Welcome GRINNERS!

A warm welcome to the 18th (we think that's accurate) GRIN conference in Oxford. There has been scholarship on this site for almost a thousand years. Penicillin was first given to a human in Oxford and cephalosporin was discovered here. GRIN is a modern-day jewel in the crown of this tradition!

A lot of water has flowed under Balls Bridge since far-sighted people like Theo Verheij, An de Sutter, Ian Williamson and other giants in our field got together in Dublin in 1998 to establish GRIN. Since then, GRIN has met in many of the great cities of Europe, and brought more and more people into collaborations: there are over 100 delegates to this meeting. GRIN has broadened its scope beyond the respiratory tract to include all primary care infections. GRIN stands out as a monument to pan European International collaborative research to address key issues that do not respect national boundaries. The program is much enriched now e.g. by major studies on urinary tract infections as well as skin and soft tissue infections. Diagnostics and viral infections have also become major themes. Furthermore, we have grown in rigor: in rating abstracts, we were just amazed by the stratospheric quality of the submissions. And all this has been achieved through an informal 'collective' rather than a formal committee structure.

GRIN has always been known for its friendly, supportive atmosphere. Was it not at our Oslo meeting when Morten Lindbaek coined the immortal phrase, the "GRIN Family"? And we are like a family: we support, work brilliantly together, and encourage each other, which has led to stellar national and international collaborations. We don't always agree, but somehow manage to argue in the finest spirit of constructive academic discourse; I can't think of anyone being sent to the naughty step at GRIN!

It's a particular pleasure to welcome Ben Goldacre, the legendary 'Bad Science' guy, who has done so much to raise consciousness of rigor in research among researchers, clinicians and the public: we keenly anticipate hearing more about the implications for infections research in primary care.

Many thanks to all who have helped make this Conference happen; Linnemore Jantjes, Emma Butterfield and Dan Richards-Doran have done a tremendous organisational and communications job. We thank Lady Margaret Hall for hosting us. We are deeply grateful too for the support we have received from the Translational Research on Antimicrobial resistance and Community-acquired infections in Europe (TRACE), and from the University of Oxford's Nuffield Department of Primary Care Health Sciences.

Enjoy the science, the friendship, the collaborations, the setting, the history and the traditions of GRIN 2016!

THE 2016 GRIN COMMITEE

Chris Butler
Emma Butterfield
Dan Richards-Doran
Gail Hayward
Oliver van Hecke
Linnemore Jantjes
Sarah Tonkin-Crine
Jan Verbakel
Kay Wang

Friday 30th September

08:15-08:45 **Registration** (Simpkins Lee Theatre/Monson Room)

08:45-09:00 **Welcome to Oxford/University by Chris Butler** (Simpkins Lee Theatre)

09:00-10:00 **Session 1:** UTI (Simpkins Lee Theatre)

Chair: Jochen Cals

1. DUTY-PCAAR: retrospective cohort study investigating the prevalence of, and risk factors for, resistance in paediatric urinary bacteria - a follow-up to the DUTY study | Abstract: p.16

Ashley Bryce, Ceire Costelloe, Mandy Wootton, Chris Butler, Alastair Hay

2. What clinicians want from decision aids for children with urinary tract infections (UTI): implications for antibiotic prescribing interventions | Abstract: p.17

Christie Cabral, Rohini Terry, Harriet Downing, Alastair Hay

3. Uropathogen distribution and antimicrobial susceptibility in uncomplicated cystitis in a high antibiotics prescribing country: results of three observational studies over the past 20 years | Abstract: p.18

Stefan Heytens, An De Sutter, Thierry Christiaens, Jerina Boelens, Geert Claeys

4. What do women with symptoms of cystitis but a negative urine culture have? PCR based quantification of *Escherichia coli* indicates that they have an infection after all | Abstract: p.19

Stefan Heytens, An De Sutter, Liselotte Coorevits, Piet Cools, Jerina Boelens, Mario Vaneechoutte, Thierry Christiaens, Leen Van Simaey, Geert Claeys

09:00-10:00 **Session 2:** Methods (Monson Room)

Chair: Anthony Harnden

1. Comparison between treatment effects in a trial versus an observational study: the example of the GRACE study | Abstract: p.20

Beth Stuart, Louise Grebel, Christopher Butler, Kerenza Hood, Theo Verheij, Paul Little

2. Educating parents about childhood fever and common infections in well-child clinics. Does it lead to reductions in physician consultations and improve medication management? A systematic review | Abstract: p.21

Kirsten Peetoom, Jacqueline Smits, Luc Ploum, Jan Verbakel, Geert-Jan Dinant, Jochen Cals

3. (Cost)-effectiveness of Antivirals for Influenza-like-illness in primary care: Set-up and progress of the ALIC4E trial in 17 European Countries | Abstract: p.22

Alike van der Velden, Johanna Cook, Theo Verheij, Christopher Butler

4. Global illness severity assessment and determinants for children presenting to primary care with cough and RTI: do parents and clinicians agree? | Abstract: p.23

Esther T van der Werf-Kok, Niamh N Redmond, Sophie Turnbull, Hannah Christensen, Hannah Thornton, Peter S Blair, Brendan Delaney, Matthew Thompson, Paul Little, Alastair D Hay

10:00-10:20 **Tea/Coffee Break with Posters** (Denke Dining Hall)

Poster abstracts pp.88–92

10:20-11:20 **Session 3:** Diagnosis/Prognosis (Simpkins Lee Theatre)

Chair: Annelies Colliers

1. Are we fair to the adventitious lung sounds in our research? | Abstract: p.24

Hasse Melbye

2. Complications and new visits after pharyngotonsillitis in relation to etiology: a prospective two-year follow-up | Abstract: p.25

Jon Pallon, Martin Sundqvist, Katarina Hedin

3. A Systematic Review of the Clinical Diagnosis of Bordetella Pertussis | Abstract: p.26

Mark Ebell, Christian Marchello, Maria Callahan

4. Investigating symptom trajectories in children presenting to primary care with acute cough and respiratory tract infection: analysis of the 'TARGET' prospective cohort study | Abstract: p.27

Alastair Hay, Knut-Arne Wensaas, Niamh Redmond, Sophie Turnbull, Hannah Christensen, Hannah Thornton, Tim Peters, Peter Blair, Jon Heron

10:20-11:20 **Session 4:** Prescribing (Monson Room)

Chair: An de Sutter

1. Clinical indications for antibiotic use. First data from a nationwide electronic prescription database in Danish General Practice | Abstract: p.28

Rune Aabenhus, Malene Hansen, Laura Saust, Lars Bjerrum

2. Comparison of Out-of-hours and Office hours Antibiotic Prescribing Quantity and Quality in Primary Care | Abstract: p.29

Alike van der Velden, Vera Debets, Theo Verheij

3. Patterns in antibiotic dispensing by non-medical prescribers in primary care across England: A retrospective analysis of data collected routinely between 2011 and 2015 | Abstract: p.30

Molly Courtenay, David Gillespie, Rosemary Lim

4. Paediatric antibiotic prescriptions in primary care in the Alpes Maritimes area of Southeastern France between 2008 and 2013 | Abstract: p31

Pia Touboul, Pascale Bruno, Brigitte Dunais, Christian Pradier

11:20-12:20 **Session 5:** Stewardship (Simpkins Lee Theatre)

Chair: Margaretha Minnaard

1. General Practitioners' views on the acceptability of using quality indicators to reduce unnecessary prescription of antibiotics in South-America | Abstract: p.32

Gloria Cordoba, Nieves Hernandez, Sandi Oliveira, Lidia Caballero, Miguel Suarez, Monica Olinisky, Luis Roushel, Marjukka Makela, Lars Bjerrum

2. An antibiotic stewardship gap? Exploring the views of A&E clinicians on antibiotic prescribing for children with fever | Abstract: p.33

Sarah Tonkin-Crine, Sarah Walker, Shelley Segal, Mike Sharland, Derrick Crook, Chris Butler

3. Beat The Bugs: An educational programme on hygiene, antibiotics and self-care for the community setting | Abstract: p.34

Vicki Young, Katie Tucker, Gill Parkinson, Nick Francis, Cliodna McNulty

4. A modified McNulty-Zelen design randomised controlled trial to evaluate the TARGET Antibiotics toolkit (Treat Antibiotics Responsibly, Guidance, Education, Tools) and its implementation | Abstract: p.35

Cliodna McNulty, Meredith Hawking, Leah Jones, Rebecca Owens, Nick Francis, Chris Butler, Philippa Moore, Andre Charlett, Donna Lecky

11:20-12:20 **Session 6:** Flu (Monson Room)

Chair: An de Sutter

1. A systematic review and decision analytic model on the early use of antibiotics for ‘at risk' children with influenza in primary care (ARCHIE) | Abstract: p.36

Jane Wolstenholme, Kay Wang, Lucy Abel, Danielle Bargo, Anthony Harnden

2. Risk factors for influenza-related complications in children | Abstract: p.37

Joseph J. Lee, Clare Bankhead, Margaret Smith, Antonis A. Kousoulis, Christopher Butler, Kay Wang

3. Barriers to the uptake of influenza vaccination in children under the age of 5 - primary care providers' and parents' perspectives | Abstract: p.38

Ruby Biezen, Danilla Grando, Bianca Brijnath, Danielle Mazza

4. Influenza epidemic surveillance and prediction based on electronic health record data from an out-of-hours general practitioner cooperative: model development and validation on 2003-2015 data | Abstract: p.39

Barbara Michiels, Kinh Nguyen Van, Samuel Coenen, Philippe Ryckebosch, Nathalie Bossuyt, Niel Hens

12:20-13:20 **Lunch (Denke Dining Hall)**

13:20-14:00 **Keynote Speaker:** Ben Goldacre (Simpkins Lee Theatre)

Chair: Chris Butler

14:00-15:00 **Session 7:** Prevention (Simpkins Lee Theatre)

Chair: Nick Francis

1. Investigating the relationship between vaccine status and the presence of respiratory microbes in children attending primary care | Abstract: p.40

Georgina Taylor, Hannah Christensen, Niamh Redmond, Hannah Thornton, Sophie Turnbull, John Leeming, Andrew Lovering, Barry Vipond, Peter Muir, Peter Blair, Tim Peters, Alastair Hay

2. What are the effects of providing real-time data on locally circulating microbes on clinician management of common infections in primary care? A systematic review | Abstract: p.41

Isabel Lane, Ashley Bryce, Suzanne Ingle, Alastair Hay

3. Colonisation rates of and risk factors for extended-spectrum beta-lactamase producing coliforms (ESBLPCs), and carbapenamase producing Enterobactericaeae (CPE), in different sections of the asymptomatic general population in England | Abstract: p.42

Cliodna McNulty, Donna Lecky, Li Xu, Deborah Ssenabulya, Keun-Taik Chung, Tom Nichols, Adela Bullya, Kim Turner, Sahida Shabir, Susan Manzoor, Lucy Thomas, Mike Thomas, Stephen Smith, Linda Crocker, Rebecca Owens, Peter Hawkey

4. An internet-delivered handwashing intervention to modify respiratory infection transmission (PRIMIT): sub-group analysis of potential high risk groups | Abstract: p.43

Beth Stuart, Paul Little, Michael Moore, Richard Hobbs, Judy Joseph, Sasha Miller, Lucy Yardley

14:00-15:00 **Session 8:** RTI in Children (Monson Room)

Chair: Morten Lindbaek

1. Paediatric respiratory tract infection surveillance: a community-based feasibility inception cohort study | Abstract: p.44

Emma Anderson, Suzanne Ingle, Peter Muir, Charles Beck, Adam Finn, John Leeming, Christie Cabral, Alastair Hay

2. Parent and child experiences and views of a paediatric respiratory tract infection (RTI) community surveillance feasibility study: a qualitative study to inform future research | Abstract: p.45

Joanna Kesten, Emma Anderson, Isabel Lane, Suzanne Audrey, Alastair Hay, Christie Cabral

3. Real-time paediatric respiratory tract infection (RTI) community surveillance: A qualitative interview study of clinicians' perspectives on the use, design and potential impact of a planned intervention | Abstract: p.46

Emma Anderson, Isabel Lane, Joanna Kesten, Alastair Hay, Timothy Moss, Christie Cabral

4. Paracetamol (acetaminophen) or non-steroidal anti-inflammatory drugs, alone or combined for pain relief in children with acute otitis media: a Cochrane review | Abstract: p.47

Alies Sjoukes, Roderick P. Venekamp, Alma C. Van de Pol, Alastair D. Hay, Paul Little[4], Anne G.M. Schilder, Roger A.M.J. Damoiseaux

15:00-15:20 **Tea/Coffee Break with Posters** (Denke Dining Hall)

Poster abstracts pp.88–92

15:20-16:20 **Session 9:** UTI (Simpkins Lee Theatre)

Chair: Gail Hayward

1. Bacteriological findings in uncomplicated urinary tract infections: current status, developing resistance and future situation | Abstract: p.48

Ingvild Vik, Marianne Bollestad, Nils Grude, Morten Lindbæk

2. Protocol for clinical trial: “Randomized clinical trial comparing fosfomycin vs. nitrofurantoin for treatment of uncomplicated lower urinary tract infection in female adults at increased risk of antibiotic-resistant bacterial infection, AIDA”. | Abstract: p.49

Anna Kowalczyk, Stephan Harbarth, Angela Huttner, Leonard Leibovici, Johan Mouton, Johan Mouton, Maciek Godycki-Cwirko

3. The development of a "TARGET antibiotics" UTI leaflet to improve communication in GP consultation around the diagnosis and management of urinary symptoms and UTIs with patients. Increasing self-care and reducing antibiotic use, bacteraemia and recurrence | Abstract: p.50

Donna Lecky, Jessica Thomas, Cliodna McNulty

4. Effect of a diagnostic algorithm for urinary tract infection in general practice on appropriate use of antibiotics and costs- a cluster randomized trial | Abstract: p.51

Anne Holm, Lars Bjerrum, Gloria Cordoba

15:20-16:20 **Session 10:** Point-Of-Care Testing (Monson Room)

Chair: Kerry Hood

1. Should all acutely ill children in primary care be tested with point-of-care CRP: a cluster randomised trial | Abstract: p.52

Jan Verbakel, Marieke Lemiengre, Tine De Burghgraeve, An De Sutter, Bert Aertgeerts, Bethany Shinkins, Rafael Perera, David Mant, Ann Van den Bruel, Frank Buntinx

2. Point-of-care CRP matters: low CRP values substantially improve immediate antibiotic prescribing in acutely ill children in primary care | Abstract: p.53

Marieke Lemiengre, Jan Verbakel, Kaat Van Roy, Tine De Burghgraeve, Bert Aertgeerts, Frans De Baets, Frank Buntinx, An De Sutter

3. Associations between throat swab microbiology and clinical outcome in children presenting to primary care with respiratory tract infection: results from the NIHR 'TARGET' Cohort Study | Abstract: p.54

Hannah V Thornton, Peter S Blair, Niamh M Redmond, Sophie L Turnbull, Hannah Christensen, Tim J Peters, John Leeming, Andrew Lovering, Barry Vipond, Peter Muir, Alastair Hay

4. Supporting antibiotic prescribing decisions for diabetic foot ulcer: an investigation of the diagnostic accuracy of inflammatory biomarkers (INDUCE study) | Abstract: p.55

Nick Francis, John Ingram, Scott Cawley, Elinor Coulman, Kerenza Hood, Clive Gregory, Emma Thomas-Jones, Tim Pickles, Vincent Piguet

16:20-17:20 **Session 11:** Stewardship (Simpkins Lee Theatre)

Chair: Gail Hayward

1. Self-assessment of antimicrobial stewardship in primary care: analysis of self-reported practice using the TARGET Primary Care Self-Assessment Tool | Abstract: p.56

Leah Jones, Rebecca Owens, Meredith Hawking, Michael Moore, Dirk Pilat, Donna Lecky, Cliodna McNulty

2. A feasibility cluster randomised controlled trial of a complex intervention to reduce antibiotic prescribing in children presenting to primary care with acute respiratory tract infection and cough; results from the CHICO trial | Abstract: p.57

Niamh M Redmond, Sophie Turnbull, Patricia Lucas, Christie Cabral, Jeremy Horwood, Jenny Ingram, Padraig Dixon, Sandra Hollinghurst, Tim J Peters, Nick Francis, Alastair D Hay, Peter S Blair

3. Investigating cultural determinants for antibiotics prescribing and consumption in Europe | Abstract: p.58

Siri Jensen, Pia Touboule-Lundgren, Maicek Godycki-Cwirko, Morten Lindbæk

4. Continuing professional development concerning AMR for teachers in Europe | Abstract: p.59

Pia Touboul Lundgren, Rebecca Robbemond

16:20-17:20 **Session 12:** Diagnosis/Prognosis (Monson Room)

Chair: Kerry Hood

1. Clinical decision rules to diagnose acute rhinosinusitis among adults in primary care | Abstract: p.60

Mark Ebell, Jens Hansen

2. Disease course of lower respiratory tract infection with a bacterial aetiology in primary care | Abstract: p.61

Jolien Teepe, Lidewij Broekhuizen, Katherine Loens, Christine Lammens, Margareta Ieven, Herman Goossens, Paul Little, Chris Butler, Samuel Coenen, Maciek Godycki-Cwirko, Theo Verheij

3. Predicting poor prognosis in adults presenting to primary care with acute cough | Abstract: p.62

Robin Bruyndonckx, Niel Hens, Marc Aerts, Margareta Ieven, Chris C. Butler, Paul Little, Theo Verheij, Herman Goossens, Samuel Coenen

4. Predicting pneumonia in primary care: The 3C cohort study of lower respiratory tract infection in primary care | Abstract: p.64

Michael Moore, Beth Stuart, Paul Little, Mark Lown, Sue Smith, Kyle Knox, Matthew Thompson, David Mant

17:30 **Meet for guided walking tour around Oxford**

Lead: Helen Ashdown

Please meet at LMH Porters Lodge if you would like to attend the walking tour

19:00-19:30 **Drinks Reception** (Talbot Hall)

19:30 **Dinner** (Deneke Dining Hall)

Saturday 1st October

09:00-10:00 **Session 13:** Prescribing (Simpkins Lee Theatre)

Chair: Theo Verheij

1. Do general practitioners (GPs) prescribe more anti-bacterials for acute respiratory tract infections (ARTIs) on Fridays than on other days of the week? A retrospective cohort study from Norway | Abstract: p.65

Håkon Lerstad, Svein Gjelstad, Morten Lindbaek

2. Investigating the effect of suboptimal antibiotic prescribing in primary care for patients with a UTI or community-acquired pneumonia on hospital admission due to a bloodstream infection | Abstract: p.66

Hannah Lishman, Ceire Costelloe, Myriam Gharbi, Mariam Molokhia, Alan Johnson, Paul Aylin

3. Adverse events in patients taking macrolide antibiotics for any indication | Abstract: p.67

Malene Plejdrup Hansen, Amanda McCullough, Sarah Thorning, Jeffrey Aronson, Elaine Beller, Paul Glasziou, Tammy Hoffmann, Justin Clark, Chris Del Mar

4. Antibiotics for acute respiratory tract infections: A mixed methods study of patient experiences of non-medical prescriber management | Abstract: p.68

Molly Courtenay, Samantha Rowbotham, Rosemary Lim, Rhian Deslandes, Karen Hodson, Katie Maclure, Sarah Peters, Derek Stewart

09:00-09:45 **Session 14:** Stewardship (Monson Room)

Chair: Alike van der Velden

1. Taking steps: Country Dialogue Meetings to formulate national action plans to stimulate a more prudent use of antibiotics | Abstract: p.69

Dominique Lescure, John Paget, Francois Schellevis, Ann Versporten, Herman Goossens, Liset van Dijk

2. Long-term effect of a practice-based intervention aimed at improving antibiotic prescribing in patients with respiratory tract infections | Abstract: p.70

Carl Llor, Ana Moragas, Beatriz Gonzalez Lopez-Valcarcel, Lars Bjerrum

3. An illness-focussed interactive booklet to optimise management and medication for childhood fever and common infections in out-of-hours primary care: a cluster randomised trial | Abstract: p.71

Eefje G.P.M. de Bont, Geert-Jan Dinant, Gijs Elshout, Gijs van Well, Nick A. Francis, Bjorn Winkens, Jochen W.L. Cals

10:00-10:50 **Session 15:** Budding Ideas (Simpkins Lee Theatre)

