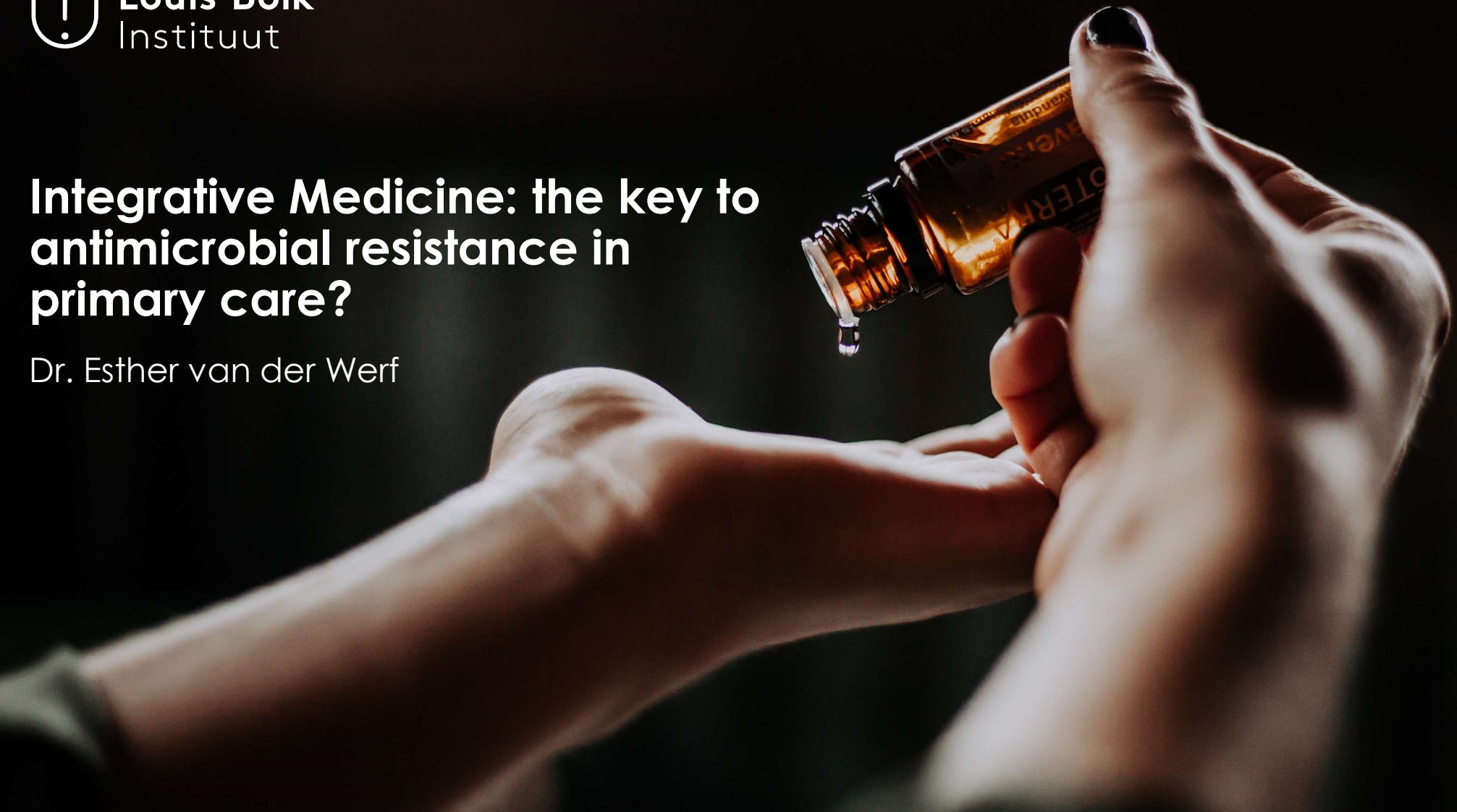


# **Integrative Medicine: the key to antimicrobial resistance in primary care?**

Dr. Esther van der Werf



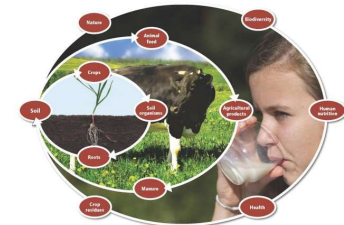
## 2001-2011: The Netherlands (Rotterdam, Utrecht, Leiden)



