these will have recurrent infections (≥3 episodes in 12 months)
- The symptoms associated with UTIs are distressing.
  - usually settle without complications within 3 - 4 days
  - but antibiotics shorten the duration of symptoms
- A delayed prescription strategy may help, but is unlikely to be accepted without better symptom relief
- Prophylactic antibiotics are given for recurrent UTIs, but resistance is increasing

Alternative Treatments for Adult Female Urinary Tract Infection: a randomised controlled trial

PI: Dr Mike Moore, University of Southampton

Prof Paul Little, Prof George Lewith, Prof Alastair Hay, Prof Simon Gibbons, Jeanne Trill, Dr Merlin Willcox

NHS
National Institute for Health Research

Arctostaphylos uva-ursi (Bearberry)

- First documented in *The Physicians of Myddfai*, a 13th century Welsh herbal
- Commonly prescribed by herbalists in UK for UTIs
- Available over the counter in pharmacies in the UK and Germany

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Research question

- P: In adult women with suspected UTI
- I: does Uva-Ursi, or ibuprofen, or a combination of both
- C: compared to placebo
- O: provide relief from urinary symptoms?

Trial design: a factorial RCT

	Ibuprofen	Placebo
Uva-ursi	Group 1	Group 3
Placebo	Group 2	Group 4

- Patients were advised to take the study medicines for 5 days:
  - Ibuprofen 400mg tds
  - Uva Ursi, 3 caps 3x daily (as a 20% arbutin extract, prepared to GMP and IMP standards)
- A matching placebo (brown rice flour and some brown malt colouring + 30 mg Spirulina to produce a herbal flavour)
- Quality control: extraction of materials from each batch and fingerprinting by NMR spectroscopy and mass spectrometry

Trial population

- Adult women (18-70) presenting to primary care with suspected lower urinary tract infection
- Willing to accept a delayed antibiotic prescription
- Study sites: 60 primary health care centres in the UK
- Recruitment: GPs or experienced nurses invited suitable patients to take part in the trial

“Rescue” treatment

- NHS prescription was issued for an antibiotic (clinician’s choice, according to local guidelines)

- If symptoms failed to settle or worsened, participants were instructed to collect and commence their delayed antibiotic prescription after 3-5 days.

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Primary outcome: symptoms

- Intention To Treat analysis of mean score for frequency symptoms assessed on day 2-4
- No differences between groups: all improved equally
  - Uva-ursi vs. placebo -0·06 (95% CI -0·33 to 0·21) p=0·661
  - ibuprofen vs. no ibuprofen advice -0·01 (95% CI -0·27 to 0·26) p=0·951.

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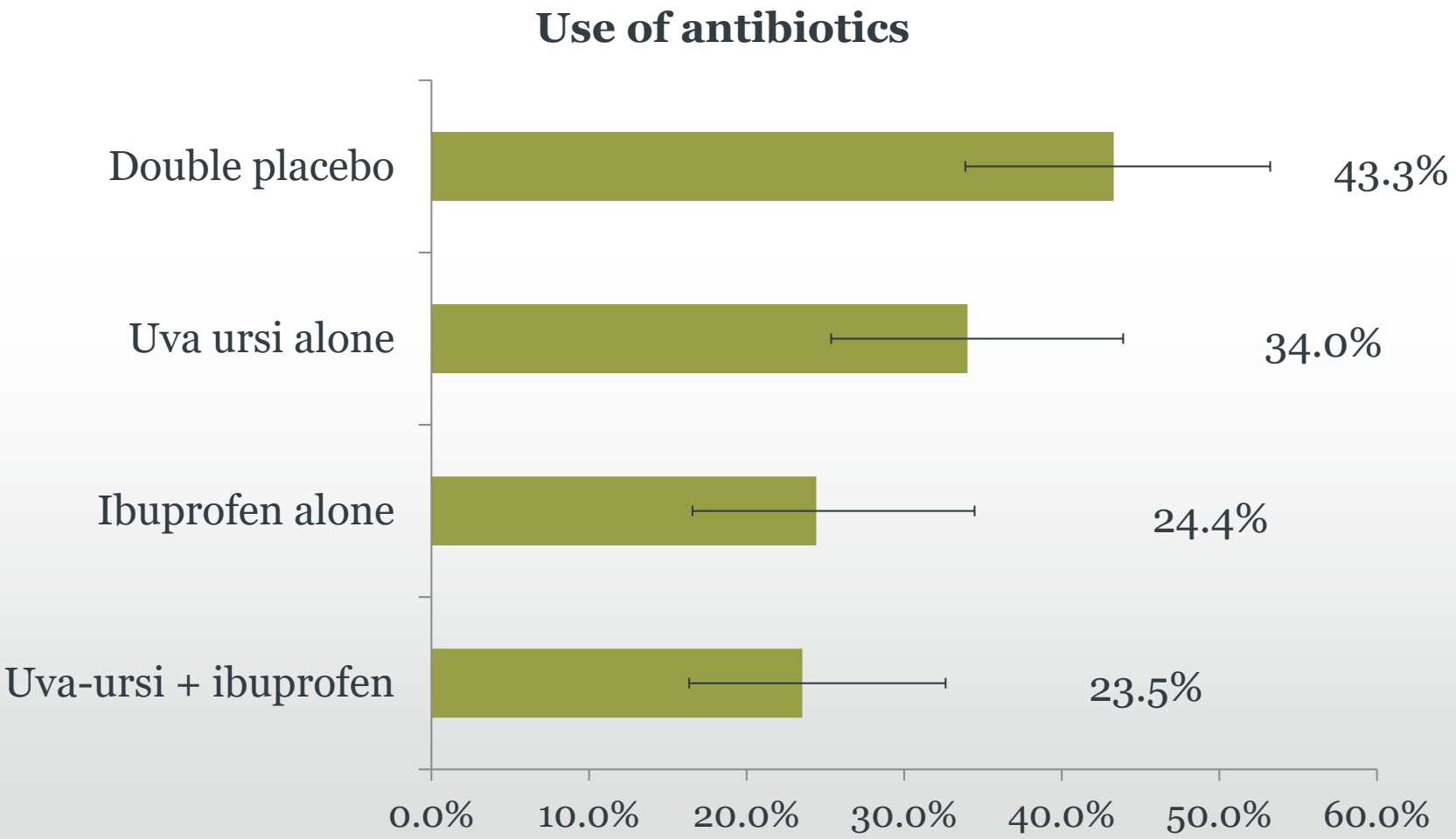
Secondary outcome measure: antibiotics