Chair: Paul Little

1. Prescribing antibiotics in general practice: The use of microbiological testing and other factors influencing decision-making and prescribing behaviour | Abstract: p.72

Rikke Vognbjerg Sydenham, Malene Plejdrup Hansen, Line Bjørnskov Pedersen, René dePont Christensen, Dorte Ejg Jarbøl

2. The clinical and cost-effectiveness of spironolactone versus lymecycline for moderate or severe persistent acne in adult women: proposal for a multicentre parallel-arm randomised controlled trial | Abstract: p.73

Miriam Santer, Nick Francis, Matthew Ridd, Ingrid Muller, Alison Layton, Beth Stuart, Paul Little

3. Comparison of guidelines on acute sore throat | Abstract: p.74

Jan Matthys

4. Will routinely collected data [RCD] ever surpass self-report? Using routine data for infections research | Abstract: p.75

Fiona Lugg

5. Intervention on promoting prudent antibiotic use in long term care facilities, a cluster-randomised trial, using a stepped wedge model | Abstract: p.76

Nicolay Harbin, Hege Salvesen Blix, Jon Birger Haug, Morten Lindbæk

6. Increase in antibiotic prescriptions in Out of Hours primary care in contrast to in-hours primary care prescriptions: service evaluation in a population of 600,000 patients | Abstract: p.77

Gail Hayward, Rebecca Fisher, Graeme Spence, Daniel Lasserson

7. An audit of the treatment of female urinary tract infections in a General Practice using the electronic health record | Abstract: p.78

Francis Collett-White, Gwyneth Rogers

10:50-11:00 **TRACE Update** (Simpkins Lee Theatre)

A ten minute TRACE e-learning to disseminate GRACE results to primary care clinicians | Abstract: p.79

Veronique Nussenblatt, Sibyl Anthierens, Sarah Tonkin-Crine, Jochen Cals, Niels Adriaenssens, Katelijn Nijsmans, Nick Francis, Theo Verheij, Chris Butler, Paul Little, Herman Goossens, Samuel Coenen on behalf of the TRACE project group

11:00-11:20 **Tea/Coffee Break with Posters** (Denke Dining Hall)

Poster abstracts pp.88–92

11:20-12:20 **Session 16:** UTI (Simpkins Lee Theatre)

Chair: Ann van den Bruel

1. The Point Of carE testing for urinary Tract Infection in primary Care (POETIC) study (Stage 4): A qualitative study to explore the barriers and benefits of using a POCT to aid the management of uncomplicated UTI in primary care | Abstract: p.80

Khurram Hashmi, Emma Thomas-Jones, Lucy Brookes Howell, Nick Francis, Paul Little, Michael Moore, Carl Llor, Janine Bates, Kerry Hood, Theo Verheij, Chris Butler

2. Use of methenamine as preventive treatment in women with recurrent urinary tract infections. Is it effective? | Abstract: p.81

Linda Rui, Morten Lindbaek, Svein Gjelstad

3. Ibuprofen versus mecillinam for uncomplicated cystitis in women - a double blind randomized trial | Abstract: p.82

Ingvild Vik, Marianne Bollestad, Nils Grude, Anders Bærheim, Sigvard Mölstad, Lars Bjerrum, Morten Lindbæk

4. Clinical and bacteriological effects of per oral pivmecillinam on uncomplicated cystitis caused by ESBL producing *E. coli*: a clinical controlled trial | Abstract: p.83

Marianne Bollestad, Nils Grude, Morten Lindbæk

11:20-12:20 **Session 17:** Diagnosis/Prognosis (Monson Room)

Chair: Hasse Melbye

1. Predicting adverse outcome from lower respiratory tract infection in primary care: The 3C cohort study of LRTI in primary care | Abstract: p.84

Michael Moore, Beth Stuart, Paul Little, Mark Lown, Sue Smith, Kyle Knox, Matthew Thompson, David Mant

2. The impact of an immediate or delayed antibiotic prescription on re-consultations, hospital admission and death for lower respiratory tract infections: 3C cohort study in UK primary care | Abstract: p.85

Paul Little, Beth Stuart, Sue Smith, Matthew Thompson, Kyle Knox, Ann Van Den Bruel, Mark Lown, Michael Moore, David Mant

3. Management of sepsis in out-of-hours primary care: a retrospective study of patients admitted to the intensive care unit | Abstract: p.86

Feike Loots, Marleen Smits, Carlijn van Steensel, Rogier Hopstaken, Paul Giesen, Arthur R.H. van Zanten

4. Association between antibiotic class and recovery from symptoms of uncomplicated urinary tract infection (UTI) | Abstract: p.87

Mandy Lau, David Gillespie, Kerenza Hood, Janine Bates, Nick Francis, Nigel Kirby, Paul Little, Carl Llor, Michael Moore, Timothy Pickles, Emma Thomas-Jones, Theo Verheij, Christopher Butler

12:20-12:30 **Date and venue of next conference**

12:30 **Lunch (Deneke Dining Hall)**

Delegate List

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Session 1: UTI

1. **DUTY-PCAAR: retrospective cohort study investigating the prevalence of, and risk factors for, resistance in paediatric urinary bacteria - a follow-up to the DUTY study**

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Objectives

Bacterial resistance to antibiotics is an internationally recognised health threat, particularly in primary care where 80% of antibiotics are prescribed. Children are high frequency recipients of primary care services, and as such receive disproportionately high numbers of antibiotics compared to middle-age populations. Currently, there is limited knowledge around the prevalence of resistant bacteria in children, and even less known about risk factors associated with resistance. This study aims to explore the prevalence of resistance to common primary care prescribed antibiotics in children's urinary bacteria, and identify risk factors associated with resistance, including the relationship between previous antibiotic exposure and resistance.

Method

DUTY-PCAAR was a follow-up to the DUTY study. Children were aged between 0-5 years presenting to primary care across England and Wales with acute illness. *Escherichia coli* urinary isolates were obtained from a subset of DUTY children's urine samples and antimicrobial susceptibility testing was conducted. Risk factor information was collected including demographics, symptoms, medical history and previous exposure to antibiotics. Logistic regression analysis was used to obtain crude and adjusted odds ratios.

Results

Antimicrobial sensitivities were obtained for 824 *E. coli* urinary isolates, 79 were laboratory-diagnosed UTI and 745 non-laboratory-diagnosed UTI. Resistance was highest against amoxicillin (38.5%), co-amoxiclav (21.0%) and trimethoprim (17.6%). No isolates were nitrofurantoin-resistant. Children with a UTI were more than twice as likely to carry a resistant *E. coli* isolate as those without a UTI (aOR: 2.36, 1.26-4.48). There was no association between being prescribed an antibiotic in the 12 months prior to urine sampling and resistance.

Conclusions

Prevalence of resistance to several common primary care prescribed antibiotics in children's *E. coli* isolates is high. Being prescribed an antibiotic did not appear to increase the likelihood of resistance in children's urinary *E. coli*. There is a need for prescribing guidelines to reflect local resistance patterns to prolong their effectiveness as first-line treatments.

2. **What clinicians want from decision aids for children with urinary tract infections (UTI): implications for antibiotic prescribing interventions**

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Objectives

The Diagnosis of Urinary Tract infection in Young children (DUTY) study produced a clinical decision rule to support the diagnosis of UTI in pre-school children. Clinical decision aids can be difficult to integrate into practice and GPs are coming under increasing pressure to reduce antibiotic prescribing. This qualitative study investigated the credibility and acceptability of the DUTY decision aid and evaluated how it might be used in practice.

Method

We recruited 24 clinicians (GPs and nurses) from primary care sites. Sites were located in urban and rural areas with different levels of deprivation. Clinicians were sent a schema of the DUTY decision rule and out study information sheet in advance of the interviews. Most interviews were conducted by telephone, with one face to face interview. The interviews covered normal management of UTI in children, views of the DUTY decision rule and facilitators and barriers to use of the rule. Interviews were audio-recorded, transcribed and analysed thematically.

Results

Clear themes emerged regarding the desired characteristics of decision rules. Clinicians wanted the decision aid to be:1) safe - they wanted to be sure that focussing to those few was a clinically safe course of action; 2) credible - they questioned the symptoms and signs that were included and excluded from the rule; 3) timely and quick - it was going to fit into a normal consultation and not add time unnecessarily; 4) valid and useful - it would help with children about whose management the clinician feels uncertainty; 5) support their sense of professional judgement and clinical autonomy.

Conclusions

When designing interventions and decision support aids, researchers need to take account not just of the immediate requirements for safety and speed, but also ensure the intervention can support clinical decision-making while respecting normal practice, clinical judgement and self-perception.

3. Uropathogen distribution and antimicrobial susceptibility in uncomplicated cystitis in a high antibiotics prescribing country: results of three observational studies over the past 20 years.

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Objectives

Empirical treatment of cystitis in primary care is guided by susceptibility data of regional microbiological laboratories, often derived from urine samples of complicated urinary tract infections (UTI) and therefore not representative for uncomplicated cystitis. To re-evaluate empirical treatment guidelines the actual distribution of uropathogens and their susceptibility patterns were examined and compared with two previous surveys in Belgium over the past 20 years. Because of the alarming increase in carriage of extended beta-lactamase (ESBL) and carbapenemase producing *E. coli*, this specific resistance was explored.

Method

From May 2014 to December 2015, 120 general practitioners (GP's) in 30 practices in the Ghent region collected midstream urine specimens from adult pre- and postmenopausal female patients with suspected cystitis. According to the European Federation for Urinalysis Guidelines (2001), significant bacteriuria was defined as > 10^3 cfu/mL for primary uropathogens (*E. coli* and *S. saprophyticus*) and > 10^4 cfu/mL for secondary uropathogens (mainly other gram negative rods and Enterococcus spp.). The presence of ESBL's and carbapenemases was tested on enterobacteriaceae in urine and faeces.

Results

Two hundred and fifty six patients were enrolled. Two hundred and three women (79.3%) had a positive culture. *E. coli* (81.6%) was the most frequent isolated uropathogen, followed by *S. saprophyticus* (8%). The distribution was nearly identical to 1995 and 2005. The susceptibility of *E. coli* remained 100% for nitrofurantoin and fosfomycin, decreased from nearly 100% in 1995 to 94.2%% for quinolones, from 73.2% to 55.5% for ampicillin, from 83.3% to 76.3% for trimethoprim-sulfamethoxazole (TMP-MSX). ESBL's were found in 2.5% of the positive urine cultures and in 7.9% of the rectal swab specimens. Carbapenemases were not detected.

Conclusions

Over a 20 year period the distribution of uropathogens in women with cystitis remained unchanged. The susceptibility of *E.coli* remained excellent for nitrofurantoin and fosfomycin. For TMP-SMX, ampicillin and quinolones there was a decrease. The recommendation of nitrofurantoin and fosfomycin as empirical first choice antimicrobials can be maintained. Whether TMP can still be recommended is dependent from local surveillance data.Faecal carriage rate of ESBL is similar to recent data from Western Europe, but is not reflected in urinary isolates. ESBL-production seems not linked to uropathogenic potential.

4. What do women with symptoms of cystitis but a negative urine culture have? PCR based quantification of *Escherichia coli* indicates that they have an infection after all.

Stefan Heytens[1], An De Sutter[1], Liselotte Coorevits[2], Piet Cools[2], Jerina Boelens[2], Mario Vaneechoutte[2], Thierry Christiaens[3], Leen Van Simaey[2], Geert Claeys[2]
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Objectives

Dysuria in women represents 2-5% of the reason for encounter in general practice. Although typical urinary symptoms are considered to have a high predictive value for a urinary tract infection in primary care, still 20 to 30% of these women have a negative culture, even with lower thresholds Richards showed that antibiotic treatment had an effect on the symptoms in culture negative women. To contribute to a better understanding of this anomaly in symptomatic women, we used the quantitative polymerase chain reaction technique (qPCR) to quantify *E. coli* in their urine samples.

Method

Between May 2014 and December 2015 two hundred and twenty women with dysuria and/or frequency and/or urgency were enrolled in the study. Between August and September 2016 eighty six women without symptoms of a cystitis were recruited in non-clinical departments of the Ghent University Hospital campus. Both culture and qPCR were performed on urine samples of the symptomatic and asymptomatic group.

Results

Of the symptomatic women 78.6% was culture positive (> 10^3 cfu/mL for *E. coli* and *S. saprophyticus*) while qPCR for *E. coli* was positive in 90.9% (> 10^3 cfu/mL). In the asymptomatic group culture and qPCR for *E. coli* was positive in 4.7% of the samples, taking into account a cut-off for asymptomatic bacteriuria of > 10^5 cfu/mL, although it is not know if these thresholds, used for bacterial culture techniques, can be applied to qPCR results.qPCR for *Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium* (MG) and *Trichomonas vaginalis* (TV) yielded one positive sample for TV and one for MG.

Conclusions

In nearly 91% of all symptomatic women *E. coli* can be found with qPCR while in asymptomatic women qPCR remains negative, except for the normal rate of asymptomatic bacteriuria. Symptoms in women with a negative culture cannot be explained by the presence of a sexual transmitting disease nor by an infection by other bacteria as extended quantitative urine culture results in finding different organisms that are also detected in asymptomatic women. This strongly suggests that women consulting with typical urinary complaints do have an infection with *E. coli*, regardless the result of the culture.

Session 2: Methods

1. **Comparison between treatment effects in a trial versus an observational study: the example of the GRACE study**

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Objectives

Although randomized controlled trials are considered the “gold standard” evidence, they are not always feasible or desirable appropriate and may represent a select population. Observational studies provide a useful alternative design to enhance applicability, but the results can be biased due to confounding. This study aimed to compare the effect of amoxicillin on symptom duration and symptom severity in an international trial and an observational study of lower respiratory tract infections using propensity score methods to control for confounding by indication in the observational data.

Method

Propensity scores were calculated and applied as probability weights in the analyses. The adjusted results were compared to the effects previously reported in the randomized controlled trial.

Results

Groups were well balanced in the RCT whilst there was significant imbalance in the observational study, with evidence of confounding by indication; patients receiving antibiotics tended to be older and more unwell at baseline. In the trial duration of symptoms (hazard ratio 1.06, 95% CI 0.96 - 1.18) and symptoms severity (mean difference -0.07, 95% CI -0.15, 0.007) did not differ between groups. Weighting by propensity score in the observational study resulted in essentially the same hazard ratios for duration of symptoms (1.06, 95% CI 0.80-1.40) and same difference for symptom severity (-0.07, 95% CI -0.34- 0.20)

Conclusions

Although randomized controlled trials are considered the “gold standard” evidence, they are not always feasible or desirable appropriate and may represent a select population. Observational studies provide a useful alternative design to enhance applicability, but the results can be biased due to confounding.

2. **Educating parents about childhood fever and common infections in well-child clinics. Does it lead to reductions in physician consultations and improve medication management? A systematic review.**

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Objectives

Childhood fever is common in children 0 to 4 years and often leads to anxiety in parents and subsequently physician consultations, while most childhood infections are self-limiting and do not require treatment. A lack of parental knowledge regarding pathophysiology and fever management is an important cause of this fever anxiety. Educating parent in well-child clinics, prior to illness episodes, may better prepare parents, reduce anxiety and ultimately healthcare use and costs. Our study systematically reviews the effect of educating parents on fever and common infections in well-child clinics, prior to illness episodes, on parental healthcare seeking behaviour and medication management.

Method

We systematically searched for literature in Medline, Embase, CINAHL, PsycINFO, Cochrane Library, Web of Science. We included randomized controlled trials evaluating educational interventions, provided to parents when their child was not ill, in well-child clinic settings, to improve parental practices during episodes of childhood fever and common infections. Data were extracted on study design, sample characteristics, type of intervention, outcome measures and results. Quality of included studies was assessed with the Cochrane risk of bias tool.

Results

Our search yielded 4252 references. We included 8 articles in our review. Overall, educating parents in well-child clinic settings, prior to episodes of childhood fever and common infections, decreases daytime physician consultations and improves medication management. However, single component and multicomponent interventions differ in their potential to reduce frequency of daytime physician consultations, number of home visits, and out-of-hours contacts. Only multicomponent interventions target telephone consultations and medication management, and show significant improvements.

Conclusions

Educating parents in well-child clinics prior to episodes of childhood fever and common infections show predominantly positive effects regarding parental practices in terms of health-care seeking behavior and medication management. However, a number of included RCTs suffered from a high risk of bias and not all outcome measures were investigated by both single and multicomponent interventions. Future educational interventions should be systematically developed, by combining theory- and evidence based behavior change methods with knowledge and experiences obtained in clinical practice.

3. (Cost)-effectiveness of Antivirals for Influenza-like-illness in primary care: Set-up and progress of the ALIC4E trial in 17 European Countries.

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Objectives

Neuraminidase inhibitors decrease illness duration in patients with influenza. However, there has never been a large-scale, publically funded trial assessing clinical and cost-effectiveness of antivirals in routine primary care.

We aim to investigate benefits and costs of treating patients with influenza-like-illness with antivirals. Secondly, we aim to identify subgroups of patients receiving more, or a particular benefit from antiviral treatment.

Method

ALIC^{4}E is an open, platform, response-adaptive randomised trial aiming to recruit up to 4000 patients with influenza-like-illness from 22 primary care Networks in 17 European countries. Patients are treated according to usual primary care practice in their country, with or without Oseltamivir. A new antiviral might be added.

Results

Approvals were obtained from local ethical boards and national competent authorities, and contracts, patient insurance, medication distribution and all trial logistics were arranged in: Norway, Sweden, Denmark, Ireland, United Kingdom, Netherlands, Belgium, Switzerland, Lithuania, Poland, France, Spain, Hungary, Romania, Czech Republic, Croatia and Greece. We have found considerable variation in focus and legal, ethical and procedural requirements between these countries. During the influenza season 2016, 16 Networks had all requirements in place and included the first 500 patients.

Conclusions

The opportunities, barriers and challenges of large-scale, innovative primary care trials in 17 countries, and the trial progress will be further highlighted and discussed.

4. Global illness severity assessment and determinants for children presenting to primary care with cough and RTI: do parents and clinicians agree?

Esther T van der Werf-Kok[1], Niamh N Redmond[1], Sophie Turnbull[2], Hannah Christensen[2], Hannah Thornton[1], Peter S Blair[2], Brendan Delaney[3], Matthew Thompson[4], Paul Little[5], Alastair D Hay[1]

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Objectives

Parent perception of illness severity in children with respiratory tract infections (RTIs) is one of the reasons parents choose to consult primary care, and clinician illness severity assessment is a guiding factor for antibiotic treatment choice. The factors that determine illness severity assessment, are likely to differ between parents and clinicians. Knowledge of these differences and (dis)agreement may be important in improving parent-clinician communication and management of children with acute cough and RTI in primary care. Our study aimed to 1) investigate (dis) agreement between clinicians' and parents' illness severity scores; and 2) establish and compare the determinants.

Method

The 'TARGET' study, a multicentre prospective cohort study of 8394 children aged 3 months to 16 years with acute (≤28days) cough and RTI was used. Demographics, parent reported symptoms, clinician reported physical examination findings and illness severity visual-analogue scale (VAS) scores (0 to 10) by parent and clinician were independently recorded at recruitment.
Medians and Inter-Quartile-Ranges [IQR] were used as descriptive statistics and the Mann-Whitney test to investigate differences between groups. Agreement was measured using kappa statistic, and uni- and multivariable logistic regression used to identify the socio-demographic and clinical factors independently associated with parent and clinician reported illness severity.

Results

Mean severity of illness noted by clinicians was 3.1 (SD= 1.7, median= 3) [Range 0-9, IQR 2-4] for the 8360/8394 (99.6%) children with complete data, compared to mean parental assessment of 5.2 (SD= 1.8, median= 5) [Range 0-10, IQR 4-7] for the 8368/8394 (99.7%) children ($p<0.0001$). We found a moderate positive correlation (Spearmans $\rho = 0.434$, $p=<0.001$) between clinician and parent reporting of the severity of the child's illness. 15% of parents and clinicians agreed on the exact score, and in 39% the score was within one point of each other. Uni- and multivariable analyses will be presented.

Conclusions

Parent and clinician global severity illness assessment differ in children with RTI consulting primary care, with parents considering their child more severely ill than their clinician. Understanding the reasons for this discrepancy are important in order to provide parents with other ways of assessing severity, which may in turn alter consulting (and re-consulting) behaviour and improve parent anxiety. Symptoms, signs and demographic factors associated with high illness severity scores will be presented at the conference.