## 2011-2019: Bristol (UK), Kuala Lumpur (Malaysia)



## September 2019 : Louis Bolk Instituut, Bunnik, The Netherlands



- Antibiotic consumption in primary care
  - Reduction of antibiotic use
  - Definitions of health
  - Integrative Medicine & AMR
- Example of RCT
  - Antibiotic prescription in primary care
  - Ongoing collaborative AMR projects



# Antibiotic use

- Widespread use of antibiotics saved millions of human lives
- Antibiotic consumption – a major driver for **Antimicrobial resistance (AMR)**
- AMR - one of greatest challenges for public health (WHO, 2014)

“*A **post-antibiotic** era, in which common infections and minor injuries **can kill**, far from being an apocalyptic fantasy, is instead a **very real possibility** for the 21st century.*”  
– World Health Organization, May 2014

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## The Netherlands: the lowest consumer of Antibiotics in Europe

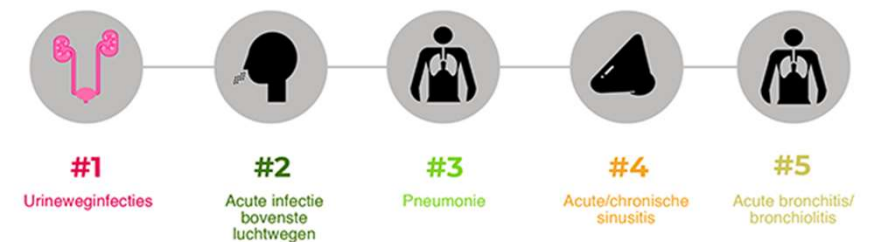




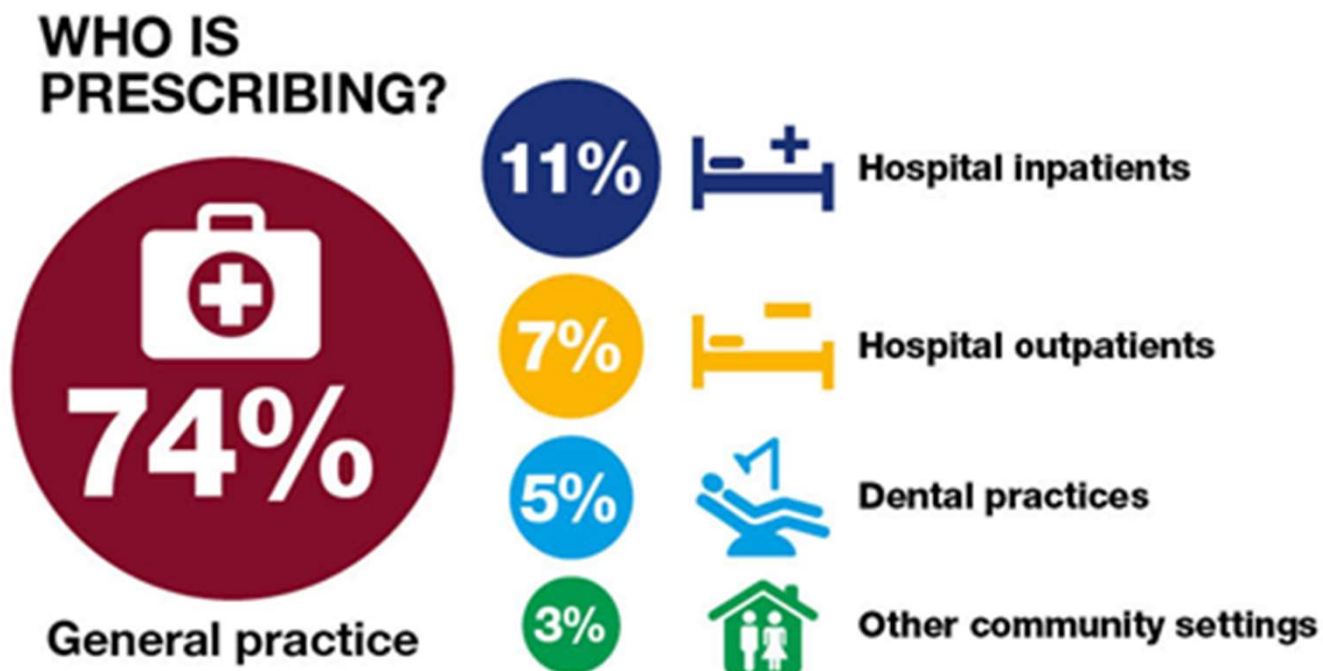
## Primary Care in The Netherlands:

- Between 1 and 59% of antibiotic prescriptions for respiratory tract infections (RTI) are **inappropriate**;
- Highest percentage for sore throats;
- Large variations between Dutch GPs.

### Most common reason to prescribe antibiotics



## GPs at the top



# Reduction in primary care- Why?

## Primary care

- Responsible for highest proportion of prescribing
- Majority are prescribed for self limiting conditions:
  - Sore throats
  - Acute bronchitis
  - Urinary tract infection
- Important target for antimicrobial stewardship\* interventions

## Biological costs of antibiotics

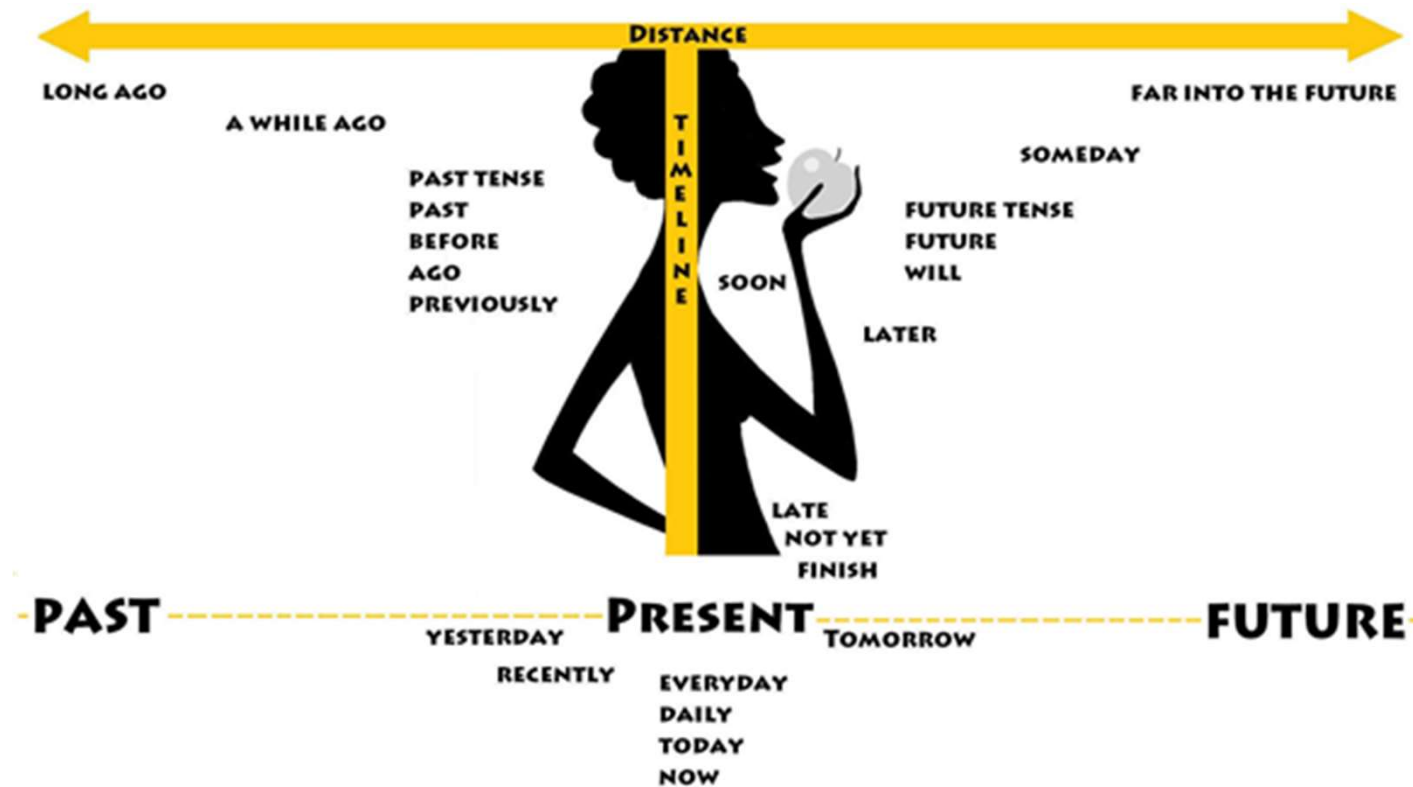
- Short and long term health effects
- Patient and GP views