National Institute for Health Research

University of Southampton

RUTI: A double blinded, randomised, placebo controlled feasibility study exploring the possible role of Chinese herbal medicine in the treatment of **R**ecurrent **U**rinary **T**ract **I**nfections.

Primary objectives:

- Feasibility of delivering CHM in UK primary care
- Safety of CHM
- Exploratory estimates of effect size on reducing the frequency and severity of infection
- Impact on antibiotic use

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RUTI Trial

- Groups
  - Standardised active herbs vs standardised placebo, delivered by GP
  - Individualised active herbs vs individualised placebo, administered by practitioners of Chinese herbal medicine

- Aims to explore:
  - Differences between active and placebo herbs (specific effect)
  - Differences between standardised and individualised herbs
  - A comparison between contextual effects of CHM via a GP clinic consultation versus a CAM clinic consultation

Formulae

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Standardised formulae

Acute formula:

- Bai Hua She She Cao
- Huang Bai
- Jin Qian Cao
- 4 x 0.4g capsules q.d.

Preventative formula:

- Huang Qi
- Ku Shen
- Wu Yao
- 4 x 0.4g capsules b.d.

Individualised formula - example

- Bai Hua She She Cao 20
- Ban Zhi Lian 15
- Bai Jiang Cao 15
- Pu Gong Ying 15
- Ku Shen 9
- Huang Qin 12
- Shi Wei 15
- Jin Qian Cao 15
- Qu Mai 15
- Bian Xu 12
- Wu Yao 9
- Yi Mu Cao 15
- Gan Cao 6

Formula provided as herbal granules and made into a decoction.

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Recruitment

- 62 women recruited (31 in each arm)
- Standardised arm
  - Recruited via doctors (health centres)
  - Slow recruitment
  - 16/31 (52%) withdrew or lost to follow-up

- Individualised arm
  - Self-referral
  - 9/31 (29%) withdrew or lost to follow up
  - Placebo control failed due to misunderstanding of herbal pharmacy…who added active herbs to the placebo mix!