Session 3: Diagnosis/Prognosis

1. **Are we fair to the adventitious lung sounds in our research?**

Hasse Melbye
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Objectives

Auscultation has played an important role in diagnosing chest infections since the invention of the stethoscope in 1816. The inventor, Laennec, was convinced that certain sounds were pathognomonic for pneumonia and lung tuberculosis, but after 200 years' use of the stethoscope in less severe conditions, the confidence in lung sounds as diagnostic measure has been weakened. All the same, adventitious lung sounds are still strongly emphasized when GPs decide on antibiotic prescribing. We still need more knowledge about the diagnostic value of chest signs in airway infection. The question is whether our research methods are good enough.

Method

Two sources of bias are discussed with reference to recent research: selection bias and bias due to dichotomizing complex findings. Results from a recent study on 88 patients with exacerbation of asthma or COPD will be included, evaluating indicators of drop in Forced Expiratory Volume in one second (FEV_1) during exacerbations (≥10% and ≥200 ml) compared to stable state.

Results

Selecting patients with suspected lower respiratory tract infection leads to under estimation of the diagnostic value of crackles for pneumonia. Wheezing, as a severe problem experienced by the patient, was strongly associated with a drop in lung function during exacerbation (P=0.001), whereas "wheezes" dichotomously recorded after auscultation was not associated with this drop. "Crackles" dichotomously recorded was associated with a significant drop in FEV_1 (P=0.001).

Conclusions

Dichotomous descriptions of chest findings are not satisfactory when evaluating their diagnostic usefulness, this is at least the case for wheezes. Our methods for documenting the presence of lung sounds should be further developed.

2. Complications and new visits after pharyngotonsillitis in relation to etiology: a prospective two-year follow-up

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Objectives

In recent years potential pathogens other than Streptococcus pyogenes (GAS) have been discussed as a cause of pharyngotonsillitis. Among these, we have showed *F. necrophorum*, in addition to GAS, to be significantly more common in patients with pharyngotonsillitis as compared to healthy controls. Little is known about the frequency of new visits and complications after pharyngotonsillitis caused by different pathogens. Therefore we aimed to investigate the complications and visits due to sore throat within two years from inclusion in this cohort and relate that to initial microbiological findings.

Method

During 2011-2012, 220 patients aged 15-45 with the suspicion of pharyngotonsillitis, and 128 controls, were enrolled in a prospective cohort study in Swedish primary care. Throat cultures and nasopharyngeal samples for the detection of Betahemolytic streptococci, *Fusobacterium necrophorum* and respiratory viruses were obtained. Two years after inclusion a retrospective review of medical records was conducted. All visits to a primary or secondary care physician due to a sore throat, a complication or tonsillectomy were recorded. A complication was defined as a diagnosis of peritonsillitis, cellulitis, otitis media, meningitis, sepsis, impetigo, glomerulonephritis or rheumatic fever within 30 days from inclusion.

Results

Of the patients 13 (6%) were lost to follow-up: Of the remaining, 43% (90/207) had at least one consultation during the two year follow-up. One patient had a complication and 5 patients underwent or were planned for tonsillectomy. A finding of GAS only at inclusion was associated with a significantly higher number of new visits within 30 days compared to patients without GAS (20% and 6% (p=0,017)). Patients with an initial finding of *F. necrophorum* showed the same rate of complications and visits as other pathogens after two years.

Conclusions

The proportion of complications and tonsillectomies after a pharyngotonsillitis was low regardless of pathogen found at inclusion. An initial finding of GAS only was associated with a new visit within 30 days but no significant differences were found after two years when comparing.

3. A Systematic Review of the Clinical Diagnosis of Bordetella Pertussis

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Objectives

To perform a systematic review of the clinical diagnosis of bordetella pertussis (BP) in children and adults.

Method

We searched PubMed for prospective cohort studies of patients presenting with cough or clinically suspected pertussis infection. We only included studies that gathered data at the time of the patient's initial presentation. Data were abstracted in parallel by at least two reviewers, and study quality was assessed using the QUADAS-2 framework. We used the mada procedure in R version 3.2.2 to perform a bivariate meta-analysis to calculate summary estimates of sensitivity, specificity, and likelihood ratios where at least 4 studies reported a sign or symptom, and created summary receiver operating characteristic curves to explore heterogeneity by vaccination status and age.

Results

Of 380 studies initially identified, 20 met our inclusion criteria, of which 12 were at low risk of bias, 4 at moderate risk, and 4 at high risk. The overall clinical impression was the most accurate predictor of pertussis (LR+ 4.9, LR- 0.57). The presence of whooping (LR+ 2.05) and post-tussive vomiting (LR+ 1.66) increased the likelihood of pertussis somewhat, while the absence of paroxysmal cough (LR- 0.58) and absence of sputum (LR- 0.63) decreased it. It appears that in a vaccinated population, typical signs and symptoms of pertussis are more sensitive but less specific than in an unvaccinated population.

Conclusions

The clinician's overall impression is the most accurate way to determine the likelihood of BP infection at the time that a patient initially presents. The presence of whooping cough and post-tussive vomiting modestly increase the likelihood of BP, while the absence of paroxymsal cough or sputum decrease it somewhat. Clinical decision rules that combine signs and symptoms, perhaps with point of care tests such as c-reactive protein, are needed.

4. Investigating symptom trajectories in children presenting to primary care with acute cough and respiratory tract infection: analysis of the 'TARGET' prospective cohort study

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Objectives

To investigate if distinct post-consultation symptom trajectory groups can be defined among children presenting to primary care with acute cough and RTI.

Method

Parents of 2296 children were invited to complete a symptom diary recording the severity of six symptoms (cough, shortness of breath, disturbed sleep, being unwell, coping with normal activities and fever) on a 7-item Likert scale (from zero 'normal' to six 'as bad as can be') for 28 days or until they scored `normal` on all symptoms on two consecutive days. We used survival analysis to estimate symptom duration and latent class analysis to identify post-consultation trajectory groups.

Results

Cough was the most persistent symptom from symptom diary data: median duration 'moderately bad or worse' (≥3) cough 3 days (interquartile range 1-5) and overall duration of 9 days (6-14). Median duration of other symptoms: shortness of breath 4 days (1-8), disturbed sleep 6 days (3-9), unwell 7 days (4-10), interference with daily activities 5 days (3-8), fever 2 days (0-5). Preliminary latent class analyses of cough severity defined 4 groups: (i) 'severe' (6%), experienced a deterioration post-consultation; (ii) 'short' (49%) resolving by day 5; (iii) 'delayed' (35%) resolving by day 11; (iv) 'persistent' (10%) still symptomatic at day 15.

Conclusions

Parents can be advised that most (94%) of children's coughs exclusively improve post-consultation. Further analyses will be conducted to identify predictors of group membership, which could be used to further reduce clinical uncertainty and improve the accuracy of safety-netting advice for parents.

Session 4: Prescribing

1. **Clinical indications for antibiotic use. First data from a nationwide electronic prescription database in Danish General Practice.**

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Objectives

In 2011 a novel system on electronic prescriptions (FMK) was introduced in Denmark. This included the mandatory designation of a clinical indication from a drop down menu when prescribing an antibiotic (J01). This feature was introduced to promote rational use of antibiotics and provide insights into the associated prescribing pattern.

Aim: To characterize the pattern of antibiotic use for acute respiratory tract infections as stated on electronic prescriptions (FMK) in regard to national guidelines on antibiotic prescribing in Danish general practice.

Method

Register based study on Danish national prescription and provider databases. Included participants had redeemed an antibiotic prescription (ATC J01) at a Danish pharmacy between July 2012 and June 2013. Cumulative antibiotic use in specific acute respiratory tract infections, including acute otitis media (AOM), acute tonsillitis, acute rhinosinusitis, pneumonia, AECOPD and acute bronchitis, was characterized in total and by age group (0-4y, 5-14y, 15-44y, 45-64y, 65-75y, 75y+) and gender. Clinical relevant prescribing for acute respiratory tract infections according to Danish national clinical guidelines was assessed.

Results

Fifty-five percent of practices had implemented the FMK system in the study period. 1.6 million prescriptions (67% of total) contained an indication from FMK. 0.4 million were unspecific indications (*e.g.* "against infection") leaving 1.2 million prescriptions with a specific clinical indication.

The major clinical indications for antibiotic prescribing were respiratory tract (456.533) and urinary tract infections (acute UTI 454.650; chronic UTI 51984). In acute respiratory tract infections penicillin V accounted for 58% of all prescriptions, macrolides 18%, amoxicillin 15% and co-amoxiclav 9%. Quinolone and tetracycline use were below 1%. Use of non-penicillin V agents increased with age.

Conclusions

FMK was not fully implemented but subsequent legislation may have improved this aspect. The present study confirms that penicillin V is the most used antibiotic agent in ARIs in Danish general practice. However, part of the observed antibiotic use in regard to age groups and the high rates of second and third line agents prescribed may be inappropriate. This was especially the case concerning AOM, acute rhinosinusitis and pneumonia. Future initiatives to promote rational use of antibiotics should address these specific infections regarding initiation of antibiotic therapy and the associated rational drug choice.

2. Comparison of Out-of-hours and Office hours Antibiotic Prescribing Quantity and Quality in Primary Care

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Objectives

Unnecessary- and non-1st choice antibiotic prescribing is a significant problem in primary care. It is often argued that irrational prescribing is higher during out-of-hours consultations as compared to office hours practice. Evidence to support this is however lacking.

We aim to obtain insight in the quantity and quality of out-of-hours antibiotic prescribing for frequently presented infectious diseases, in comparison to office hours.

Method

At a national level, we evaluated numbers of dispensed antibiotic courses and types according to the moment of prescription (data: Dutch Foundation of Pharmaceutical Statistics). At a regional level, we compared prescribing rates, choice of antibiotic and the appropriateness of prescribing for acute otitis media, sinusitis, tonsillitis, bronchitis, cystitis and impetigo between office- and out-of-hours practice. For assessment of appropriate prescribing, information from electronic medical files (patient characteristics, symptoms, clinical investigation) was compared to the recommendations from the national guidelines.

Results

In the Netherlands, 6% of GP-prescribed antibiotics were prescribed out-of-hours, with relatively more amoxicillin, amoxicillin/clavulanate and nitrofurantoin, and less tetracyclins and macrolides. For all indications 1st-choice prescribing was comparable between the two settings, whereas prescribing rates were higher out-of-hours, especially for tonsillitis and sinusitis. Evaluation of patient files, however, revealed that over-prescribing was comparable or even lower than was determined earlier for daily care.

Conclusions

The assumption that out-of-hours antibiotic prescribing quality is worse than in daily practice doesn't seem to be correct. The higher prescribing rates found out-of-hours can be explained by the triage system selecting for patients needing urgent care. The appropriateness of prescribing, therefore, is the best quality measure. Similar interventions to reduce antibiotic use can be developed for the two settings.

3. Patterns in antibiotic dispensing by non-medical prescribers in primary care across England: A retrospective analysis of data collected routinely between 2011 and 2015

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Objectives

To describe patterns of antibiotic dispensing by non-medical prescribers (including nurses, pharmacists, optometrists, physiotherapists, radiographers, and chiropodists/podiatrists) in primary healthcare services across England between January 2011 and December 2015 using routinely collected data.

Method

A retrospective analysis of observational data between 2011 and 2015 was conducted. Data related to antibiotics that were dispensed from prescriptions issues by non-medical prescribers (NMPs), including quantity, type and dose of antibiotic were obtained from the NHS Business Services Authority via a Freedom of Information request. Data were provided for all Clinical Commissioning Groups (CCGs) across England at the CCG-level. For four specific CCGs (two urban, two rural), practice-level data were also obtained. Descriptive statistical analyses were undertaken.

Results

Over 12 million antibiotic courses were dispensed from prescriptions issues by NMPs between 2011 and 2015 across England. This represented 6.5% of all antibiotics dispensed from primary care over this time period. The percentage of antibiotics dispensed in primary care that were from NMPs steadily increased over time (from 5.4% to 7.6%). The percentage of all NMP dispensing that were antibiotics steadily decreased over this time period (from 14.7% to 10.9%). Further work will be presented investigating variation across CCGs and practices.

Conclusions

Our analysis indicates that the volume of antibiotics prescribed by NMPs is becoming an increasing contributory influence to total antibiotic prescribing in primary care. Groups working on antimicrobial stewardship interventions must include NMPs in their approach or risk losing the ability to influence a large body of antibiotic prescribers.

4. Paediatric antibiotic prescriptions in primary care in the Alpes Maritimes area of South eastern France between 2008 and 2013

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Objectives

France has remained among the top 5 European countries for ambulatory antibiotic consumption since such monitoring began in 1998. Young children are major antibiotic consumers in spite of the viral origin of most infections in this population. Recommendations were updated in 2011 to limit prescriptions. In order to assess their impact, diagnoses and prescriptions were compared in a population of children attending day-care centres (DCC) in South-eastern France in 2008 and 2012. Trends in reimbursement of paediatric antibiotic prescriptions by the National health insurance (NHI) for the whole area were also studied.

Method

Distribution of diagnoses accounting for antibiotic treatment and type of antibiotic prescribed over the previous 3 months to children below 4 years attending day-care centres in the Alpes Maritimes in South-eastern France were compared between 2008 and 2012 prior to and following the availability of these new recommendations. Trends in reimbursed ambulatory antibiotic prescriptions by general practitioners and paediatricians in the area were studied for this age group from 2008 to 2012 and in 2013

Results

The majority of recorded diagnoses concerned upper respiratory tract infections (URTI). Inappropriate antibiotic prescription persisted for colds and bronchitis in similar proportion during both surveys. Improvement in choice of antibiotic with fewer prescriptions for 3rd generation cephalosporins was observed both in day-care centres and according to NHI data, however this was mainly recorded among paediatricians.

Conclusions

Although progress in antibiotic stewardship in pædiatric primary care appeared to have been limited between 2008 and 2012, fewer reimbursed prescriptions in 2013 compared to 2010 by both pædiatricians and GPs may reflect some degree of improvement. Investigating the reasons for persisting antibiotic prescription for colds and bronchitis in children attending French DCCs and addressing these with an appropriate approach may contribute to improve France's performance in terms of antibiotic consumption.

Session 5: Stewardship

1. **General Practitioners' views on the acceptability of using quality indicators to reduce unnecessary prescription of antibiotics in South-America**

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Objectives

To explore GPs views about the acceptability of using quality indicators to reduce the unnecessary prescription of antibiotics in patients with suspected Respiratory Tract Infections (RTIs) across 4 countries in South-America.

Method

In March 2015, General Practitioners (GPs) from Argentina, Bolivia, Paraguay and Uruguay participating in a quality improvement program were invited to participate in focus groups in which a previously developed discussion guide was followed. Data was analysed through systematic text condensation with an inductive approach.

Results

171 GPs were invited to the focus groups and 48 % participated. There were not statistically significant differences between those attending or not de focus groups. The breadth of acceptability ranged from totally acceptable to slightly acceptable. The reasons behind this can be classified into the following domains: a) Health system barriers and facilitators, b) GPs as a professional group, c) Decision-making process, d) doctor-patient relationship and e) content and face validity of the indicator.

Conclusions

In general, there was a positive view towards the use of quality indicators as a tool to help GPs to reduce the unnecessary use of antibiotics. Nonetheless, applicability challenges arisen from the above-mentioned domains have to be taken into consideration and hopefully sorted out in order to consider the use of quality indicators an effective tool to be implemented in General Practice within the South-American context.

2. An antibiotic stewardship gap? Exploring the views of A&E clinicians on antibiotic prescribing for children with fever.

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Objectives

Antibiotic resistance is a global threat and antibiotic stewardship across all healthcare contexts is key to containing antimicrobial resistance. The majority of outpatient antibiotic prescribing is for children with respiratory tract infections. Qualitative studies investigating clinicians' views of antibiotic prescribing have mostly concentrated on general practitioners (GPs) as the usual first health care contact for patients. Whilst accident and emergency (A&E) is not recommended for initial consultations, children with acute infections do commonly attend. So far no research in the UK has explored the views of clinicians working in A&E about managing children with acute infections including antibiotic prescription.

Method

Semi-structured interviews were carried out with doctors and nurses working in two A&E departments in South East England, which served contrasting patient populations. A mixture of purposive and opportunistic sampling was used to sample clinicians with variation in job role (doctor, nurse) and speciality (emergency medicine, paediatrics). Clinicians were asked about how they managed children (under 8 years) with fever and related infections and their views on antibiotic prescribing for such children. Interviews were audio-recorded, transcribed verbatim and analysed following thematic analysis.

Results

30 interviews were completed. Clinicians reported seeing children with fever in A&E on a daily basis. All clinicians felt there was a proportion of unnecessary attendance for such children as a result of both self-presenters and referral by NHS 111 and GPs. Antibiotic stewardship was discussed in terms of the pressure on GPs to prescribe fewer antibiotics. Most clinicians felt that over-prescription of antibiotics was not relevant to the A&E context. However, a few felt there were instances of unnecessary prescribing and that improvement was possible. Clinicians had mixed views on whether they felt parental pressure to prescribe antibiotics.

Conclusions

Whilst clinicians working in A&E often manage similar patients to those managed in general practice, awareness about prudent antibiotic prescribing for children with acute infections is not common in this context. A&E may be a suitable target area for antibiotic stewardship interventions, which currently appear not to be making a specific impression. Identifying feasible and effective ways to promote prudent prescribing in A&E will support joined-up messages being delivered by general practice to patients and the public across all acute sectors.

3. Beat The Bugs: An educational programme on hygiene, antibiotics and self-care for the community setting

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Objectives

Education of the public is a key driver in the fight against the rising number of antibiotic resistant bacteria seen today. Through education we can raise awareness of the issue, increase knowledge and begin to change behaviour around antibiotic use and prescribing. e-Bug, led by the Public Health England Primary Care Unit, educates children and young people on hygiene, the spread of infections and antibiotics. e-Bug is expanding into the community to groups outside schools, including hard to reach adults. In line with NICE guidance we aim to increase public awareness around antibiotics and hygiene.

Method

e-Bug have worked alongside the Kingfisher Treasure Seekers community group to develop Beat The Bugs: a 6-week hygiene course for different types of community settings. The course covers an Introduction to Microbes, Hand and Respiratory Hygiene, Food hygiene, Oral hygiene, Antibiotics and a final session on self-care and action planning. During a pilot course with adults with learning disabilities we collected qualitative feedback from participants and the course leader. The sessions were observed for fidelity by members of the e-Bug team.

Results

The results from the pilot indicate the course was flexible and improved knowledge and awareness in vulnerable adults. Qualitative feedback identified that the number of visual components and interactive activities should be increased and reading decreased. Feedback from the course leader suggested a training session for those delivering the course would increase uptake and use of the materials. Further feedback from potential course leaders has suggested a more flexible resource of standalone sessions, rather than a 6-week course, would be more suitable for community groups.

Conclusions

This e-Bug community resource, whether a course or standalone sessions, will be a very useful addition to the e-Bug materials, to help implement NICE guidance 2016 to improve the public's knowledge and behaviour around hygiene, self-care and antibiotic use. We would now like to plan a full evaluation.

4. A modified McNulty-Zelen design randomised controlled trial to evaluate the TARGET Antibiotics toolkit (Treat Antibiotics Responsibly, Guidance, Education, Tools) and its implementation

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Objectives

The TARGET Antibiotics Toolkit has been developed by the Public Health England Primary Care Unit, the Royal College of General Practitioners and the Antimicrobial Stewardship in Primary Care group. The toolkit aims to influence personal attitudes, social norms and perceived barriers to optimal prescribing.

The aim of the study was to determine whether the addition of a one hour outreach workshop covering the importance of AMR and discussing available materials through the TARGET website results in fewer antibiotic prescriptions dispensed, compared to controls who have usual support by local medicine managers.

Method

Four CCGs across England were purposively selected and practices stratified by area, ethnicity, antibiotics dispensed and list size. Surgeries were randomly allocated to intervention or control using block randomisation. All intervention surgeries were invited to participate in a practice based workshop.

For the year prior to the workshop and the year following the workshop (1st January 2013 - 30th July 2015) we analysed total oral antibiotic items dispensed /1000 patients and items per STAR-PU (excluding minocycline, antifungals, antivirals and anti TB), items of oral penicillin /1000 patients, items of cephalosporins /1000 patients and items of quinolones /1000 patients.

Results

Out of 80 intervention practices, 42 agreed to receive the TARGET workshop. 318 attended the workshops in total.