*\*coordinated interventions to improve and measure appropriate use of antimicrobials (NICE Guidelines, 2015)*



## Side effects of Antibiotics



# Antibiotics and the Human Gut Microbiome

## Short term effects

- Acutes: nausea, diarrhea and skin rash.

## Long term effects

- Microbes in the human body interact with many physiological processes, and participate in the regulation of the immune and metabolic systems;
- Alteration of the human gut or vaginal microbiome can **indirectly** affect health in long term



# Antibiotics and the Human Gut Microbiome



## Potential longer term effects due to microbiome modulation- increased risk on

- depression, anxiety, or psychosis (Lurie et al. 2015)
- dysfunctioning of the immune system and its ability to resist infection (Denny et al. 2016)
- developing Parkinson's disease (Padua et al., 2016)
- for several diseases in children including obesity, types 1 and 2 diabetes, inflammatory bowel diseases, coeliac disease, allergies and asthma (Blaser, 2016)

## It appears that these effects are:

- most pronounced if the antibiotics are **consumed within the first two years of life.**
- may be cumulative.

# A new approach

## Time for a new and promising approach

- that may be effective both for healthcare and for agriculture, and that is based on health promotion.

## Health promotion

- The promotion of health in a professional way requires a clear vision on 'health'
- Different definitions of health



# Definitions of Health

Conventional definition of health: “**Absence of disease**”

- Logical approach to prevent and to fight disease: **Fighting disease approach**

New definition of health\*: “***the ability to adjust and to self-manage***”

- Indicates a professional strategy of health promotion as a necessary **complement** to the fighting disease approach, and emphasises the strengthening of the resilience of a system: **Health promotion approach**

Foundation for Traditional and Complementary Medicine (TCM)

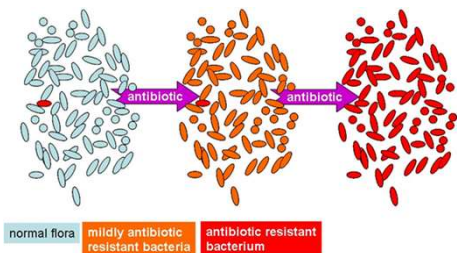
\*(Huber et al., BMJ 2011, 343, adopted by WHO)



# AMR and Integrative Medicine

## TCM as non-antibiotic strategy

1. To strengthen the self-healing capacities of the organism (**health promotion**)
  - TCM as an alternative for antibiotics, but not directly based on the antimicrobial properties of the therapy itself
  - TCM as symptom reliever (delayed prescription strategy)
2. To control/treat infectious diseases (**Fighting disease**).
  - TCM as an alternative for antibiotics, directly based on their own antimicrobial properties



# Primary Care Infection Research

## 1. “beat the bad bugs”:

To investigate if TCM, as an adjunct or alternative to standard care, can cost-effectively reduce the consumption of antibiotics whilst maintaining symptom control, and to distinguish its clinical effect of placebo effects.