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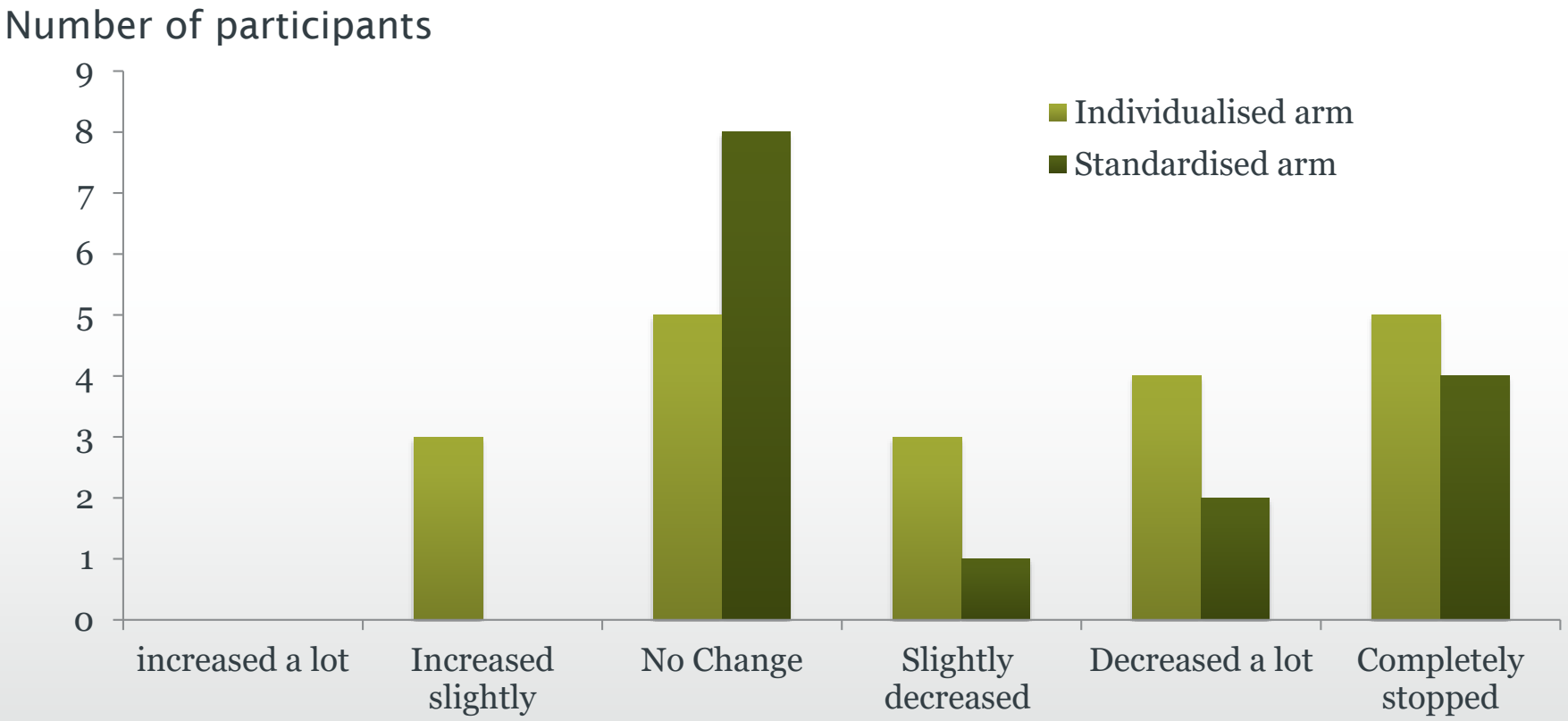
Results from individualised group (n=31) using -50 to +50 VAS scale (no placebo control)

- Overall change in urinary symptoms +22.4/50 (SE 3.7) = 44.8% improvement
- Reduction in frequency of infections +22.8/50 (SE 4.5)= 45.6% reduced frequency of UTIs
- Severity of infection: reduction of +15.5/50 (SE 4.9) = 31% reduction in severity of UTIs

Reported use of antibiotics



Initial feasibility findings

- It was easier to recruit and retain patients on individualised Chinese medicine
- Recruitment to via health centres was challenging
- It is possible to do a CTIMP trial on Chinese Herbal Medicine in the UK
- Descriptive statistics suggest positive reduction in symptoms and decrease in antibiotic use

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How to prioritise herbal remedies and TCM for future clinical trials?

- There are thousands of herbal medicines
- There is little money for conducting trials
- Many trials produce a “negative” outcome
- -> How to maximise chances of picking the best remedy for a trial?
  - Plant(s) and plant part(s)
  - Preparation
  - Dosage

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The RTO

(Retrospective treatment-outcome study)

Ask patients – or relatives – about treatment recently used, and health outcome of this treatment.

⇒ which treatment is followed by the best or the worst outcomes?