Initial time series analysis indicates that there was no significant change in total antibacterial prescribing in intervention practices after the workshop. However in control practices the total prescribing increased by 3.8%. Intervention practices that accepted workshops had a significant decrease in co-amoxiclav prescribing (7.6%), control practices had a significant increase (7.8%), and practices randomised to the intervention group that refused workshops had a significant increase (12.4%). There were no significant changes in any groups in prescribing of cephalosporins, quinolones or trimethoprim/nitrofurantoin.

Conclusions

Educational sessions such as the TARGET workshop can be an effective method for promoting behaviour change in relation to antibiotic prescribing.

As a result of qualitative feedback, changes have been made to the resources. Which are freely available from the RCGP website: www.rcgp.org.uk/targetantibiotics.

Session 6: Flu

1. **A systematic review and decision analytic model on the early use of antibiotics for 'at risk' children with influenza in primary care (ARCHIE)**

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Objectives

The objective of this study is to determine the cost-utility of early prescribing of antibiotics (co-amoxiclav) to 'at risk' children (children most at risk of complications following influenza) for the treatment of influenza and influenza like illness (ILI) in comparison to standard care.

Method

A systematic review was completed to provide the current health economic evidence available regarding the cost-utility of prescribing antibiotics to 'at risk' children for influenza and ILI. Using the information obtained from the systematic review, a decision analytic model was developed to estimate the potential cost-utility of prescribing co-amoxiclav to 'at risk' children with influenza/ILI based on the previous research.

Results

The systematic review found that no previous health economic studies on prescribing antibiotics specifically to 'at risk' children with influenza/ILI exist. The model estimated that treating 'at risk' children with co-amoxiclav for influenza/ILI is cost effective with an ICER of £1217/QALY. The mean (SE) cost of antibiotic treatment was £353 (£64) and standard care £343 (£63). The mean (SE) QALY was 0.9269 (0.05) for antibiotic treatment and 0.9188 (0.04) for standard care. A subgroup analysis found antibiotic treatment is slightly more cost-effective in children age 6 months-23 months, due to a reduction in complications and hospitalisations.

Conclusions

Antibiotic treatment was found to be cost-effective. Cost-effectiveness was primarily driven by the reduction in the probability of complications, re-consultations and improved patient reported quality of life due to the children being prescribed with antibiotics.

2. Risk factors for influenza-related complications in children

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Objectives

Most research exploring risk factors for influenza-related complications in children examines risk of all-cause hospitalisation in children who present with influenza/influenza-like illness (ILI) to hospital ambulatory care. In order to identify risk factors for influenza-related complications in children who present to primary care we undertook a retrospective cohort study, including children aged 0-17 years who attended Clinical Practice Research Datalink (CPRD) practices coded with influenza-like illness during the 2009-10 H1N1 influenza pandemic (27th April 2009 to 23rd May 2010).

Method

Where possible, CPRD records were linked to data from the Hospital Episode Statistics and Index of Multiple Deprivation (IMD) databases. We estimated the risk associated with neurological disorders, premature birth, haematological and immunological conditions, metabolic conditions (including diabetes), and asthma. Analyses were adjusted for potential confounders including age, sex, IMD score, acute hospitalisations during the previous year, prescriptions during the index consultation (antibiotics, antivirals or asthma medications), and vaccination status. The primary outcome was influenza-related complications within 30 days of initial presentation. Secondary outcomes were influenza-related complications requiring further intervention, pneumonia, influenza-related hospitalisations, and all-cause hospitalisations.

Results

The records of 16,032 children were analysed-1,292 (8%) with influenza-related complications. Age under two years (n=2,053) was a statistically significant risk factor for IRC (OR_{adj}1.63-95%CI 1.38-1.92). In children over five years old asthma (n=2,068) was a significant risk factor for IRC (OR_{adj}1.48-95%CI:1.19-1.85) and complications requiring further intervention (OR_{adj}1.36-95% CI:1.01-1.84). Neurological conditions (n=172) appeared to increase all-cause hospitalisation risk on univariate analysis, but not after adjustment (OR_{adj}1.46-95% CI:0.82-2.63). No other significant associations were found between pre-specified conditions and outcomes. Children prescribed antibiotics, antivirals, or asthma medications (n= 4,953) had significantly lower risk of IRC (OR_{adj}0.35-95%CI:0.30-0.41).

Conclusions

Our findings support the inclusion of asthma and age under two years in current definitions of risk factors for influenza-related complications, as well as influenza vaccination strategies aiming to vaccinate all young children, irrespective of whether or not they have a known underlying condition. Further research is needed to understand the role of early intervention for influenza-like illness in children who present in primary care, particularly in relation to use of antibiotics and antivirals.

3. Barriers to the uptake of influenza vaccination in children under the age of 5 - primary care providers' and parents' perspectives.

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Objectives

Influenza vaccination has been shown to be safe and effective against influenza and in the prevention of complicating secondary respiratory illnesses, however its uptake in children under 5 remains low. We explore the views of parents and primary care providers (PCPs) on their knowledge and acceptance of influenza vaccination in children under 5.

Method

We conducted 30 in-depth interviews with PCPs (i.e., general practitioners, practice nurses, maternal and child health nurses, and pharmacists) and five focus groups with parents (n=50) between June 2014 and July 2015 in Melbourne, Australia. Data were thematically analysed.

Results

PCPs expressed concerns regarding the efficacy of the vaccine, out-of-pocket costs incurred by families, and uncertainty of the mortality and morbidity of influenza for otherwise healthy children. However, they would recommend the vaccine to high-risk groups (e.g. chronic disease(s), and asthma).

The majority of parents were aware of the availability of the influenza vaccine, however, they believed the vaccine could cause influenza. Some parents also believed symptoms of the disease would be more severe if they had received the vaccine. Additionally, most parents thought influenza vaccination was not necessary for their children as they needed to build their own ‘immunity'.

Conclusions

Our study revealed a gap between current influenza vaccination recommendations and PCPs' practice. Barriers exist such as concerns regarding influenza vaccine, administration schedule and PCPs' knowledge of influenza and its severity. There were also misconceptions and lack of knowledge among parents regarding influenza and the influenza vaccine. Interventions such as practitioner education and training, and increasing parents' knowledge on influenza vaccination are required to overcome the barriers identified in this study.

4. Influenza epidemic surveillance and prediction based on electronic health record data from an out-of-hours general practitioner cooperative: model development and validation on 2003-2015 data

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Objectives

Annual influenza epidemics significantly burden health care. Anticipating them allows for timely preparation. The Scientific Institute of Public Health in Belgium (WIV-ISP) monitors the incidence of influenza and influenza-like illnesses (ILIs) and reports on a weekly basis. General practitioners working in out-of-hour cooperatives (OOH GPCs) register diagnoses of ILIs in an instantly accessible electronic health record (EHR).

The objective is to explore the possibility of modelling seasonal influenza epidemics based on EHR ILI data of the OOH GPC Deurne-Borgerhout, Belgium and to develop a model accurately predicting new epidemics to complement the national influenza surveillance by WIV-ISP.

Method

Validity of the OOH GPC data was assessed by comparing OOH GPC ILI data with WIV-ISP ILI data for the period 2003-2012 and using Pearson's correlation. The best fitting prediction model based on OOH GPC data was developed on 2003-2012 data and validated on 2012-2015 data. Comparison with existing well-established surveillance methods was performed. A one-week and one-season ahead prediction was formulated.

Results

In the OOH GPC, 72,792 and 31,844 contacts were recorded from 2003 until 2012 and from 2012 until 2015, respectively. Correlation between OOHs and WIV-ISP ILI incidence is high ranging from 0.83 up to 0.97. Adding a secular trend (5 year cycle) and using a first-order autoregressive modelling for the epidemic component together with the use of Poisson likelihood produced the best fitting results. The selected model had the best one-week ahead prediction performance compared to existing surveillance methods. The prediction of the starting week was less accurate (± 3 weeks) than the predicted duration of the next season.

Conclusions

OOH GPC data can be used to predict influenza epidemics both accurately and fast one-week and one-season ahead and can be used complementary to the national influenza surveillance.

Session 7: Prevention

1. **Investigating the relationship between vaccine status and the presence of respiratory microbes in children attending primary care.**

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Objectives

Respiratory tract infections (RTIs) are a common cause of primary care (PC) attendance, predominantly in children, and antibiotics are frequently prescribed. Identifying the underlying microbial cause and prognosis of these children can be challenging. As several vaccines are known to reduce the prevalence of targeted pathogens, we aimed to describe the relationship between vaccine status, and microbe presence and prognosis, in children attending PC with RTI, to determine the potential for immunisation history to inform clinical decision making and advice given at consultation.

Method

The TARGET cohort study recruited children from 4 centres in England between 2011 and 2013. Demographic, and clinical sign and symptom data were collected at recruitment and vaccine data obtained through a PC notes review. At the Bristol centre a parent-reported symptom diary was kept for up to 28 days following consultation and a throat swab was taken and analysed for the presence and density of 26 potentially pathogenic microbes. Univariable and multivariable analysis were used to investigate association between vaccine status, the presence of microbes and prognosis, including long cough (25 days or more), re-consultation and symptom duration.

Results

Of the 2,296 children recruited from the Bristol centre, 1750 had been vaccinated with Pneumococcal Conjugate Vaccine (PCV); no vaccination data were available for 12 children. 2,159 children with vaccine status had *S.pneumoniae* results available for analysis, of which 321 (14.9%) were positive. Preliminary multivariable analysis indicated some evidence for increased odds of pneumococcal isolation in vaccinated compared to unvaccinated children (OR 1.82 95%CI 0.98-3.38 p=0.055) adjusting for age, the number of other bacteria and viruses isolated within the TARGET study and swab transit time. We found no association between PCV vaccine and long cough adjusting for age (p=0.804).

Conclusions

We found that PCV vaccination may be associated with pneumococcal detection in the throat in children attending PC with RTI. This could be due to replacement by non-vaccine serotypes; future work typing the strains within the TARGET study could allow for greater distinction. We found no association with long cough. Full results for additional vaccines, microbes and prognosis markers will be presented at conference. These results indicate vaccine status alone cannot be used to rule out the presence of particular species in children with RTI attending PC or be used to inform advice about prognosis.

2. What are the effects of providing real-time data on locally circulating microbes on clinician management of common infections in primary care? A systematic review.

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Objectives

The WHO describes antimicrobial resistance (AMR) as one of the greatest challenges to global public health. Over-consumption of antibiotics is a major driver for the development of AMR. Clinician uncertainty has been identified as a key driver of antibiotic prescribing in primary care. In a Bayesian framework, clinicians first establish a pre-test diagnostic probability, which is modified (post-test probability) as further clinical evidence becomes available. This study aims to investigate if interventions to inform clinicians about locally relevant population-based microbiological and syndromic surveillance change antibiotic prescribing (with or without evidence of changing diagnostic probabilities).

Method

Databases searched included Medline, EMBASE, CINAHL, Web of Science, grey literature sources, thesis databases and trial registries. Additional studies were identified through screening references and contacting experts. Studies were eligible if investigating effects on primary care clinician management of common infections in OECD member countries where the intervention included dissemination of real-time, population-based data on locally relevant microbes or syndromic presentations. The main outcomes of interest were antibiotic prescribing, secondary care referrals and changes in diagnostic probability.

Quality assessments specific to study design: Cochrane Risk of Bias tool for RCTs; and the ROBINS-I tool for non-randomised intervention studies.

Results

Electronic searches identified 9292 hits (1693 duplicates). Screening identified 38 records to retrieve in full-text. Findings will be presented on papers for which data extraction has been completed by conference dates. Parameters of interest include effect sizes (antibiotic prescribing and secondary care referrals), quality and validity of studies, with meta-analyses conducted if appropriate. Changes to diagnostic certainty resulting from the intervention will be reported. We will assess the development, execution and evaluation of the interventions in line with the MRC guidelines on complex interventions, as well as any use of behaviour change models.

Conclusions

Thorough evaluation of the included studies will determine the effectiveness and efficacy of this type of intervention. This systematic review will contribution to the design and implementation of future interventions and guide the design of ethical and robust studies seeking to evaluate complex interventions in a primary care setting.

3. Colonisation rates of and risk factors for extended-spectrum beta-lactamase producing coliforms (ESBLPCs), and carbapenamase producing Enterobactericaeae (CPE), in different sections of the asymptomatic general population in England

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Objectives

ESBLPCs are common in the gut of populations where antibiotics are over used. Most prevalence data comes from patients with diarrhoea. We aimed to estimate how many of the general population in England carry ESBLPCs and determine independent risk factors for their presence.

Method

Patients 18+ from 15 practices in four Primary Care Trusts with different ethnicity across England were stratified by antibiotic use, gender and ethnicity. Randomly selected patients were invited by letter to submit a stool and complete a questionnaire. Stools were cultured directly on chromogenic agar. We used MALDI-TOF mass spectrometry to determine bacterial species, and multiplex PCR and sequencing to determine presence of the *bla*$_{\text{CTX-M}}$ gene and genotype. Second specimens were collected from a subset. We used 2011 census data, practice population and return rate to give a weighted prevalence of ESBLPCs, and used multivariate analysis to explore risk factors.

Results

2296 (3.9%) of 58,337 invitees returned a stool and questionnaire. The estimated prevalence of ESBLPCs in England was 7.3% [CI5.6, 9.4] (Shropshire 4·9%, Southampton 9·2%, Newham 12·7%, Birmingham 16%). The greatest risk factors for colonisation included: being born in India, Pakistan, Bangladesh or Sri Lanka (aOR5·4, we estimate 24% of all people colonised), born in Afghanistan (aOR 46); born in Middle East (aOR4·7), travel in last year to Indian subcontinent (aOR2.9, accounting for 12%); After allowing for the aforementioned risk factors, hospitalisation, travellers' diarrhoea, and antibiotic use, were not independent associated with ESBLPCs. Only 2/2430 were positive for CPEs.

Conclusions

These findings have implications for healthcare as they demonstrate that ESBLPCs are established in England, and there is a larger reservoir of ESBLPCs in defined sections of the population. The main risk factors for colonisation appear to be travel to, or association with, countries with a high prevalence of colonisation with ESBLPCs. As the prevalence of ESBLPCs is likely to be at least 4.9% across the England, any empirical antimicrobials prescribed for the treatment of suspected sepsis due to possible coliforms, should cover ESBLPCs; a broader spectrum antimicrobial should also be considered for UTI in patients with risk factors.

4. An internet-delivered handwashing intervention to modify respiratory infection transmission (PRIMIT): sub-group analysis of potential high risk groups

Beth Stuart[1], Paul Little[1], Michael Moore[2], Richard Hobbs[1], Judy Joseph[1], Sasha Miller[1], Lucy Yardley[1]

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Objectives

An internet-delivered handwashing intervention reduced episodes of respiratory tract infection (RTI) by 25% among healthy adults in winter. The aim of this subgroup analysis was to determine whether the intervention was equally effective in pre-specified subgroups known to be at higher risk of infection.

Method

20,666 adults were randomised to receive either access or no access to a customised tailored web-based intervention to encourage increased handwashing behaviour in the winter. The primary outcome was the number of participants reporting one or more episodes of RTI at 16 weeks, analysed using generalised linear models for the binomial family. This analysis explored the effect of the intervention in pre-specified higher risk subgroups: households with children under 11, larger households, participants with lung comorbidities, participants with heart disease, participants who consulted for RTI 2+ times in the previous year and more deprived households.

Results

In the full trial after 16 weeks, 51% in the intervention group reported one or more episodes of RTI compared with 59% in the control group (multivariate risk ratio 0·86, 95%CI 0·83-0·89). All subgroups reported a higher rate of infection than the whole study population. However, there was no evidence of any significant interactions terms and the intervention group reported significantly fewer episodes of any RTI than the control group in all subgroups, with RRs of a similar magnitude to those reported in the whole study population. There was no increase in re-consultation or antibiotic use over the study period.

Conclusions

In the sub-groups patients at higher risk of infection within the PRIMIT trial, the reduction in RTIs was comparable to that observed in the whole study population, suggesting that the intervention is effective and suitable for use in these groups.

Session 8: RTI in Children

1. **Paediatric respiratory tract infection surveillance: a community-based feasibility inception cohort study**

Emma Anderson[1], Suzanne Ingle[1], Peter Muir[2], Charles Beck[3], Adam Finn[4], John Leeming[5], Christie Cabral[6], Alastair Hay[1]

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Objectives

Much epidemiological research into respiratory tract infection (RTI) is conducted at the point of healthcare consultation, leaving the community burden, microbiology, symptom duration and proportion consulting unknown. This study sought to: (1) establish the feasibility of (predominately online) recruitment and retention to a paediatric RTI community surveillance study, with collection of syndromic and microbiological data (parent and research nurse [RN] collected); and (2) estimate RTI symptom duration and primary care consultation rates using data from over 300 RTI illnesses.

Method

Children aged ≥3 months and <16 years and their parents/carers were recruited via GP surgery invitation letters. Parents provided baseline data (including household demographics and parent health anxiety) online, and responded to weekly emails to confirm the absence/presence of new RTI symptoms. Once symptomatic, parents provided daily data online (presence and severity of symptoms, days off work/school, health service and medication use). RNs visited to collect clinical examination data and nasal and saliva swabs. Parents took same day (symptomatic) and subsequent (asymptomatic) swabs. Medical history and consultation details were collected from primary care medical notes.

Results

We invited 10,310 children and their parents/carers to participate. A total of 485 (4.7% of the 10310) children were recruited (baseline data complete) from 331 families. Initial results indicate 351 new onset RTI symptom episodes reported in 259 children from 195 families (in addition to 121 (25%) of the recruited children reported existing RTI symptoms at baseline). 200 RN home visits were completed with 190 symptomatic (parent and nurse) and 258 asymptomatic (parent) swabs collected to date. Illness resolution was confirmed for 305 (91%) of the new onset RTIs.

Symptoms duration results will be presented and parent-reported consultation rates.

Conclusions

Initial results indicate that community infection surveillance is feasible, as assessed by recruitment, retention and data completeness rates. We will present these results at the conference as well as symptom duration and preliminary evidence around consultation rates.

2. Parent and child experiences and views of a paediatric respiratory tract infection (RTI) community surveillance feasibility study: a qualitative study to inform future research

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Objectives

The objectives of this qualitative study with parents and children were: (1) to understand the acceptability of the community-based feasibility inception cohort study and the collection of paediatric RTI data (microbiological swabs and online symptomatic surveillance); and (2) to understand parent views on the content, design and potential impact on home care and primary care help seeking of RTI infection surveillance information.

Method

Semi-structured interviews were conducted with 30 mothers and 11 children (≥7 years). Participants were selected purposefully based on deprivation (index of multiple deprivation decile), child age and whether RTI symptoms had been reported. Interviews explored experiences of participating in the feasibility study in relation to the acceptability of recruitment and data collection methods (symptom surveys and parent and research nurse taken microbiological swabs). Participants were then presented with example information on circulating viruses and symptoms and asked about the value and impact it might have on perceptions of child illness and management practices. Interviews were analysed using the framework method.

Results

Recruitment and data collection were experienced as acceptable. Modifications to the swab equipment and instructions would enhance acceptability.
Positive responses to infection surveillance information related to information regarding symptom duration and currently circulating symptom information. Parents anticipated the information would help them identify their child's illness and reassure them that similar infections were prevalent locally. Increased parent concern and misdiagnoses were proposed as potential negative consequences and without more guidance on caring for children with a circulating virus minimal impact on parent management was anticipated.
Parents approved of clinicians' using the information to diagnose their child's RTI with greater certainty.

Conclusions

Preliminary findings from this study suggest that collecting paediatric RTI symptom and microbiological data is likely to be acceptable to parents and children, and improvements to the study components have been identified. Diverse responses to the infection surveillance information were elicited and there was some support for the intended behavioural outcomes. Responses will be used to develop a pilot randomised controlled trial to assess the interventions impact on primary care utilisation. The initial findings suggest the intervention will need to focus on symptom duration information and provide guidance on management.

3. Real-time paediatric respiratory tract infection (RTI) community surveillance: A qualitative interview study of clinicians' perspectives on the use, design and potential impact of a planned intervention.

Emma Anderson[1], Isabel Lane[2], Joanna Kesten[1], Alastair Hay[1], Timothy Moss[3], Christie Cabral[2]
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Objectives

The overall aim of this study is to investigate the feasibility of the provision of locally relevant real-time syndromic and microbiological surveillance information and its potential to improve the care of children with RTIs by reducing diagnostic uncertainty, which could help reduce unnecessary antibiotic prescribing.