## 2. “keep the good bugs healthy”:

To determine microbiota prevention and intervention strategies to conserve and steward the effects of antibiotics.



Traditional & Complementary Medicine

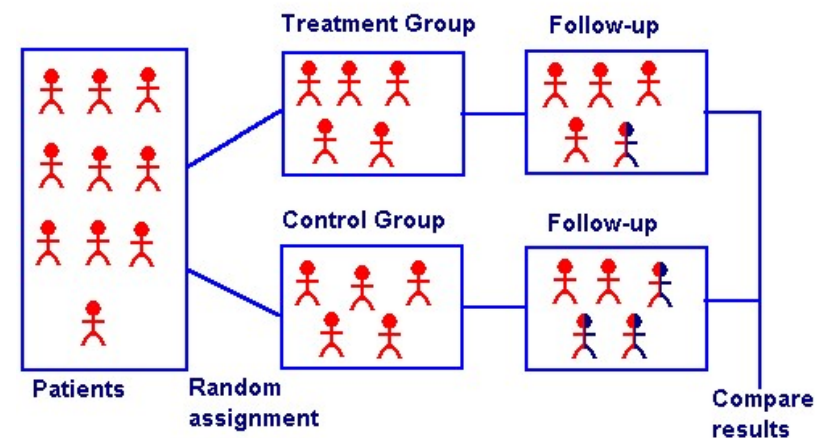
Probiotics & prebiotics



## Primary Care Infection Research

### Not without evidence!

- All interventions, no matter conventional or complementary, have to be tested on **efficacy, safety and cost effectiveness.**





Contents lists available at ScienceDirect

## Clinical Microbiology and Infection

journal homepage: [www.clinicalmicrobiologyandinfection.com](http://www.clinicalmicrobiologyandinfection.com)

## Original article

## Uva-ursi extract and ibuprofen as alternative treatments for uncomplicated urinary tract infection in women (ATAFUTI): a factorial randomized trial

M. Moore<sup>1,\*</sup>, J. Trill<sup>1</sup>, C. Simpson<sup>2</sup>, F. Webley<sup>2</sup>, M. Radford<sup>2</sup>, L. Stanton<sup>2</sup>, T. Maishman<sup>2</sup>, A. Galanopoulou<sup>2</sup>, A. Flower<sup>1</sup>, C. Eyles<sup>1</sup>, M. Willcox<sup>1</sup>, A.D. Hay<sup>3</sup>, E. van der Werf<sup>3</sup>, S. Gibbons<sup>4</sup>, G. Lewith<sup>1</sup>, P. Little<sup>1</sup>, G. Griffiths<sup>2</sup>

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## ARTICLE INFO

## Article history:

Received 12 September 2018

## ABSTRACT

**Objectives:** The aim was to investigate if offering symptomatic therapy (Uva-ursi or ibuprofen) alongside a delayed prescription would relieve symptoms and reduce the consumption of antibiotics for adult

# Primary Care Infection Research

## Objectives:

To investigate if offering symptomatic therapy (Uva-Ursi or ibuprofen) alongside a delayed prescription would relieve symptoms and reduce the consumption of antibiotics for adult women presenting with acute uncomplicated UTI.

**Methods:** factorial design (randomised double-blind placebo controlled trial of Uva Ursi, and open pragmatic trial of advice/no advice to take ibuprofen)

## Conclusions:

1. No evidence of an effect of either intervention on the severity of frequency symptoms;
2. There is evidence that advice to take ibuprofen will reduce antibiotic consumption without increasing complications;
3. For seven women given this advice, one less will use antibiotics.