= “Epidemiological ethnopharmacology”

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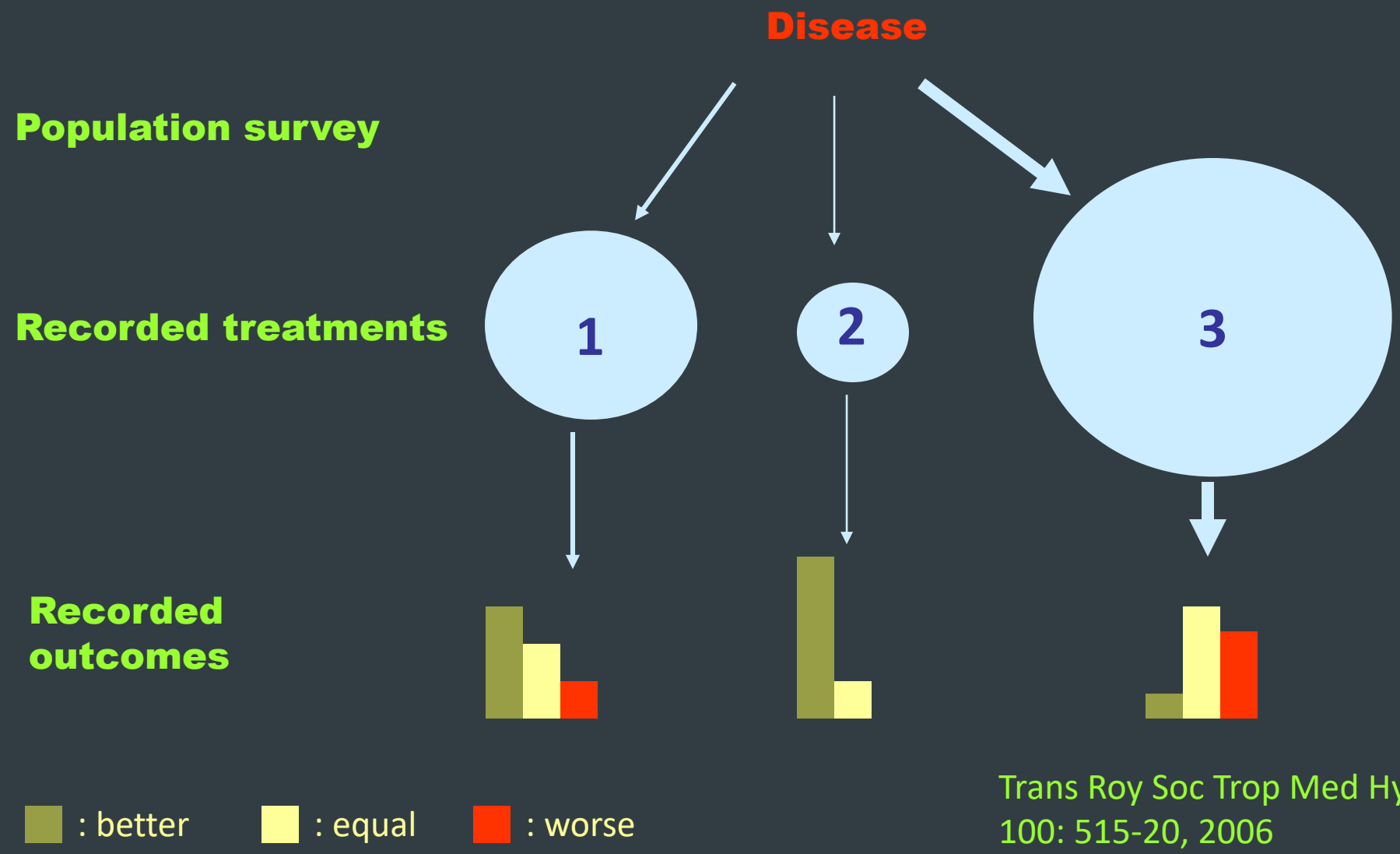
The RTO is novel because:

- Patients, not healers, are interviewed
- Information is collected on outcomes
- Statistical methods are used to explore correlations between treatments and outcomes

Are the most commonly used plants also the most effective?



Trans Roy Soc Trop Med Hyg, 100: 515-20, 2006

Statistical analysis

(full tables included 66 plants and 166 recipes for 952 cases).