The objectives of this qualitative study are 1) to understand clinicians' perspectives on the content, design, integration into practice and anticipated impact of an outline intervention of microbiology and real-time virus symptoms data; and 2) to explore the barriers and facilitators to the desired behavioural outcomes of such an intervention to inform intervention development.

Method

Semi-structured one-to-one interviews were conducted with 19 clinicians (16 GPs; 3 Nurse Practitioners) representing a range of clinical experience from a range of Bristol GP surgeries (deprivation deciles 1 to 8).

Interviews explored clinicians' current approaches to managing paediatric RTIs, knowledge of circulating infections, and views of a mock-up example of viral and syndromic surveillance information including information on normal symptom duration. Clinicians' perceptions of the value, use, and impact on clinical practice of infection surveillance information were explored alongside preferences for content, design and mode of delivery.

Interviews were audio recorded, transcribed verbatim and analysed using the framework method.

Results

Clinicians agreed there is currently no formal primary care system for identifying circulating infections, and the surveillance information was novel and potentially useful.

While symptom duration was perceived as useful, clinicians queried the relevance of knowing community viral microbiology, reporting their role as to identify the truly sick (requiring treatment) amidst general ‘viruses going around', and to treat each child individually. Without explicit instructions within the intervention to change their clinical practice, clinicians predicted limited impact on their decision-making, focusing instead on perceived benefits in supporting their patient explanations/expectation management. Barriers/facilitators identified included time pressures, information overload and parent self-efficacy.

Conclusions

Initial results (will be complete by time of conference) indicate complex, mixed responses from clinicians to the provision of paediatric RTI microbiological and symptomatic surveillance information in terms of perceived value for use in practice. Whilst clinicians viewed the information as beneficial for supporting consultations with parents, they questioned how knowledge of viral microbiology could or should inform their practice of treating each patient individually. Intervention development will ensure it meets clinicians' clinical decision-making needs and takes account of time pressures and information overload.

4. Paracetamol (acetaminophen) or non-steroidal anti-inflammatory drugs, alone or combined for pain relief in children with acute otitis media: a Cochrane review

Alies Sjoukes[1], Roderick P. Venekamp[2], Alma C. Van de Pol[1], Alastair D. Hay[3], Paul Little[4], Anne G.M. Schilder[5], Roger A.M.J. Damoiseaux[1]

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Objectives

To systematically review 1) the effectiveness and safety of paracetamol (acetaminophen) or non-steroidal anti-inflammatory drugs (NSAIDs), alone or combined, as compared with placebo or no treatment in relieving pain in children with acute otitis media (AOM); and 2) the effectiveness and safety of NSAIDs as compared with paracetamol in relieving pain in children with AOM.

Method

We used the standard methodological procedures expected by Cochrane. The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, LILACS and Web of Sciences were searched for published trials. Clinicaltrials.gov, ICTRP and additional sources were searched for published and unpublished trials. The search date was 2 June 2015. We included trials comparing the effectiveness of paracetamol or NSAIDs, alone or combined, in relieving pain in children with AOM. We also included trials conducted in children with fever or URTI if they allowed us to extract subgroup data of children with AOM either directly or upon request by original trial authors.

Results

Three randomised controlled trials including a total of 327 children with AOM were included. We found moderate quality evidence that both paracetamol and ibuprofen as monotherapy were more effective than placebo in relieving pain at 48 hours (*paracetamol versus placebo*: RR 0.38, 95% CI 0.17-0.85; *ibuprofen versus placebo*: RR 0.28, 95% CI 0.11-0.70) but not in terms of relieving fever at 48 hours (quality of evidence: low). We found evidence of varying quality that paracetamol and ibuprofen were equally effective in achieving short-term pain relief. Evidence on the effectiveness of *NSAIDs and paracetamol versus paracetamol* was inconclusive.

Conclusions

Current evidence suggests paracetamol or ibuprofen as monotherapy should be used to relief ear pain in children with AOM. Clinicians should be aware that even with analgesia, around ten percent of the children may experience inadequate pain control. Further research is needed to provide insights in the role of NSAIDs and other analgesics such as anaesthetic eardrops as an adjunct to paracetamol in children with AOM.

Session 9: UTI

1. **Bacteriological findings in uncomplicated urinary tract infections: current status, developing resistance and future situation.**

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Objectives

Empirical treatment of acute uncomplicated urinary tract infections is based on current resistance patterns and national guidelines. In Norway these resistance patterns are based on national data from urine cultured at medical laboratories. The urine samples are taken mostly from patients with complicated urinary tract infections. Are these bacteriological findings representative for what we will find in women with uncomplicated cystitis? And if they are not, will they differ to such an extent that we should consider changing the national guidelines for empirical treatment of uncomplicated cystitis in women?

Method

We have compared bacteriology and resistance patterns in urine samples taken from women with uncomplicated cystitis in three different periods over the last 15 years. The material consists of 184 urine cultures from 2001, 406 urine cultures from 2010-11 and 259 urine cultures from 2013-15.

Results

E. coli is the main bacterial agent in 80 % of the cultures. Staphylococcus saprophyticus represent between 5-17 %. Our resistance patterns differ somewhat from the national numbers, but both suggest a quite stable and low level of resistance towards mecillinam and nitrofurantoin, and an increase in resistance towards trimethoprim and ampicillin. Antibiotic resistance in Staphylococcus saprophyticus has been known to be uncommon, but in our comparison Staphylococcus saprophyticus seems to become increasingly resistant to Ampicillin, and also developing resistance towards trimethoprim. All results are preliminary.

Conclusions

Despite a substantial rise in use of mecillinam in Norway, we do not see a corresponding increase in the level of resistance to mecillinam in E.coli. The opposite is the case for trimethoprim. This confirms that mecillinam has a low resistance driving effect and can stay on as a first choice antibiotic in the empirical treatment of uncomplicated cystitis. Nitrofurantoin has very low resistance levels and should be used more often, whereas trimethoprim should be considered removed as a first choice.

2. **Protocol for clinical trial: "*Randomized clinical trial comparing fosfomycin vs. nitrofurantoin for treatment of uncomplicated lower urinary tract infection in female adults at increased risk of antibiotic-resistant bacterial infection, AIDA*".**

Anna Kowalczyk[1], Stephan Harbarth[2], Angela Huttner[2], Leonard Leibovici[3], Johan Mouton[4], Johan Mouton[5], Maciek Godycki-Cwirko[6]
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Objectives

To demonstrate the superiority of 5 days nitrofurantoin over once 3g fosfomycin for the treatment of lower, uncomplicated UTI in women at high risk of antibiotic-resistant uropathogens.

Method

Adult, non-pregnant female patients with uncomplicated UTI, at high risk of antibiotic-resistant pathogens after providing consent form will be randomly assigned into one of the treatment arms. The clinical and bacteriological cure evaluation will be made at day 1, 14 and 28 after treatment.

Results

Primary: clinical response 28 days after completion of therapy; secondary: clinical response 14 days after completion of therapy, bacteriological response 14 and 28 days post treatment incidence of "true UTI" among all included patients, duration of symptoms after treatment initiation, hospital admission in the 33-day study period, progression to pyelonephritis or urosepsis in the 33-day study period, 28-day mortality. Incidence of adverse events, with particular emphasis on toxicity of nitrofurantoin, including chronic hepatitis and pneumonitis, emergence of antibiotic resistance.

Conclusions

This trial will provide an answer to the key scientific and clinical question regarding the superiority of two antimicrobial regimens of the two off patent antibiotics nitrofurantoin and fosfomycin in the treatment of lower uncomplicated UTI. In addition, the study will provide answers to relevant clinical questions, in particular the risk of adverse events. The results of this trial will provide the data for the PK/PD analyses.

3. **The development of a "TARGET antibiotics" UTI leaflet to improve communication in GP consultation around the diagnosis and management of urinary symptoms and UTIs with patients. Increasing self-care and reducing antibiotic use, bacteraemia and recurrence.**

Jessica Thomas, Donna Lecky, Cliodna McNulty
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Objectives

UTIs are one of the most common bacterial infections seen in General Practice, accounting for many antibiotic prescriptions. A recent study stated 95% of women consulted a health professional, and 74% reported being prescribed an antibiotic, yet only 63% reported taking them. Unnecessary prescribing of antibiotics could be minimised by improving syndromic based diagnosis and facilitating communication between the GP and patient in consultation. Enhanced communication may also improve self-care and reduce recurrence of *E.coli* bacteraemia.

Method

We undertook two focus groups and interviews with women who had experienced recent urinary symptoms as well as telephone interviews with GPs. We explored women's attitudes to and experiences of self-caring for their urinary symptoms and women's needs from a GP consultation. We also explored GPs perception of time spent in consultation with patients, exploring antibiotic resistance, infromation shared, guidelines used and common consultations. In addition we discussed the content of the "TAREGT antibiotics" leaflet to be shared with patients during consultation about possible urinary symptoms and UTIs and this was discussed with all participants.

Results

Women valued an explanatory leaflet that they could share in consultation and take home, giving advice on their diagnosis of their urinary symptoms, self-care and prevention measures. Women were unlikely to recall being given advice on self-care and information whilst in consultation. Women had little understanding of the different types of UTIs and did not attribute antibiotic resistance to the overuse of antibiotics. Younger women had a higher expectation to be prescribed antibiotics for their urinary symptoms whilst older women relied more on commonly known self-caring measures such as: hydration and hygiene.

Conclusions

An explanatory leaflet would be a useful tool to encourage better patient diagnosis, the relationship between antibiotic use and resistance as well as self-care and prevention of urinary tract associated symptoms. Simple messaging could help patients re-evaluate the risk of antibiotics. GPs should be encouraged to explore their patient's knowledge, share information on self-care and prevention measures and antibiotic resistance when in consultation.

4. **Effect of a diagnostic algorithm for urinary tract infection in general practice on appropriate use of antibiotics and costs- a cluster randomized trial**

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Objectives

The aim of this study was to investigate the effect of diagnostic algorithm for UTI on appropriate prescribing of antibiotics and total price of point-of-care diagnostics for patients with symptoms of urinary tract infection consulting their general practitioner.

Method

This study was a cluster randomized controlled single blinded study of a diagnostic aid in general practice. 90 general practices were randomized to either receiving a diagnostic algorithm supplemented with a smart-phone integrated web-page, aiming to guide in use and interpretation of point-of-care diagnostics, or to not receiving anything. Practices registered diagnostics and treatment on 20 consecutive patients with symptoms of UTI each and sent a urine sample to the microbiological department as reference on each patient. Primary outcomes were appropriate primary choice of antibiotics and total costs per patient for consultations and point-of-care diagnostics.

Results

The trial includes patients until the 1st of June. At submission, 74 practices have completed inclusion of 1505 patients. Final results will be presented in the conference.

Conclusions

This is to our knowledge the first study investigating the immediate effect of distributing a diagnostic algorithm for UTI to general practice. Knowing the actual impact of having access to an algorithm can guide decision makers in how to design quality intervention aiming to increase effectiveness and reduce inappropriate use of antibiotics.

Session 10: Point-Of-Care Testing

1. **Should all acutely ill children in primary care be tested with point-of-care CRP: a cluster randomised trial.**

Jan Verbakel[1], Marieke Lemiengre[3], Tine De Burghgraeve[2], An De Sutter[3], Bert Aertgeerts[2], Bethany Shinkins[4], Rafael Perera[1], David Mant[1], Ann Van den Bruel[1], Frank Buntinx[2]
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Objectives

Point-of-care blood CRP testing has diagnostic value in helping clinicians rule out the possibility of serious infection. We investigated whether it should be offered to all acutely ill children in primary care or restricted to those identified as at risk on clinical assessment.

Method

Cluster RCT involving acutely ill children presenting to 133 GPs at 78 GP practices in Belgium. Practices were randomised to undertake point-of-care CRP testing in all children (1730 episodes) or restricted to children identified as at clinical risk (1417 episodes). Clinical risk was assessed by a validated clinical decision rule (presence of one of breathless, temperature ≥ 40°C, diarrhoea and age 12-30 months, or clinician concern). Main trial outcome was hospital admission with serious infection within 5 days. No specific guidance was given to GPs on interpreting CRP levels but diagnostic performance is reported at 5, 20, 80, 200 mg/L.

Results

Restricting CRP testing to those identified as at clinical risk substantially reduced the number of children tested by 79.9% (95%CI 77.8-82.0%). There was no significant difference between arms in the number of children with serious infection who were referred to hospital immediately (0.16% vs 0.14%, p=0.88). Only one child with a CRP < 5 mg/L had an illness requiring admission (a child with viral gastroenteritis admitted for rehydration). However, of the 80 children referred to hospital to rule out serious infection, 24 (30.7%, 95%CI 19.6-45.6%) had a CRP < 5 mg/L.

Conclusions

CRP testing should be restricted to children at higher risk after clinical assessment. A CRP < 5 mg/L rules out serious infection and could be used by GPs to avoid unnecessary hospital referrals.

2. **Point-of-care CRP matters: low CRP values substantially improve immediate antibiotic prescribing in acutely ill children in primary care.**

Marieke Lemiengre[1], Jan Verbakel[2], Kaat Van Roy[1], Tine De Burghgraeve[2], Bert Aertgeerts[2], Frans De Baets[2], Frank Buntinx[2], An De Sutter[1]
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Objectives

Antibiotics are prescribed too often for acutely ill children in primary care. A possible explanation could be found in the physicians' diagnostic uncertainty. To promote rational prescribing, EBM practice guidelines were drawn up. However, they are not always clear-cut and still leave some room for doubt and subjective assessment. CRP has been put forward as an objective mean to increase diagnostic certainty. Family physicians pointed that POC CRP will not reduce antibiotic prescribing as long as its diagnostic value in children is not clear. But, does this really mean that FPs wouldn't take CRP into account once it is measured?

Method

Acutely ill children (1 month – 16 years) consulting their FP were consecutively recruited. Based on the preliminary diagnosis, age, and clinical presentation, the presence of a rational indication for antibiotics according to the Belgian guidelines was evaluated. CRP values were dichotomized at a cut-off point of 5 mg/L. The primary outcome was the immediate antibiotic prescribing rate. A mixed logistic regression analysis was performed to investigate if antibiotic prescribing rates differed across children with higher, lower or unknown CRP-levels, while testing for interaction with the presence or absence of a rational indication for antibiotics.

Results

133 family physicians from 79 practices in Flanders recruited 3147 children between January 2013 and March 2014. Following the ERNIE2-protocol, 60% of the children got a POC CRP test. CRP-levels were < 5 mg/L in 41,1%. After adjusting for covariates, a CRP < 5 mg/L was associated with lower prescribing rates compared to unknown values. This was the case when there was a rational reason to prescribe antibiotics following the guidelines (OR 0.24, 95%CI 0.12-0.46); when there was no rational reason to prescribe (OR 0.26, 95%CI 0.13-0.49) and when it was unclear if there was a rational reason to prescribe (OR 0.19, 95% CI 0.07-0.47). There were no differences in prescribing rates when comparing cases with CPR values > 5 mg/L to unknown values, except a borderline significance in case the indication for antibiotics was unclear (OR 1.8, 95%CI 1.00-3.26).

Conclusions

Low CRP levels substantially reduced immediate antibiotic prescribing, regardless of a rational indication to prescribe antibiotics. FPs overruled practice guidelines when CPR-levels were low.

3. Associations between throat swab microbiology and clinical outcome in children presenting to primary care with respiratory tract infection: results from the NIHR 'TARGET' Cohort Study

Hannah V Thornton[1], Peter S Blair[3], Niamh M Redmond[2], Sophie L Turnbull[1], Hannah Christensen[3], Tim J Peters[4], John Leeming[5], Andrew Lovering[5], Barry Vipond[6], Peter Muir[6], Alastair Hay[1]

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Objectives

Children with respiratory tract infections (RTIs) are frequent primary care users and antibiotic recipients. Antibiotic prescribing leads to antimicrobial resistance; however, point-of-care testing (POCT) could potentially reduce inappropriate antibiotic use. We aimed to investigate the potential prognostic value of microbe detection in children presenting to primary care with cough, adjusting for subsequent antibiotic consumption.

Method

The TARGET cohort study was a prospective multicentre (Bristol, London, Oxford and Southampton) study of children presenting to primary care with acute cough and RTI between July 2011 and May 2013. A novel bacterial-viral dual throat swab was taken from children in the Bristol centre to identify 26 respiratory microbes; 12 bacteria and 14 viruses.

Outcomes (hospitalisation for RTI, reconsultation, prolonged cough (defined as lasting >25 days) and symptom duration) were recorded for 28 days post-recruitment. Associations between microbe detection and outcomes were determined using chi-squared tests and survival analyses.

Results

Data were available from 2,109 of 2,296 (92%) children, median age 3 years. 74% were positive for ≥1 microbe (≥1 bacterium only 32%; ≥1 virus only 14%; co-detection 28%; no detection 26%).

In children who did not consume antibiotics, bacterial detection was associated with increased odds of prolonged cough (OR 2.38 [1.07-5.31]). There was no evidence of this association in children who consumed antibiotics (OR 0.85 [0.38-1.89]).

Odds of hospitalisation were increased in children with viral detection (OR 4.28 [1.10-16.65], p=0.036). Due to the small number of children hospitalised, it was not possible to stratify this analysis by antibiotic consumption.

Conclusions

We found that bacterial detection from the throat was associated with prolonged cough in children with RTI who do not consume antibiotics. Additionally, viral detection was associated with hospitalisation in this preliminary analysis. Use of POCT to identify microbes from the throat could potentially be useful in providing tailored advice about expected symptom duration, or in directing antimicrobial treatment.

Further analysis will focus on establishing whether individual microbe detection provides prognostic value over and above clinical presentation, adjusting for antibiotic consumption. These results could contribute to POCT development strategy.

4. Supporting antibiotic prescribing decisions for diabetic foot ulcer: an investigation of the diagnostic accuracy of inflammatory biomarkers (INDUCE study)

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Objectives

In 2011-12, the financial cost of diabetic foot ulcers (DFUs) and amputation in NHS England was £650 million, approaching 1% of its budget. Diagnosis of DFU infection remains entirely clinical and antibiotics are often prescribed empirically, risking increased antibiotic resistance. Conversely, missing early bacterial infection increases the risk of serious infection and amputation. Our aim was to explore the diagnostic discriminatory value of inflammatory biomarkers and clinical signs.

Method

Patients with a DFU and either mild or no infection were eligible. Exclusion criteria were immunosuppression or receipt of antibiotics within the previous two weeks. Four inflammatory biomarkers were investigated to develop a composite assay for mild DFU infection: venous white cell count (WCC), C-reactive protein (CRP), procalcitonin, and a novel wound exudate calprotectin assay. Antibiotic prescribing decisions were based on clinician's baseline assessments and patients were reviewed one week later. Ulcer infection was defined by the clinician's overall impression based on their two assessments, incorporating response to antibiotics, but blinded to test results.

Results

67 of 363 potential participants were recruited from community podiatry clinics in two UK regions. Two withdrew early, leaving 28 (43%) mildly infected and 37 (57%) non-infected DFUs. Median baseline CRP levels were 7.50 mg/ml and 6.00 mg/ml, and median calprotectin levels were 1437ng/ml and 879ng/ml, in the infected and uninfected groups respectively. The area under the receiver operating characteristic curve (AUROCC) for a composite assay incorporating calprotectin, CRP and WCC was 0.632 (95% CI 0.479-0.785). Combining with ulcer area the AUROC was 0.683 (95% CI 0.535-0.830), sensitivity 0.640 & specificity 0.806.

Conclusions

A composite assay including CRP, calprotectin and WCC has shown some value in being able to assist antibiotic stewardship in DFU infection. However, this composite score has insufficient accuracy to recommend clinical use in isolation, and would need to be combined with a further biomarker or other clinical information in order to have clinical utility. Ulcer area improves discrimination marginally. Venous procalcitonin is unhelpful for mild DFU infection.

Session 11: Stewardship

1. **Self-assessment of antimicrobial stewardship in primary care: analysis of self-reported practice using the TARGET Primary Care Self-Assessment Tool**

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Objectives

The Primary Care Self-Assessment Tool within the TARGET Antibiotics Toolkit eLearning module (www.rcgp.org.uk/targetantibiotics), enables prescribers to assess their antimicrobial stewardship (AMS). It provides a baseline for prescribers to assess their behaviour in comparison to others in their locality and nationally (UK), and to determine changes in their practice over time.