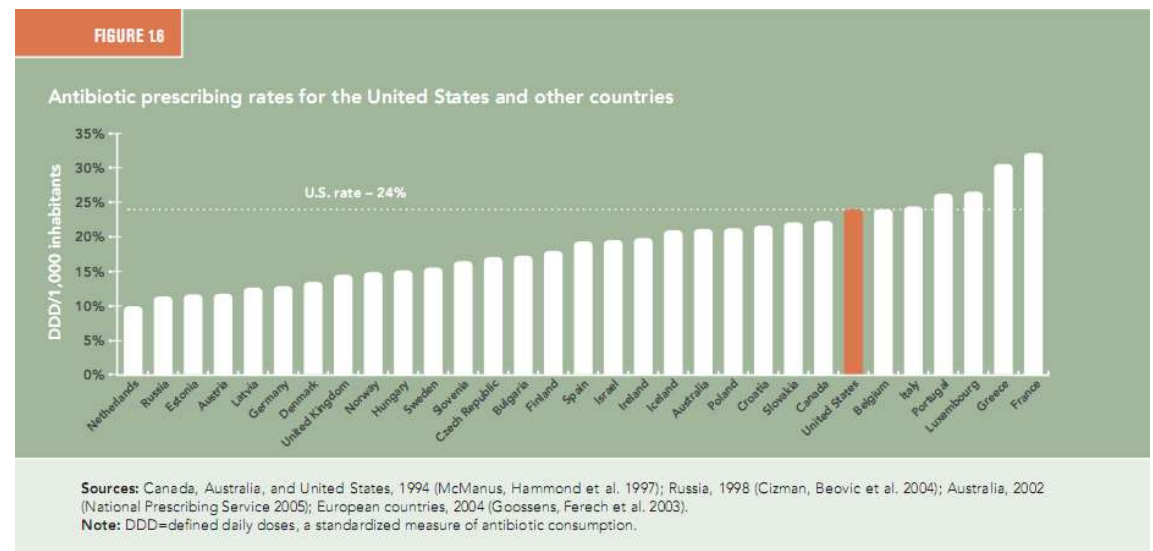
Uva Ursi extract not effective- important result as lots of women using this without prescription!



# Antibiotic prescription Rates

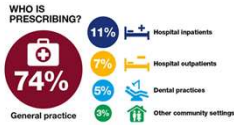
There is also large variations in **outpatient antibiotic prescriptions:**

- In the Netherlands, the level of prescriptions has traditionally been one of the lowest in Europe.
- In Germany and the UK, generally the prescription level is also relatively low.



Reference: The Center For Disease Dynamics, Economics & Policy

# Antibiotic prescription Rates



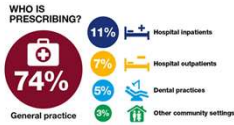
GPs as a professional group are **expected to react homogenously** to external demands, basing their prescription on objective measures and guidelines.

But **different views on medicalisation** and the use of traditional and complementary (TCM)/integrative medicine (IM) could result in variations in antibiotic prescribing.

The association between the use of TCM/IM by GPs and antibiotic prescribing has so far not been widely scrutinised.



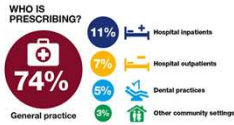
# Antibiotic prescription Rates



Is there a the differences in antibiotic prescription rates between ‘conventional GPs surgeries’ and GP surgeries employing GPs additionally trained in IM/TCM within NHS Primary Care in England?



# Antibiotic prescription Rates



**Design:** retrospective study on antibiotic prescription rates (measured as total antibiotics, respiratory tract infection (RTI) specific antibiotics and urinary tract infection (UTI) specific antibiotics) **per GP surgery**.

**Participants:** 7283 NHS GP surgeries in England

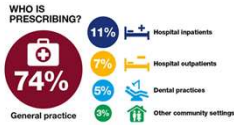
**TCM:** Chiropractic, osteopathy, acupuncture, herbal medicine and homeopathy and Anthroposophic Medicine

**IM GP surgeries:** IM GPs were identified and a current working link was made to an NHS General Practice

**Data:** Monthly prescribing data was obtained from NHS Digital\* (Jan 2016 – Dec 2016).



## Antibiotic Prescription rates



IM GPs (N=9) were **comparable** to conventional GPs in terms of list sizes, demographics, deprivation scores and comorbidity prevalence.