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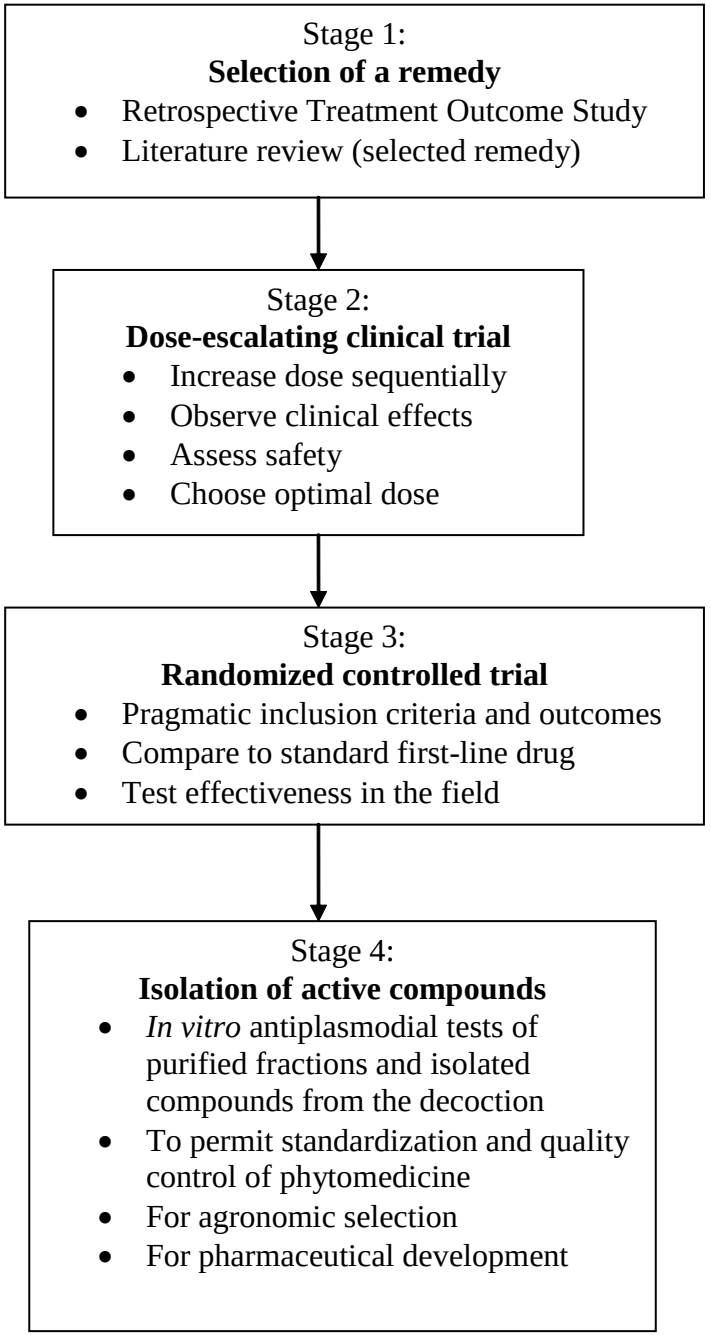
Plant	Number who used	Number Improved	Number Failed	% Improved (95% CI)	P (Fisher exact)
Argemone mexicana	30	30	0	**100%** (88-100)	reference
Carica papaya	33	28	5	85% (68-95)	0.05
Anogeissus leiocarpus	33	27	6	82% (64-93)	0.03

Reverse Pharmacology

- Took 6 years to develop an “improved traditional phytomedicine” in Mali
- Cost about 0.4m Euros
- End product is easily affordable and available



RTO – treatment of cough in China, 2019

- Online survey distributed through social medial networks in China
  - Have you had a cough in the last 3 months?
  - If yes, which treatment(s) did you take?
  - How long did your symptoms last?
- 26,000 participants recruited in 3 weeks!
- Analysis ongoing…

Centre for Evidence-based Chinese Medicine

- Group led by Prof Jianping Liu
- Working on systematic reviews and clinical trials

UNIVERSITY OF Southampton

Innovate-UK

UK - China AMR Competition Scope

1) Explore Traditional Chinese Medicine (herbal medicines and/or botanicals) for the treatment and/or prevention of infectious diseases in humans and/or animals

- *Evaluate TCM in combination with existing antibiotics. A small scale clinical trial must be included in this strand.*
  - *Projects could explore, for example:*
  - *reduced side effects (including the impact on the microbiome)*
  - *improved efficacy at lower antibiotic doses*
  - *the prevention of drug resistant infection in high-risk immunocompromised patient cohorts*

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Adding Chinese herbal medicine to antibiotic treatment for acute exacerbation of chronic obstructive pulmonary disease

- Preclinical: to investigate the antimicrobial properties of Shufeng Jiedu (SFJD) on *Haemophilus influenzae* in a lung explant model of infection
- Clinical: To determine the feasibility of conducting a fully powered trial of SFJD as an addition to antibiotics for the treatment of acute exacerbations of COPD in the UK primary care setting
- Parallel trial in China in patients hospitalised with COPD
- Evidence synthesis – aim to register SFJD in UK

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  - Pukka herbs
  - Schwabe
- Southampton Clinical Trials Unit
- Thank you for your kind invitation!

A question for you: could we do similar research in Uganda?