Method

Before completion of the Royal College of General Practitioners' eLearning module 'Antibiotic Resistance in Primary Care' participants are asked to complete an electronic Self-Assessment Tool. We analysed responses between November 2014 and June 2016.

Results

1634 healthcare professionals completed the self-assessment. 97% used antibiotic guidance for the treatment of common infections, although only 61% reported that this was made available to all temporary prescribers. 49% reported undertaking a practice-wide antibiotic audit in the last two years and 57% kept a written record and practice action plan.

93% of GPs reported that they used back-up/delayed prescribing when appropriate. 37% had a strategy in place to avoid patients re-consulting with other clinicians to obtain antibiotics. 66% used patient focused strategies to highlight the importance of responsible antibiotic use. 31% had undertaken an antibiotic related educational module.

Conclusions

Antibiotic guidance and delayed prescribing are used by most prescribers. However to help optimise antimicrobial use GP staff need to also make guidance available to temporary prescribers, perform regular audits with action planning, and maximise patient focused strategies. Professional education and use of this tool should be encouraged locally to monitor AMS.

2. A feasibility cluster randomised controlled trial of a complex intervention to reduce antibiotic prescribing in children presenting to primary care with acute respiratory tract infection and cough; results from the CHICO trial.

Niamh M Redmond[1], Sophie Turnbull[2], Patricia Lucas[2], Christie Cabral[2], Jeremy Horwood[1], Jenny Ingram[2], Padraig Dixon[2], Sandra Hollinghurst[2], Tim J Peters[2], Nick Francis[3], Alastair D Hay[2], Peter S Blair[2]

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Objectives

Children with respiratory tract infections (RTIs) frequently visit primary care services and receive antibiotics, despite many illness resolving without treatment. Recent literature suggests solutions to reduce indiscriminate antibiotic use are likely to involve multifaceted, complex interventions. Combining empirical evidence and a behavioural model we developed a 'within-consultation' web-based intervention to reduce antibiotic prescribing by reducing uncertainty about hospitalisation risk, eliciting parental concerns, and providing individualised care advice. A feasibility cluster randomised controlled trial (RCT) was conducted to explore recruitment, retention and acceptability of the intervention (main outcomes), test health economic data collection, and inform a future trial.

Method

32 GP practices in south west England were recruited and randomised (stratified by prescribing rate and practice size) into either an intervention or usual care group. With informed consent, children aged 3 months-12 years consulting with acute cough and RTI were recruited by GPs or prescribing nurses (clinicians). Baseline patient characteristics, symptoms, signs and final treatment decisions were recorded. Fidelity measures were collected and qualitative interviews with clinicians and carers were conducted and analysed. Carers were followed up by telephone, paper or electronically to collect health economic and outcome data. Medical notes were reviewed for the 30 days post recruitment.

Results

Between October 2014 and March 2015, 501 children were recruited (92.4%). Antibiotic prescribing rate was 25% (intervention) and 15.8% (control) groups. Evidence of differential recruitment between the two groups (intervention n=292 vs. control n=209) was found. Children in intervention group were younger (p=0.03) had a higher respiratory rate (p<0.0001), wheeze prevalence (p=0.007) and higher parental (p=0.045) and clinician illness severity scores (p=0.01). Clinician interviews suggested preferential recruitment of less unwell children to both groups. Fidelity measures indicated clinicians used the web-based system and median time was 5-6 mins. Electronic data and medical reviews were comprehensive health economic data sources.

Conclusions

Although trial recruitment, retention and intervention acceptability rates were positive, differential recruitment and possible Hawthorne effects may explain the paradoxical antibiotic prescribing rates. Future studies should consider using processes that reduce differential recruitment and promote intervention use for all eligible children. This may be achievable by incorporating the intervention into electronic care records, incentivising intervention use and removing the need for individual patient consent.

3. Investigating cultural determinants for antibiotics prescribing and consumption in Europe

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Objectives

To identifiy cultural determinants for patient preconceptions and expectations of respiratory tract infections and antibiotic treatment and health seeking behaviour.

Method

Semi structured in-depth interviews with adult patients in Norway, France and Polen seeing their doctor with a respiratory tract infection. Patients were interviewed before and after consultation. Each country included approximately 30 patients. The interviews were conducted in the language of each country and later transcribed and translated into English for analysis.

Results

Preliminary results will be presented at the conference

Conclusions

An identification of cultural determinants for antibiotic use and health seeking behaviour related to RTI's, will enable tailor made interventions targeting specific groups and cultures.

4. Continuing professional development concerning AMR for teachers in Europe

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Objectives

Education is one of the strategies recommended by the WHO and EC to combat Antimicrobial resistance (AMR). E-Bug, an educational project for European schools, develops teaching resources for different age groups of students, concerning microbes spread, prevention and treatment of infections. Surveys in France showed teachers don't feel familiar with AMR but consider they have an important role in health education that could be optimized through continuing professional development (CPD).
The aim of this study was to explore characteristics of CPD for upper secondary teachers in Europe in order to identify relevant CPD features for a European training module.

Method

In this survey study online databases were used to gain general data concerning CPD for teachers in different European countries. Most of the information was found in the databases of the Eurydice network and the Organisation for Economic Co-operation and Development (OECD) and the Teaching and Learning International Survey (TALIS). Information about characteristics of CPD for upper secondary teachers in 26 European countries involved in e-Bug was collected concerning types, obligation, organisers, location, facilitators and barriers. The study describes the main differences and similarities in characteristics of CPD activities.

Results

The main characteristics of CPD activities for teachers were: Obligation to undertake CPD activities or not: in 12 of the investigated countries, CPD activities were mandatory. Type of CPD: courses and workshops were the most followed, conferences, seminars, teacher networks and research were also popular. The organisers were often independent professional organisations, education institutions and schools at local or national levels. The main facilitators were financial, scheduled time to attend CPD and promotion. The main barriers were lack of incentives, conflict with work schedule, high costs of CPD, lack of relevant CPD activities and family responsibilities.

Conclusions

Considering the similarities and differences of CPD characteristics between countries it seems reasonable to develop a free, open, easily accessible online course for European teachers concerning AMR, adaptable to each country's specific practice. Close collaboration with educational institutions and accreditation would be an advantage. Several studies have shown that if teacher's knowledge increases, the achievement of students' increases and it becomes more likely that students implement this knowledge into their lifestyle. Developing relevant courses for teachers about AMR adapted to their specific needs could help teachers optimizing their teaching and thus contribute to improving antibiotic use.

Session 12: Diagnosis/Prognosis

1. Clinical decision rules to diagnose acute rhinosinusitis among adults in primary care

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Objectives

Acute rhinosinusitis (ARS) is commonly treated with antibiotics, although fewer than half of episodes represent acute bacterial rhinosinusitis (ABRS). The objective of our study was to develop clinical decision rules (CDRs) for the diagnosis of ARS and ABRS.

Method

Reference standards for the diagnosis of ARS were purulent antral puncture fluid or abnormal computed tomography scan (CT), and for ABRS was positive bacterial culture of antral fluid. For each reference standard, we developed two CDRs: a point score based on a logistic regression model and an algorithm based on a classification and regression tree (CART) model. We identified low, moderate, and high risk groups for ARS or ABRS for each CDR**.**

Results

The point scores each had between 5 and 6 predictors, and an area under the receiver operating characteristic curve (AUROCC) between 0.721 and 0.767. For positive bacterial culture as the reference standard, low, moderate and high risk groups had a 16%, 49% and 73% likelihood of ABRS, respectively. CART models had an AUROCC ranging from 0.783 to 0.827. For positive bacterial culture as the reference standard, low, moderate and high risk groups had a likelihood of ABRS of 6%, 31% and 59% respectively.

Conclusions

We have developed a series of clinical decision rules integrating signs, symptoms and CRP that diagnose ARS and ABRS with good accuracy. They now require prospective validation and an assessment of their effect on clinical and process outcomes.

2. Disease course of lower respiratory tract infection with a bacterial aetiology in primary care

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Objectives

Bacterial pathogens are assumed to cause a different illness course than non-bacterial causes of acute cough, but evidence is lacking. Insight into the illness course of bacterial lower respiratory tract infection (LRTI) that is not treated with antibiotics could help guide empirical antibiotic prescribing, support a strategy of watchful waiting, and improve patient information. We evaluated the disease course of LRTI with a bacterial aetiology in adults presenting with acute cough in primary care.

Method

Secondary analysis of a multi-centre European trial in which 2061 adults with acute cough (≤ 28 days' duration) were recruited from primary care and randomised to amoxicillin or placebo. For this analysis only patients in the placebo group (n=1021) were included reflecting natural course of disease. Standard microbiological and serological analysis were performed at baseline to define bacterial aetiology. All patients recorded symptoms in a diary each day for four weeks. Disease course of patients with a bacterial aetiology was compared to those without bacterial aetiology on symptom severity, duration of symptoms rated 'moderately bad or worse' and re-consultation.

Results

Of 1021 eligible patients, 187 were excluded because of missing diary results, leaving 834 patients of whom 162 (19%) had bacterial LRTI. Patients with bacterial LRTI had worse symptoms at day 2-4 after presentation (difference= 0.19, 95% CI 0.01-0.36; p=0.038) and more often re-consulted 27% (44/162) vs. 17% (114/660) than those without bacterial LRTI (OR 1.80, 95% CI 1.20-2.71; p=0.005). Resolution of symptoms rated ‘moderately bad or worse' did not differ between patients with and without bacterial LRTI (HR 0.92, 95% CI 0.77-1.10; p=0.363).

Conclusions

Patients who present in primary care with acute bacterial LRTI have a slightly worse course of disease when compared to those without an identified bacterial aetiology, but the relevance of this difference is doubtful.

3. Predicting poor prognosis in adults presenting to primary care with acute cough

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Objectives

Identification of acute cough patients at high risk of poor prognosis (hospitalisation or re-consultation with new or worsened complaints) could improve the outcome, while safely reducing antibiotic use. We developed a prediction rule to identify adults presenting to primary care with acute cough at greater risk of poor prognosis (GRIN 2015). We now aim to ❶ stabilize that prediction rule, ❷ compare the new prediction rule to existing ones (PSI, CRB, CURB, CRB-65 and CURB-65), ❸ assess the effect of antibiotic prescribing on prognosis, and ❹ assess the added predictive value of C-reactive protein (CRP) and blood urea nitrogen (BUN).

Method

The prediction rule presented at GRIN 2015 was constructed using data collected within the GRACE (Genomics to combat Resistance against Antibiotics in Community-acquired LRTI in Europe) suit of prospective LRTI studies in primary care, and a random forest approach. This prediction rule was stabilized by adjusting the random forest approach. Performance of the new and existing prediction rules was compared using their area under the receiver operating characteristic curve (AUROC). The effect of antibiotic prescribing on prognosis and the added predictive value of CRP and BUN was assessed through their parameter estimates and p-values.

Results

The new prediction rule accounts for differences between countries, and includes information on phlegm severity, blood pressure, crackles, interference with daily activities and time stopped smoking. Performance characteristics indicate that this prediction rule outperforms existing ones in predicting poor prognosis in adult LRTI patients, although there is room for further improvement.

AUROC (standard error)

PSI

0.5127 (0.0003)

CRB

0.5287 (0.0008)

CURB

0.5348 (0.0021)

CRB-65

0.5339 (0.0008)

CURB-65

0.5336 (0.0017)

New

0.6080 (0.0028)

Antibiotic prescribing (-0.0129, p = 0.9103) did not affect prognosis, and neither BUN (-0.0003, p = 0.9896) nor CRP (0.0007, p = 0.6853) improved the new prediction rule.

Conclusions

Existing prediction rules should not be used to predict poor prognosis in adults presenting to primary care with acute cough. Our prediction rule could be used, although its performance should be improved further. Antibiotic treatment had no effect on prognosis, and inclusion of CRP or BUN did not improve the prediction rule. We suggest to use the prediction rule to identify patients that would benefit from more intensive follow-up. To assess whether this will safely reduce antibiotic prescribing, a prospective evaluation is needed.

Future research will focus on the added predictive value of microbial aetiology and chest X-ray.

4. Predicting pneumonia in primary care: The 3C cohort study of lower respiratory tract infection in primary care

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Objectives

To assess predictors to aid diagnosis of pneumonia in routine primary care

Method

Design: Observational cohort study **Setting**: Adult patients presenting in UK general practice with LRTI had symptoms, signs and treatment recorded. Participants were followed-up for 30 days by chart review. In those receiving chest x-ray within the 30 day window reports were reviewed and assigned a pneumonia/non-pneumonia diagnosis. The predictive value of patient characteristics, presenting symptoms, and clinical findings for the diagnosis of pneumonia was assessed. A cohort of 28867 adult patients with acute cough was recruited in 522 practices between 2009-2013

Results

1485/28867 (5%) patients were x-rayed within 30 days and 718 (2.5.%) within one week of the index consultation and of these 101/718 (14.8%) were assigned a probable pneumonia diagnosis. The significant independent predictors of X ray confirmed pneumonia within one week of consultation are temperature >37.8 degrees and crackles on auscultation. Excluding the possible pneumonia diagnosis (9 cases) resulted in the addition of pulse >100 and oxygen saturation <95% to the model. The AUC of the two factor model was 0.66 (0.61-0.71) and the PPV in those x-rayed in the first week was 32%.

Conclusions

In routine practice x-ray confirmed pneumonia as a short term complication of LRTI is unusual (0.37%). The potential utility of the clinical model and comparison with existing models will be discussed.

Session 13: Prescribing

1. **Do general practitioners (GPs) prescribe more anti-bacterials for acute respiratory tract infections (ARTIs) on Fridays than on other days of the week? A retrospective cohort study from Norway**

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Objectives

Increased use of anti-bacterials is associated with anti-bacterial resistance. A better understanding of GPs' anti-bacterial prescription patterns, including the "non-pharmacological" prescriptions, is important for implementation of a national strategy for appropriate use of anti-bacterials. We wanted to analyse whether GPs were more likely to prescribe anti-bacterials for ARTIs on Fridays than on other days of the week, driven by absence of GP-patient contact at weekends. Furthermore whether such effects were particularly GPs with high workload. And whether broader-spectrum anti-bacterials were more popular on Fridays?

Method

435 Norwegian GPs participating in the RxPAD study delivered data on antibiotic prescription for RTIs through one year before any intervention, comprising 177.262 consultations with 53895 prescriptions. Week day of prescription was the dependent variable. Multivariate logistic regression analysis adjusted for clustering was performed. Confounding variables were included.

Results

Friday's odds for an anti-bacterial were not statistically different from the odds of Monday through Wednesday, but about 9 percent higher than Thursday's odds (Friday OR 1.00 vs. Thursday OR 0.92) looking at the entire data material. Mondays had the highest odds looking at GPs with an even workload distribution through the week (Monday OR 1.0 vs. OR 0.94, 0.93, 0.90, 0.98 for Tuesday-Friday) and Fridays' odds were not significantly different from any of the other days. Thursday had the lowest odds for prescription in the same subgroup of GPs, especially GPs with few consultations (OR 0.72).

Conclusions

We found no evidence of a Friday effect, suggesting an adequate Norwegian system for out-of-hours care over the weekend. Mondays had the highest odds looking at GPs with even workload-distribution through that week, possibly driven by the length of the illness.

2. Investigating the effect of suboptimal antibiotic prescribing in primary care for patients with a UTI or community-acquired pneumonia on hospital admission due to a bloodstream infection.

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Objectives

This study will firstly determine the effect of suboptimal antibiotic prescribing in patients presenting with a urinary tract infection (UTI) or community acquired pneumonia (CAP) at the GP practice on the incidence of community-acquired bloodstream infections (BSI). Secondly, risk factors associated with developing a community-acquired bloodstream infection after a suboptimal antibiotic dose has been taken will be identified.

Method

This will be a retrospective cohort study using data from CPRD linked to HES data and ONS mortality data. All adult (18+) patients diagnosed with a UTI or CAP and have subsequently received antibiotics (2007-2014) will be included. Prescriptions will be compared with the PHE national guidelines with regard to the appropriateness of the drug, dose and treatment duration. Patients will be followed up for 60 days to monitor the incidence of BSI hospital admission. Survival analyses and logistic regression will be used to determine the association between suboptimal antibiotic treatment and BSI incidence adjusted for patient risk factors.

Results

The study population consists of 507,190 patients with a UTI and 147,219 patients with CAP who meet the inclusion criteria and have linked HES and ONS data (where applicable). All models will adjust for patient age, sex, region, pregnancy, BMI and comorbidities such as diabetes, cardiovascular disease, antibiotic allergies, smoking frequency and alcohol consumption. Only the UTI analyses will additionally adjust for STIs and only the CAP analyses will additionally adjust for COPD, asthma and pneumococcal/influenza vaccinations. This study is currently in the data cleaning/analysis phase and there are therefore no results from the survival or logistic regression analyses currently.

Conclusions

Findings from the study could serve to provide evidence to support compliance with National Antibiotic Prescribing Guidelines in primary care Trusts across England and highlight the importance of Antimicrobial Stewardship in primary care.

3. Adverse events in patients taking macrolide antibiotics for any indication

Malene Plejdrup Hansen[2], Amanda McCullough[1], Sarah Thorning[3], Jeffrey Aronson[4], Elaine Beller[1], Paul Glasziou[1], Tammy Hoffmann[1], Justin Clark[1], Chris Del Mar[1]
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Objectives

Macrolides are among the most commonly prescribed antibiotics worldwide.
However, taking macrolides exposes patients to the risks of various adverse events including diarrhoea, rash and antibiotic resistance. Current understanding of adverse events in patients taking antibiotics is largely derived from observational studies, in which estimates may be biased, because it is hard to distinguish adverse drug reactions from disease related symptoms.
One way of addressing this problem is to investigate adverse events reported in randomised placebo-controlled trials.
We have quantified the incidence of all reported adverse events in patients taking macrolide antibiotics for any indication, compared with placebo.

Method

We searched The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, LILACS, and Web of Science from inception to March 2016 for randomised, participant-blinded, placebo-controlled trials. We also searched the reference lists of all included records, the WHO International Clinical Trials Registry Platform (ICTPR), and ClinicalTrials.gov for other published, unpublished, and ongoing trials.
We limited the search to the most commonly used macrolide antibiotics: azithromycin, clarithromycin, erythromycin, and roxithromycin. Two authors independently screened potentially relevant studies, extracted data, and assessed study quality.

Results

We retrieved a total of 3662 records, after duplicates were removed, and 424 full-text records were assessed for eligibility. A total of 170 studies have been included, and data extraction and quality assessment are completed. We will summarise reported adverse events using meta-analysis, and when data cannot be combined statistically we shall report outcomes narratively.
We will present the results at the conference.

Conclusions

This review is an adjunct to the large amount of existing evidence of the benefits of antibiotic treatment, and the findings can be used when the benefit-harm trade-off of antibiotic treatment with macrolides is considered.

This abstract is based on a draft and pre-peer reviewed version of "Adverse events in patients taking macrolide antibiotics versus placebo for any indication (Protocol)". Upon completion and approval, the final version is expected to be published in the *Cochrane Database of Systematic Reviews* (www.cochranelibrary.com)."

4. Antibiotics for acute respiratory tract infections: A mixed methods study of patient experiences of non-medical prescriber management

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Objectives

To 1) explore patients' expectations and experiences of nurse and pharmacist non-medical prescriber -led management of respiratory tract infections, 2) to examine whether patient expectations for antibiotics affect the likelihood of receiving them, and 3) to understand factors influencing patient satisfaction with respiratory tract infection consultations.

Method

A mixed methods design was used in which questionnaire data was collected from patients (n=120) and interviews were undertaken with patients (n=22) and nurse and pharmacist non-medical prescribers (n=16) following consultations for respiratory tract infections.

Results

Patients had multiple expectations of their consultation and 44% expected an antibiotic. There was alignment between self-reported patient expectations and those perceived by non-medical prescribers. Patient expectations for non-antibiotic strategies, including education for self-management, were associated with receipt of those strategies, whereas patient expectations for an antibiotic were not associated with receipt of these medications. Patient-centred management strategies were received by 72.5% of patients. Regardless of patients' expectation or management strategy employed, high levels of satisfaction were reported. Taking concerns seriously, conducting a physical examination, sharing treatment decisions, and lack of time restrictions, each contributed to patient satisfaction.