Patients consulting an IM GP surgery were **22% less likely to get 'any antibiotic' prescription** compared to those who consulted a conventional GP surgery.

Receiving a RTI specific antibiotic prescription was **26% less likely** among those who consulted an IM GP surgery compared with those who consulted a conventional GP surgery.

The number of antibiotics prescribed for **UTI were similar** between both practices (RR: 0.91, 95% CI: 0.72 – 1.17).





General practice / Family practice  
Research



## Do NHS GP surgeries employing GPs additionally trained in integrative or complementary medicine have lower antibiotic prescribing rates? Retrospective cross-sectional analysis of national primary care prescribing data in England in 2016

Esther T van der Werf<sup>1</sup>, Lorna J Duncan<sup>1</sup>, Paschen von Flotow<sup>2</sup>, Erik W Baars<sup>3, 4</sup>

Author affiliations +

### Abstract

**Objective** To determine differences in antibiotic prescription rates between conventional General Practice (GP) surgeries and GP surgeries employing general practitioners (GPs) additionally trained in integrative medicine (IM) or complementary and alternative medicine (CAM) (referred to as IM GPs) working within National Health Service (NHS) England.

**Design** Retrospective study on antibiotic prescription rates per STAR-PU (Specific Therapeutic group Age–sex weighting Related Prescribing Unit) using NHS Digital data over 2016. Publicly available data were used on prevalence of relevant comorbidities, demographics of patient populations and deprivation scores.

**Setting** Primary Care.

**Participants** 7283 NHS GP surgeries in England.

**Primary outcome measure** The association between IM GPs and antibiotic prescribing rates per STAR-PU with the number of antibiotic prescriptions (total, and for respiratory tract infection (RTI) and urinary tract infection (UTI) separately) as outcome.

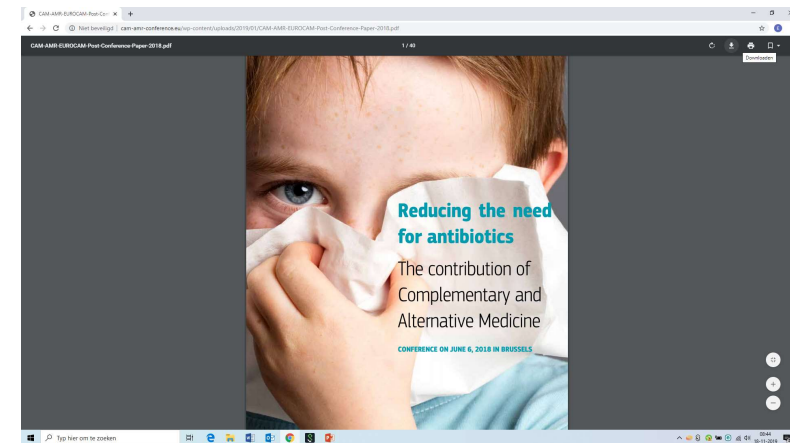
**Results** IM GP surgeries (n=9) were comparable to conventional GP surgeries in terms of list sizes, demographics, deprivation scores and comorbidity prevalence. Negative binomial regression models showed that statistically significant fewer total antibiotics (relative risk (RR) 0.78, 95% CI 0.64 to 0.97) and RTI antibiotics (RR 0.74, 95% CI 0.59 to 0.94) were prescribed at NHS IM GP surgeries compared with conventional NHS GP surgeries. In contrast, the number of antibiotics prescribed for UTI were similar between both practices.

**Conclusion** NHS England GP surgeries employing GPs additionally trained in IM/CAM have lower antibiotic prescribing rates.