Conclusions

Non-medical prescribers demonstrate an understanding of patient expectations of respiratory tract infection consultations and use a range of management strategies without recourse to antibiotics, particularly in terms of taking a patient-centred approach. Patients' expectations of respiratory tract infection consultations were met and prescribers were not influenced by patient expectations for an antibiotic. Patients were satisfied with the consultation, indicating that strategies used were acceptable. These findings illustrate that it is possible to maintain patient satisfaction without prescribing an antibiotic. Given the increasing pressure on general practice surgeries, non-medical prescribers have an important role.

Session 14: Stewardship

1. Taking steps: Country Dialogue Meetings to formulate national action plans to stimulate a more prudent use of antibiotics

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Objectives

To stimulate a more prudent use of antibiotics it is important to have efficient collaboration on a national level with all involved stakeholders. Especially in countries with higher rates of non-prudent use, there is need for more actions on the policy level. Therefore, various stakeholders from six European countries with higher rates of non-prudent use were engaged in Country Dialogue Meetings. The aim of these meetings was threefold; (1) to discuss the problem of non-prudent use of antibiotics in the country, (2) to discuss relevant policy options and (3) to formulate country-specific recommendations to stimulate the prudent use of antibiotics.

Method

The Country Dialogue Meetings were organized in six European countries where antibiotic use without a medical prescription is more prevalent than in other European countries; Cyprus, Greece, Hungary, Italy, Spain and Romania. The meetings were organized in close collaboration with local organizers. In each country a bottom-up approach was used, meaning that the local actors were leading in formulating a strategy and in selecting priorities for stimulating the prudent use of antibiotics in their country.

Results

The meetings were attended by 13 to 30 stakeholders' representatives per country. Especially the involvement of consumer organizations was considered to be essential. Each country formulated an Action Plan to enhance the prudent use of antibiotics. Overall, the most important element was patient and professional education. In addition, each country had specific elements they considered as important. For instance, Italy, Greece and Hungary noted it is essential to stimulate an effective use of vaccinations. Although stakeholders in all countries agreed about the importance of continuing their collaboration in the future, there are some hampering factors like the lack of leadership.

Conclusions

The Country Dialogue Meetings resulted in Action Plans in all six countries and it motivated stakeholders to collaborate. Yet, there was variation across the countries with regard to the level of awareness among stakeholders on the problem of antimicrobial resistance (AMR). While in some countries stakeholders agreed that AMR and the non-prudent use of antibiotics was a problem that they should jointly combat, in other countries stakeholders were more hesitant about this. It would therefore be useful to have a follow-up of the Country Dialogue Meetings in order to see how the countries proceed with the Action Plans they formulated.

2. Long-term effect of a practice-based intervention aimed at improving antibiotic prescribing in patients with respiratory tract infections.

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Objectives

A group of Spanish GPs participated in a multifaceted intervention in 2009 which consisted of discussion sessions of the results of the first registry carried out one year before, courses for GPs, guidelines on respiratory tract infections (RTI), patient information leaflets, workshops on rapid tests and the implementation of rapid antigen detection tests and C-reactive protein tests in their offices. The antibiotic prescribing halved in the second registry that took place after the intervention (95% CI, 0.44–0.57). A third audit-based registry was carried out 6 years after the intervention aimed at assessing its long-term effect on antibiotic prescribing.

Method

The 210 GPs from 8 areas who had completed the first and second registries in January-March 2008 and 2009 were invited to participate in the third registry. As in the previous registries, they were instructed to fill out a template for all the patients with RTIs during 15 working days in January-March 2015. A new group of GPs who had never participated in courses on the rational use of antibiotics from the same areas were also invited to participate and acted as controls. A multilevel logistic regression was performed considering the prescription of antibiotics as the dependent variable.

Results

121 GPs exposed to the intervention in 2009 (57.6%) and 115 control GPs agreed to participate in the present study, registering 21,172 RTIs. On adjustment for co-variables, compared to the antibiotic prescription observed after the intervention, intervened GPs prescribed slightly more antibiotics in 2015, albeit without statistically significant differences (OR, 1.1; 95% CI, 0.91–1.34), but GPs allocated to the control group prescribed significantly more antibiotics (OR, 2.75; 95% CI, 2.09–3.61). Regarding cases of pharyngitis/tonsillitis, the antibiotic prescription was significantly higher in both groups of GPs in 2015 compared to the prescription observed in the intervention group in 2009.

Conclusions

Antibiotic prescribing observed in the control group in 2015 reflects the global increase of antibiotics reported in Spain over the last years. This study shows that a multifaceted intervention still reduces antibiotic prescribing 6 years after this took place. However, the modifications of GP prescribing behaviour were maintained for only some RTIs.

3. ***An illness-focussed interactive booklet to optimise management and medication for childhood fever and common infections in out-of-hours primary care: a cluster randomised trial***

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Objectives

Fever is the most common reason for a child to be taken to a general practitioner (GP). It is mostly caused by self-limiting infections which do not require antibiotic treatment. However, antibiotic prescription rates remain high, especially during out-of-hours care. Anxiety and lack of knowledge among parents, and perceived pressure to prescribe antibiotics amongst GPs, are important determinants of excessive prescriptions. An illness-focussed interactive booklet can potentially improve this by providing parents with information on self-management strategies. This study aimed to determine the effectiveness of an interactive booklet on management of children presenting with fever at Dutch GP out-of-hours cooperatives.

Method

A cluster RCT with 20 GP out-of-hours cooperatives randomised to: GP access to the interactive booklet or care as usual. The booklet consists of: a traffic light system for parents on how to respond to fever-related symptoms, benefit and harms of medication and safety net instructions. Children <12 years with parental reported or physician measured fever were included. Primary outcome: antibiotic prescribing during initial consultation. Sample size was based on an expected difference in baseline prescribing rate of 25% in the control group and 19% in the intervention group. Secondary outcomes: (intention to) (re-)consultation, prescriptions during re-consultations, referrals, parental satisfaction and reassurance.

Results

GPs at the 20 GP out-of-hours cooperatives recruited the target of 20,000 children with fever from November 2015 to May 2016. Statistical analysis is currently ongoing using descriptive statistics and by fitting two level (GP-out-hours centre and patient) random intercept logistic regressions models. Analysis is based on intention to treat principle. This trial was registered with ClinicalTrials.gov, number NCT02594553 and approved by the ethical committee of Zuyderland-Zuyd (METC Z) in Heerlen, the Netherlands (Ref 14-N-171).

Conclusions

This will be the first and largest cluster RCT that will evaluate the effectiveness of using an illness-focused interactive booklet during GP out-of-hours consultations with febrile children on antibiotic prescriptions. It is hypothesized that the use of the booklet during consultations for febrile children at GP out-of-hours centres will result in a reduced number of antibiotic prescriptions, improved parental satisfaction and reduced intention to re-consult. The first results will be available during the 2016 GRIN meeting.

Session 15: Budding Ideas

1. **Prescribing antibiotics in general practice: The use of microbiological testing and other factors influencing decision-making and prescribing behaviour**

Rikke Vognbjerg Sydenham[1], Malene Plejdrup Hansen[2], Line Bjørnskov Pedersen[3], René dePont Christensen[1], Dorte Ejg Jarbøl[1]
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Objectives

The majority of antibiotics are prescribed from general practice. The use of broad-spectrum antibiotics increases the risk of development of bacteria resistant to antibiotic treatment. In spite of guidelines aiming to minimize the use of broad-spectrum antibiotics we see an increase in the use of these agents. The overall aim of the project is to explore factors influencing the decision process and the prescribing behaviour of the GPs when prescribing antibiotics. We will study the impact of microbiological testing on the choice of antibiotic. Furthermore the project will explore how the GPs' prescribing behaviour is influenced by selected factors.

Method

The study consists of a register-based and a questionnaire study. The register-based study is based on data from the Register of Medicinal Product Statistics (prescribed antibiotics), Statistics Denmark (socio-demographic data), Danish Provider Registry (GP characteristics and organisation), and the Danish Microbiology Database (performed microbiological testing). We will assess the use of microbiological testing prior to antibiotic prescription. Furthermore we will investigate associations between GP characteristics, use of microbiological investigations and description patterns. The questionnaire comprising a discrete choice experiment will investigate the relative importance of selected factors (e.g. microbiological diagnostics, point-of-care tests, patients' expectations) in the management of infectious diseases.

Results

This PhD project is scheduled to be carried out in 2016-2019. The hypotheses and anticipated perspectives will be discussed at the meeting.

Conclusions

This project will contribute with solid knowledge on diagnostic approaches for management of infections in Danish general practice. The results will create a base for targeted interventions aiming to optimize diagnostic approaches to infectious diseases benefitting the individual patient and society as a whole.

2. The clinical and cost-effectiveness of spironolactone versus lymecycline for moderate or severe persistent acne in adult women: proposal for a multicentre parallel-arm randomised controlled trial

Miriam Santer[1], Nick Francis[2], Matthew Ridd[3], Ingrid Muller[1], Alison Layton[4], Beth Stuart[1], Paul Little[1]

[1]University of Southampton, Southampton, UK, [2]Cardiff University, Cardiff, UK, [3]University of Bristol, Bristol, UK, [4]Harrogate & District NHS Foundation Trust, Harrogate, UK

Objectives

Over 3% of people aged 13-25 years consult for acne each year. A third of these are prescribed long courses of oral antibiotics, most commonly lymecycline. Spironolactone is used off-license in acne due to its antiandrogenic properties but there is no convincing evidence for its use.

Our proposal seeks to answer the research question: Is oral spironolactone non-inferior to oral lymecycline at reducing acne severity in adult women with moderate-severe persistent acne?

Method

We will recruit women aged 18 years or over with moderate-severe persistent acne through primary and secondary care. Following informed consent, participants will be computer randomised to either:

oral spironolactone once daily for 24 weeks; initially 50mg once daily to be increased if necessary to 100 mg once daily if insufficient treatment response after 6 weeks

or:

oral lymecycline 408 mg once daily for 24 weeks.

In both groups topical combination product of benzoyl peroxide/adapalene will be added if there is insufficient treatment response after 12 weeks. We will use a single-blind design with objective outcome assessment.

Results

Our proposed primary outcome is the Leeds Revised Acne Grading Scale (LRAGS) comparison between groups in mean change from baseline to 12 weeks. LRAGS is a 12-point pictorial scale ranging from mild to very severe. Our sample size calculation is based on a non-inferiority margin of one grade mean change between groups at 12 weeks.

Secondary outcomes include: self-assessment of LRGAS; participants' rating of overall improvement on 6-point Likert scale; antimicrobial resistance; clinical and serum biochemical markers for polycystic ovary disease.

Although primary outcome will be judged at 12 weeks we will continue to follow-up patients to 52 weeks.

Conclusions

Guidelines recommend that oral antibiotics should be used together with a non-antibiotic topical therapy but ‘usual care' is oral antibiotics as monotherapy. We are therefore assessing spironolactone against usual care.

3. Comparison of guidelines on acute sore throat

Jan Matthys
General Practice, Gent, Belgium

Objectives

PURPOSE Many countries have national guidelines for the treatment of pharyngitis. We compared the recommendations and the reported evidence in national guidelines for the management of acute sore throat in adults. The purpose is to look at evolutions in recommendations.

Method

Guidelines were retrieved via MEDLINE and EMBASE and through a Web-based search for guideline development organizations. The content of the recommendations and the underlying evidence were analysed with qualitative and bibliometric methods.

Results

Recommendations still differ with regard to the use of a rapid antigen test and throat culture and with the indication for antibiotics. American guidelines consider diagnosis of group A streptococcus essential, whereas in different European guidelines, acute sore throat is considered a self-limiting disease and antibiotics are not recommended. The evidence used to underpin these guidelines still differs.

Conclusions

Although the evidence for the management of acute sore throat is easily available, national guidelines are different with regard to the choice of evidence and the interpretation for clinical practice. These findings are important in the context of appropriate antibiotic use, the problem of growing antimicrobial resistance, and costs for the community. There is a need to evolve to a consensus about a European guideline on acute sore throat.

4. **Will routinely collected data [RCD] ever surpass self-report? Using routine data for infections research**

Fiona Lugg
Cardiff University, Cardiff, UK

Objectives

Objective 1 - To identify the current caveats of using RCD in infections research as compared with self-report data
Objective 2 - Development and evaluation of an intervention to enable research-acceptable RCD for infections research

Method

A literature review of the current publications on self-report vs. RCD in infection research and key infections outcomes that could have been reported using RCD.

The next step would be to conduct an online focus group / discussion with users of routine data for health research / infection research to identify barriers/facilitators for using RCD.

A workshop / Delphi style meeting to reach a consensus on key changes/solutions or key messages would feed into the development of an intervention. This would include academics, data providers, clinicians, public health, infection control, data analysts.

Results

Based on the findings above, an intervention / solution for researchers would be developed to enable better use of RCD for infection research. (Ideas: An intervention with clinicians or data providers / data analysts.)
Key deliverables and outcomes would be identified that could measure success of the intervention.
A natural experiment would be one way to track the effects of the intervention (changes of coding over time) or systematic literature review to track changes in publications on infections + RCD over time.

Conclusions

The major benefit for using RCD as a resource for research is the ability to access data from a large population of patients across the UK. However, it is important to remember that the data are collected primarily for clinical and routine use rather than specifically for research.
Using routine data can considerably reduce costs for a project, however it will only be possible if the data are research-acceptable.

5. Intervention on promoting prudent antibiotic use in long term care facilities, a cluster-randomised trial, using a stepped wedge model

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Objectives

Several countries have prepared national action plans to combat antibiotic resistance. Norway is currently to implement the national action plan, providing the two National centers for antibiotic use in primary care and hospitals, with an opportunity to conduct research on the implementation of interventions outlined for LTCF (Long term care facilities) and hospitals. The Norwegian action plan on antibiotic resistance aims to achieve a 30% reduction in human antibiotic consumption by 2020. However, changing prescribing behavior is complex and involves contextual factors. To date, no Norwegian studies to promote prudent antibiotic use have been published from LTCF.

Method

Antimicrobial stewardship interventions (ASI) can target to educate health personnel, publish and implement antibiotic guidelines, provide feedback on prescribing practices, restrict use of specific antibiotics, implement healthcare information technologies, such as computerized decision support systems, establish multidisciplinary antimicrobial stewardship teams, and tailor interventions to the recipient.

Forty Norwegian LTCF (clusters) from 20 counties (2 per county), will be recruited by invitation. Inpatients with an infection diagnosis are eligible for inclusion in the study. The LTCF will appoint healthcare professionals, who will be involved in the development, implementation and evaluation of the interventions. Clusters will be randomized to interventions by county.

Results

A pilot study in the county of Østfold county is planned late 2016, to test all parts of the intervention and data registrations.

Conclusions

Research questions:

1) To what degree is antibiotic prescribing in LTCF adherent to the national guidelines?

2) To what extent can ASI lead to lower total antibiotic use in LTCF?

3) To what extent can ASI reduce use of broadspectrum antibiotics in LTCF?

4) To what extent can ASI improve diagnostics of urinary tract infections (UTIs) in the LTCF?

5) To what extent can ASI lead to a more adequate use of metenamin for prevention of UTIs?

6. Increase in antibiotic prescriptions in Out of Hours primary care in contrast to in-hours primary care prescriptions: service evaluation in a population of 600,000 patients

Gail Hayward, Rebecca Fisher, Graeme Spence, Daniel Lasserson
University of Oxford, Oxford, UK

Objectives

Despite the growing importance of antimicrobial guardianship in primary care, there have been no published evaluations of antibiotic prescribing practices in Out-of-Hours services in the UK. Concerns exist that governmental drives to decrease antimicrobial prescribing in in-hours primary care may displace antibiotic prescribing to the OOH service but there is, as yet, little evidence to substantiate these fears. We aimed to describe antibiotics prescribing practices in an OOH primary care service and to compare trends in prescribing with the in hours GP services in the same population.

Method

In this retrospective service evaluation we established a database of 496942 patient contacts to Oxfordshire OOH primary care between May 2010 and August 2014, including details of patient demographics and antibiotic prescriptions. Comparison of time trends in antibiotic prescriptions from OOH primary care and in-hours primary care for the same population was made using multiple linear regression models fitted to the monthly data for out of hours prescriptions, out of hours contacts and in hours prescriptions between September 2010 and August 2014.

Results

Compared to the overall population contacting the OOH service, younger age, female sex, and lower deprivation score were all independently correlated with an increased chance of a contact resulting in antibiotic prescription. Despite a reduction in patient contacts with the OOH service, antibiotic prescriptions from this service rose during the study period (increase of 37.1 monthly prescriptions each year (CI: 10.6 to 63.7)). A matching increase was not seen for in-hours antibiotic prescriptions, and the difference between the year trend for out of hours and in hours prescriptions was significant (Z test, $p = 0.002$**).

Conclusions

We have demonstrated trends in prescribing which could represent a partial displacement of antibiotic prescribing from in hours to OOH primary care. There would be merit in examining this more closely across a range of OOH service providers to see if the trends we describe are evident nationally or internationally.

7. An audit of the treatment of female urinary tract infections in a General Practice using the electronic health record

Francis Collett-White[1], Gwyneth Rogers[2]
[1]Oxford University NHS Foundation Trust, Oxfordshire, UK, [2]West Bar Surgery, Banbury, UK

Objectives

Antibiotic resistance is an increasing problem in the UK, particularly in the treatment of urinary tract infections. General practices are well equipped to monitor their antibiotic use since much of their prescribing is recorded electronically. This audit aimed to assess compliance with the local CCG guidelines for the treatment uncomplicated urinary tract infections in females over 16 years of age. The audit method can then be used by other GP surgeries across the NHS to improve antimicrobial use in urinary tract infections (UTI).

Method

Data was collected from a large general practice of approximately 17,000 patients from a medium sized town. All consultations in April 2016 with a READ code of a UTI and related terms were linked with the prescribed antibiotic, dose, frequency and duration. All females aged greater than 16 with a first presentation of a UTI were included. Patients were excluded if they were pregnant, male, less than 16 years old, had a catheter, urinary tract abnormality or recurrent UTI. The data was grouped and analysed using Excel.

Results

In April 2016, 59 patients were diagnosed with a UTI, 44 patients were excluded, and 15 patients fitted the inclusion criteria. 12/15 (80%) of patients were treated with trimethoprim or nitrofurantoin of which 11/15 (73%) were treated for the recommended 3 days. Of those not treated according to the CCG guidelines, 1/15 (7%) treated with amoxicillin, 2/15 (13%) with co-amoxiclav and 1/15 (7%) was treated for greater than 3 days.

Conclusions

The local CCG guidelines for the treatment of an uncomplicated UTI in a female is followed in the majority of cases, however improved adherence would reduce use of broad spectrum antibiotic use. This audit also highlighted the high number of consultations for UTI in males, children and with patients with a recurrent or failed UTI. This audit can be repeated in other GP practices using the same electronic health record to assess their own adherence to local guidelines using the same method of data extraction and analysis.

TRACE Update

1. **A ten minute TRACE e-learning to disseminate GRACE results to primary care clinicians**

Veronique Nussenblatt, Sibyl Anthierens, Sarah Tonkin-Crine, Jochen Cals, Niels Adriaenssens, Katelijn Nijsmans, Nick Francis, Theo Verheij, Chris Butler, Paul Little, Herman Goossens, Samuel Coenen on behalf of the TRACE project group.

Objectives

To disseminate the GRACE results to primary care clinicians TRACE engaged in the construction of a ten minute e-learning. It aims to empower clinicians to deliver effective and safe management of patients presenting to primary care with acute cough while reducing antibiotic use.

Methods

The e-learning is based on GRACE results, effective learning theory and electronic educational approaches such as gaming.

Results

The e-learning consists of two modules:

1) The first and main module is a ten minute module based on communication skills training from GRACE INTRO and built around the seven elements for an effective consultation. The information in GRACE INTRO for each of these elements are pared down to fit an e-learning approach, including the main messages and suggested phrases to use during a patient encounter. Users will be able to view the relevant section of the GRACE INTRO booklet when hovering over key words.

2) The second module presents relevant GRACE results to provide the evidence base for the first module. It takes the format of questions and answers. The answers contain straightforward messages gleaned from the GRACE results with the references and links to abstracts on Pubmed.

Discussion

The e-learning currently is in English, but the goal is to have it translated into other European languages and to have it implemented at national level. The project group welcomes any feedback from GRIN participants.