# International network TCM & AMR

Dr. Klaus von Ammon, University of Bern, CAM center  
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Professor Dr. Philippe Hartemann, University of Lorraine  
Professor Dr. Roman Huber, University of Freiburg, Head of CAM center  
Dr. Josef Hummelsberger, International Society for TCM  
Professor Dr. David Martin, University of Tübingen  
Professor Dr. Harald Matthes, University Charité, Berlin, Head of Havelhöhe Clinic, Berlin, Hufelandgesellschaft  
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Dr. Esther van der Werf, Louis Bolk Institute, University of Bristol  
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Prof. Dr. Ursula Wolf, University of Bern, Head of CAM center

**Working group JPIAMR “Appropriate use of antibiotics: the role of CAM treatment strategies”**



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Evidence-Based Complementary and Alternative Medicine  
Volume 2019, Article ID 5365608, 29 pages  
<https://doi.org/10.1155/2019/5365608>

**Review Article**  
**The Contribution of Complementary and Alternative Medicine to Reduce Antibiotic Use: A Narrative Review of Health Concepts, Prevention, and Treatment Strategies**

Erik W. Baars<sup>1,2</sup>, Eefje Belt-van Zoen<sup>2</sup>, Thomas Breitkreuz<sup>3</sup>, David Martin<sup>4</sup>, Harald Matthes<sup>5</sup>, Tido von Schoen-Angerer<sup>6</sup>, Georg Soldner<sup>7</sup>, Jan Vagedes<sup>8</sup>, Herman van Wietmarschen<sup>1</sup>, Olga Patijn<sup>1</sup>, Merlin Willcox<sup>9</sup>, Paschen von Flotow<sup>10</sup>, Michael Teut<sup>5</sup>, Klaus von Ammon<sup>11</sup>, Madan Thangavelu<sup>12</sup>, Ursula Wolf<sup>11</sup>, Josef Hummelsberger<sup>13</sup>, Ton Nicolai<sup>14</sup>, Philippe Hartemann<sup>15</sup>, Henrik Szöke<sup>16</sup>, Michael McIntyre<sup>17</sup>, Esther T. van der Werf<sup>18,19</sup> and Roman Huber<sup>20</sup>

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Bestand Start Invoegen Ontwerpen Indeling Verwijzingen Verzendlijsten **Controleren** Beeld ACROBAT Geef aan wat u wilt doen... Esther van der Werf Delen

ABC Spelling- en grammaticacontrole  
ABC Synoniemenlijst  
ABC Aantal woorden

Slim opzoeken  
Inzichten

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Taal

Nieuwe opmerking  
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Opmerkingen

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Volgende

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Can complementary and alternative medicine treatment strategies control symptoms of uncomplicated acute RTIs and reduce antibiotic use? A systematic review of systematic reviews of observational studies and clinical trials

E.W. Baars<sup>1,2\*</sup>, E. Belt-Van Zoen<sup>1</sup>, X.-Y. Hu<sup>1</sup>, L. Lai<sup>1</sup>, M. Willcox<sup>1</sup>, R. Huber<sup>4</sup>, N. Roberts<sup>5</sup>, A. Huntley<sup>6</sup>, H. van Wietmarschen<sup>2</sup>, E.T. van der Werf<sup>6,7</sup>

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**Under Review**

Pagina 1 van 61 17100 woorden Nederlands (standaard)

Typ hier om te zoeken

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## Ongoing collaborative AMR projects Louis Bolk Institute

### Non-antibiotic treatment or prevention strategies

- Funding application multicentre randomised placebo controlled trial probiotics in women with recurrent urinary tract infections in the UK
- Funding application feasibility study honey cream and women with recurrent vaginal candidiasis infections in The Netherlands
- Systematic review of side effects on human microbiome of commonly used antibiotics in primary care
- Update of a systematic review and patient group on probiotics use and optimal probiotics for a trial.
- Introduction of E-bug in Dutch primary school education (implementation and evaluation)





## Take home message

### Reduction of antibiotic use – **Why?**

1. AMR
2. Short- and long term health effects (microbiome)

### Integrative Medicine- **What?**

- Combines conventional medicine and TCM
- Evidence based and safe

### Solving AMR in Primary care- **How?**

- A switch from **inappropriate antibiotic use to appropriate use of Integrative Medicine** for common primary care infections could help solving the problem of AMR in primary care.

# Thank you for your attention!

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Head of Department Health & Nutrition  
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