Session 16: UTI

1. The Point Of carE testing for urinary Tract Infection in primary Care (POETIC) study (Stage 4): A qualitative study to explore the barriers and benefits of using a POCT to aid the management of uncomplicated UTI in primary care

Emma Thomas-Jones[1], Lucy Brookes Howell[1], Khurram Hashmi[1], Nick Francis[1], Paul Little[3], Michael Moore[3], Carl Llor[2], Janine Bates[1], Kerry Hood[1], Theo Verheij[4], Chris Butler[5]
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Objectives

Urinary tract infection (UTI) is the most frequent bacterial infection affecting women and accounts for about 15% of antibiotics prescribed in primary care. Many other women turn out not to have a microbiologically confirmed UTI but have been prescribed antibiotics or antibiotics to which the organism is resistant. Inappropriate antibiotic prescribing unnecessarily increases risk of side effects, drives antibiotic resistance, and wastes resources.

This study aimed to explore clinicians' accounts of diagnosis and management of UTI in routine primary care, and investigated the barriers and benefits of using the Flexicult POCT as a tool for aiding management of UTI.

Method

Interviews were conducted with clinicians across the 4 research networks that took part in the trial (England, Wales, Spain and the Netherlands). The interviews were semi-structured and conducted by telephone. The topic guide consisted of: usual routine management for women with suspected UTI, opinions on the Flexicult POCT and participation in the trial.All interviews were conducted in the native language for the network and audio-recorded. Transcripts were translated were required into English. The data was coded using NVivo 10, using a coding frame based on the interview topic guide. Data was analysed thematically.

Results

35 interviews were conducted.

Diagnosis of UTIs was based on patient history, symptoms and use of dipsticks /dipslides. GPs felt more confident in diagnosing UTIs than nurses.

Advantages of the POCT were the availability of results, particularly the indication of the most appropriate antibiotic to prescribe. The POCT had a positive impact in raising awareness that a potential UTI could be attributed to something other than a bacterial infection, and had raised awareness of antibiotic resistance.

The main barriers were time and difficulty in interpreting results, timing of presentation (e.g. unable to read the plate at weekends) and staffing issues.

Conclusions

Flexicult was useful for increasing the awareness of antibiotic resistance, allowing clinicians to consider other causes of urinary symptoms, especially in the elderly. Clinicians were able to change antibiotics according to the sensitivities of the test which was deemed better for the patients. However, the main barrier was that Flexicult was not a true POCT as it took 24 hours for the results to be available.

2. **Use of methenamine as preventive treatment in women with recurrent urinary tract infections. Is it effective?**

Linda Rui, Morten Lindbaek, Svein Gjelstad
University of Oslo, Oslo, Norway

Objectives

Urinary tract infections (UTIs) are the most common bacterial infections in women of all ages. An estimate of 40% of women has a new urinary tract infection within six months after an initial infection. A Cochrane meta-analysis from 2012 has investigated the impact and benefits of methenamine as preventive treatment for urinary tract infections. The authors conclude that it may be effective to treat UTI prevention with methenamine. In Norwegian general practice, methenamine is prescribed as long term treatment, especially in older women to prevent recurrent UTIs, and accounted for 19 % of the total Norwegian antibiotic prescribing in 2014.

Method

A complete history of antibiotics dispensed from all Norwegian pharmacies, collected from the Norwegian prescription database (NorPD) 2005 to 2015, was analysed. Women > 50 years old with recurrent UTIs were included, defined by two or more incidents within six months, or three or more within twelve months. The UTI antibiotics included were nitrofurantoin, pivmecillinam, trimethoprim and ciprofloxacin. Any time span for use of methenamin was identified, and the use of UTI antibiotics during this time span was compared with the patients that did not receive methenamine treatment.

Results

Preliminary results will be presented at the conference.

Conclusions

Preliminary conclusions will be presented at the conference.

3. Ibuprofen versus mecillinam for uncomplicated cystitis in women - a double blind randomized trial

Ingvild Vik[1], Marianne Bollestad[1], Nils Grude[1], Anders Bærheim[4], Sigvard Mölstad[5], Lars Bjerrum[6], Morten Lindbæk[1]

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Objectives

Although uncomplicated cystitis is often self-limiting, most patients will be prescribed an antibiotic treatment. Previous studies have demonstrated that use of an NSAID can reduce the need for antibiotics in these patients. We wanted to investigate whether treatment with an NSAID was as effective as an antibiotic in achieving symptomatic resolution in women with uncomplicated cystitis.

Method

This was a randomized, controlled, double blind trial. Women between the ages of 18 to 60 presenting with symptoms of uncomplicated cystitis were screened for eligibility. 383 women from four sites in Norway, Sweden and Denmark were allocated to treatment with either 600 mg ibuprofen three times a day or 200 mg mecillinam three times a day for three days. The primary outcome was the number of patients who felt cured by day four. Secondary outcomes were the number of patients in need of a secondary medical consultation and, among these, how many developed an upper urinary tract infection.

Results

Data from all the sites have been collected and we are about to start working on the analysis.

Conclusions

We aim to be able to present some preliminary data at the GRIN meeting in October 2016.

4. Clinical and bacteriological effects of per oral pivmecillinam on uncomplicated cystitis caused by ESBL producing *E. coli*: a clinical controlled trial

Marianne Bollestad[2], Nils Grude[3], Morten Lindbæk[1]
[1]The Antibiotic Centre of Primary Care, Department of General Practice, Institute of Health and Society, University of Oslo, Oslo, Norway, [2]Division of Medicine, Stavanger University Hospital, Stavanger, Norway, [3]Department of Medical Microbiology, Vestfold hospital trust, Toensberg, Norway

Objectives

The number of patients infected by multiresistant microbes today is high and the rise in extended spectrum β-lactamase (ESBL) producing *Enterobacteriaceae* is especially worrisome.

Oral treatment options for ESBL producing *Enterbacteriaceae* are limited.

In vitro studies of mecillinam demonstrated significantly greater antibacterial potency and higher stability to β-lactamase hydrolysis compared to other penicillins.

The aim of the study was to investigate the clinical and bacteriological findings of pivmecillinam treatment of ESBL producing *E. coli* UTI with non-ESBL producing *E. coli* UTI.

Method

This was a prospective, controlled trial. Women aged ≥16 with community acquired UTI caused by *E. coli* and treated with pivmecillinam were included. Clinical and bacteriological findings were registered.

The study will include at least 160 patients in total of ESBL producing and non-ESBL producing *E. coli* UTI from eight different inclusion sites in Norway.

The primary outcome measure is the number of days until symptomatic resolution. Secondary outcome measures are the number of patients in need of an alternative treatment for symptom resolution and the number of patients with persisting ESBL producing *E. coli* 14 days after treatment end.

Results

Data collection will end on September 1st 2016 and we aim to present preliminary data at the GRIN meeting in 2016.

Conclusions

The study has not yielded any conclusions as the results are not known yet.

Session 17: Diagnosis/Prognosis

1. **Predicting adverse outcome from lower respiratory tract infection in primary care: The 3C cohort study of LRTI in primary care**

Michael Moore[1], Beth Stuart[1], Paul Little[1], Mark Lown[1], Sue Smith[2], Kyle Knox[2], Matthew Thompson[3], David Mant[2]
[1]University of Southampton, Southampton, UK, [2]University of Oxford, Oxford, UK, [3]University of Washington, Seattle, USA

Objectives

To assess predictors of worse outcome in LRTI presenting in routine primary care.

Method

Design: Observational cohort study **Setting**: Adult patients presenting in UK general practice with LRTI had symptoms signs and treatment recorded.

Participants were followed-up for 30 days to determine clinical outcome including admissions and deaths. All admissions were reviewed and a decision regarding whether potentially attributable to the LRTI illness. The predictive value of patient characteristics, presenting symptoms, and clinical findings for admission or death was assessed but non-attributable admissions eg elective surgery were not included.

A cohort of 28867 adult patients with acute cough was recruited with informed consent by 522 practices between 2009-13

Results

There were a total of 258 hospitalisations and 30 deaths; 234 of the 258 hospital admissions were for conditions possibly related to the LRTI and 13 relevant deaths. There are 10 variables that predict hospitalisation or death with a RR of 1.5 or higher: age 60+, comorbidity, shortness of breath, chest pain, crackles, higher severity score, high pulse, high temperature, low oxygen saturation and low blood pressure. These 10 items can be combined into a score which ranges from 0 (none of these) to 10 (all of these). The AUC of this score is 0.77 (Bootstrapped 95% CI 0.74, 0.80).

Conclusions

Hospitalisation and death is uncommon following LRTI presentation in primary care. The prediction model shares features of that predicting pneumonic infiltrates. The implications of the model and its clinical utility for predicting adverse outcomes will be discussed.

2. **The impact of an immediate or delayed antibiotic prescription on re-consultations, hospital admission and death for lower respiratory tract infections: 3C cohort study in UK primary care**

Paul Little[1], Beth Stuart[1], Sue Smith[2], Matthew Thompson[3], Kyle Knox[2], Ann VanDenBruel[2], Mark Lown[1], Michael Moore[1], David Mant[2]
[1]University of Southampton, Hampshire, UK, [2]University of Oxford, Oxfordshire, UK, [3]University of Washington, Washington state, USA

Objectives

To estimates the impact of no offer of an antibiotic, an immediate antibiotic prescription, or a delayed antibiotic prescription for chest infections on subsequent re-consultations, hospitalisation, and death

Method

Adults presenting in UK general practice with LRTI had symptoms, signs, and antibiotic prescribing strategies recorded. Re-consultation with new or non-resolving symptoms, or hospitalisation or death, were documented within 30 days. Multivariate analysis controlled for variables significantly related to the propensity to prescribe antibiotics and for clustering by general practitioner.

Results

Following uncomplicated initial presentation subsequent hospitalisation or death occurred in 48/7349 (0.65%) following no antibiotic prescription, 147/17573 (0.84%) an immediate prescription and 16/3819 (0.42%) a delayed prescription. Hospitalisation and death were reduced by immediate antibiotics (multivariate analysis risk ratio 0.32, 0.13 to 0.78, p=0.012) and delayed antibiotics (0.22, 0.10 to 0.50, p<0.001). Re-consultation for new or worsening symptoms occurred in 1444/7349 (19.6%), 4405/17573 (25.1%) and 538/3819 (14.1%) respectively, and there was no impact on re-consultation following immediate antibiotics (risk ratio 0.98, 95% confidence intervals 0.91 to 1.06, p=0.660) but a reduction associated with delayed prescriptions (0.65, 0.59 to 0.73, p<0.001).

Conclusions

For uncomplicated LRTI immediate or delayed antibiotics more than halve the incidence of subsequent hospitalisation or death, but most patients don't need antibiotics as such events are uncommon. If clinicians are considering antibiotics a delayed prescription may be preferable since it is also associated with reduced re-consultations with new or worsening symptoms.

3. Management of sepsis in out-of-hours primary care: a retrospective study of patients admitted to the intensive care unit

Feike Loots[1], Marleen Smits[1], Carlijn van Steensel[1], Rogier Hopstaken[2], Paul Giesen[1], Arthur R.H. van Zanten[3]
[1]IQ healthcare, Radboudumc, Nijmegen, The Netherlands, [2]Saltro Diagnostic Centre, Utrecht, The Netherlands, [3]Gelderse Vallei Hospital, Ede, The Netherlands

Objectives

Sepsis is a life-threatening condition. Early detection is crucial for the prognosis. In the hospital setting, major efforts have been made to detect sepsis and start treatment as soon as possible. However, often the chain of care for patients with sepsis commences in the primary care setting. Due to the acute onset of sepsis, this will often occur during out-of-hours at a general practitioner (GP) cooperative. The aim of this study is to explore the role of the GP cooperative in the pre-hospital care for sepsis patients and identify factors influencing delay to hospital treatment and outcome.

Method

We performed a retrospective cohort study of patients with community-acquired sepsis admitted to the intensive care unit (ICU) of the Gelderse Vallei Hospital (Ede, the Netherlands) between January 2011 and December 2015. We obtained all relevant data from the hospital records as well as the co-located GP cooperative serving 260,000 patients. The outcomes of interest were: time from the first GP cooperative contact until hospital arrival, urgency at triage, type of contact, referral after initial GP assessment and diagnosis by the GP. Differences in mortality rates between subgroups were analyzed with logistic regression analysis.

Results

Of 265 patients admitted to the ICU, 127 (47.9%) had contacted the GP cooperative. 59.1% received a home visit with a median delay to hospital arrival of 109 minutes; 18.1% concerned clinic consultations (median delay 108 minutes); 10.2% telephone advice (412 minutes), and 12.6% received direct ambulance care without GP assessment (57 minutes). After GP assessment, 61/100 patients were referred. In 43 of these 100 patients, the GP had not suspected an infection. The in-hospital mortality rate in this group was significantly higher than in patients with suspected infections (41.9%. versus 15.8%), and remained significant after correction for confounders.

Conclusions

GPs' clinical detection of sepsis proves to be difficult. More than one third of ICU admitted sepsis patients initially assessed by GPs in out-of-hours care was not referred to a hospital. In almost half of the patients the GP had not suspected an infection. The majority of these patients had received a home visit from the GP prior to ICU admission. The highest mortality rates were observed in the patients when GPs had not suspected an infection. Better diagnosis in GP settings is crucial to improve prognosis.

4. Association between antibiotic class and recovery from symptoms of uncomplicated urinary tract infection (UTI)

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Objectives

To investigate the association and interaction between class of antibiotic prescribed, microbiologically-confirmed UTI, and resistance to the prescribed antibiotic, on time to recovery in women with symptoms of uncomplicated urinary tract infection (UTI) in primary care using data from a prospective four-country observational study investigating the presentation, management, microbiology, and outcomes of women with uncomplicated UTI in primary care combined with data from a four-country randomised controlled trial of a of an optimised POCT guided diagnostic and treatment strategy for symptoms of uncomplicated UTI in primary care.

Method

Midstream urine samples were collected from consenting women and cultured in local laboratories, with antibiotic sensitivities determined in a central laboratory. Antibiotics were grouped into several classes. A UTI was defined as the presence of any organism cultured as pure or predominant (10^3 difference between the first and the second most abundant isolate) at ≥ 10^5 CFU/mL. Participants were given a diary to rate 11 symptoms each day for two-weeks. Multivariable Cox proportional hazards models were fitted, and time to full recovery (all symptoms normal), resolution of moderately bad symptoms, and resolution of day-time frequency/night-time frequency/urgency (DNU) outcomes were considered.

Results

Time to full recovery was shorter for women prescribed antibiotics, regardless of class. Time to resolution of DNU was shorter for participants prescribed trimethoprim, nitrofurantoin, or fosfomycin. Time to resolution of moderately bad symptoms was shorter for participants prescribed fosfomycin. UTI on culture was not associated with a difference in time to recovery, and we were underpowered to detect significant differences in time to full recovery for those with UTIs resistant to the prescribed antibiotic (median 9 days versus 7 days for those sensitive). There was no evidence of any interactions between antibiotic class and UTI on culture or resistance.

Conclusions

Primary care clinicians should consider the use of antibiotics, particularly fosfomycin, for patients presenting with symptoms of uncomplicated UTI. Our data question the value of urine culture as a gold-standard for diagnosis. Being prescribed an antibiotic for which the infecting organism is resistant may delay time to recovery, but a larger sample is needed to estimate this with greater precision. Further work should consider the short-term benefits associated with antibiotic prescribing, alongside any prevention in complications, and how this is balanced against immediate side-effects associated with antibiotic use and development of antibiotic resistance within the community.

Posters

1. **Quality of antibiotic prescribing of Swiss primary care physicians with high prescription rates: a survey**

Dominik Glinz, Lars Hemkens, Heiner C Bucher
Basel Institute of Clinical Epidemiology and Biostatistics, Basel, Switzerland

Objectives

Most antibiotics are prescribed in primary care but prescription patterns and disease specific antibiotic use are unknown in Switzerland. To assess the quality of antibiotic prescribing in primary care in Switzerland with the disease-specific quality indicators by the European Surveillance of Antimicrobial Consumption (ESAC) Project Group. The ESAC quality indicators assess 1) whether the proportions of patients treated with antibiotics lie within the ESAC-defined acceptable ranges; if treated with antibiotics, 2) whether the proportions of patients receiving the recommended antibiotic lie above 80%; and if treated with antibiotics, 3) whether the proportions of patients receiving quinolones is below 5%.

Method

In January 2015, nested in a nationwide intervention study, a structured questionnaire was mailed to the 2900 primary care physicians with the highest prescription rates in Switzerland. Participation was voluntary and anonymous. Physicians were asked to record the diagnostic procedures, diagnosis and treatment (in particular antibiotic prescribing) for 44 consecutive patients with symptoms of the most common indications for prescribing antibiotics in primary care, common cold, tonsillitis/pharyngitis, acute rhinosinusitis, acute otitis media, acute bronchitis, and community acquired pneumonia and urinary tract infection. 250 primary care physicians responded and 9281 patient records were analysed.

Results

The proportions of patients with acute bronchitis (41.0%, 95%CI: 38.3-43.6%; acceptable maximum: 30%), tonsillitis/pharyngitis (46.4%; 42.9-49.9%; 20%), acute rhinosinusitis (47.6%; 44.0-51.1%; 20%) and acute otitis media (70.7%; 65.3-76.1%; 20%) receiving an antibiotic exceeded the ESAC defined acceptable maximum by 11.0%, 26.4%, 27.6% and 50.7%, respectively. The proportion of recommended antibiotics among the prescribed antibiotics ranged between 12.2- 72.2% for all indications and was much lower than the minimal acceptable proportion of 80%. In particular, 37.0% (32.4-41.6%) of women with urinary tract infections were treated with quinolones substantially exceeding the maximal recommended range (5%).

Conclusions

Prescribing quality of primary care physicians in Switzerland for common indications for antibiotic treatment is low with substantial overtreatment of tonsillitis/pharyngitis, acute rhinosinusitis and acute otitis media, and acute bronchitis. Overuse of quinolones for urinary tract infections is of major concern given the high resistance rates of 19% for *E. coli* in Switzerland.

2. Lower urinary tract infections in primary care in Skåne, Sweden

Helena Isberg, Sigvard Mölstad, Anders Beckman
Lund University, Malmö, Sweden

Objectives

To describe pathogens and prevalence of resistance to antimicrobials in urine cultures from patients 15 years and older with urinary tract symptoms in primary care and to describe symptoms and cure in relation to treatment and bacterial findings in cultures.

Method

Patients aged 15 years and older with UTI symptoms attending one of the 8 participating health care centers were recruited during 17 months ending March 2016. Both sexes were invited. Patients recorded presence and severity of symptoms in a questionnaire and filled out a symptom diary. Clinicians were asked to manage the patients according to their usual practice. Urine samples were sent to a laboratory for culture.

Results

Data collection is completed and data analyses are underway.

Bacteria was found in 78.0 % of urine samples sent for culture. Escherichia coli (E. coli) was the most common bacteria and 79.1% of E.coli isolates were fully susceptible to all the antimicrobials tested. 3.7 % of E. coli isolates produced extended spectrum beta-lactamase enzymes (ESBL).
A prescription of antibiotics was done to 73.3 % of patients. Pivmecillinam was the most prescribed antibiotic prescribed to 55.3% of treated patients.

Conclusions

The present study will explore patients symptoms, the bacterial resistance in urine samples, and the cure in relation to background patient data in patients with suspected UTI seeking primary care.

3. Understanding antibiotic prescribing for respiratory tract infections in primary care out of hours services (The UNITE Study)

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Objectives

Respiratory tract infections (RTI) are usually brief, self-limiting conditions. Antibiotics have little or no clinical benefit in most cases, however RTIs account for over 80% of all antibiotic prescriptions issued in primary care. In addition to the risk of side effects, the unnecessary prescription of antibiotics contributes to the spread of resistant bacteria.

From 2010 to 2013, the total number of annual community prescriptions of antibiotics increased by 32%. In light of this, the study aims to explore medical and non-medical prescriber's views on and experiences of facilitators and barriers to antibiotic prescribing in this setting.

Method

30 semi-structured qualitative interviews have been conducted to elicit General Practitioner (GP) and Nurse Prescriber (NP) views and experiences of prescribing for RTIs in primary care out of hours (OOH) services. To ensure diversity, purposive maximum variation and snowballing sampling was used to identify key informants. A thematic analysis of transcribed interviews is being conducted. In line with the applied nature of the work proposed, a subtle-realist approach has been taken and standard approaches used to safeguard rigour.

Results

Three themes have emerged from initial analysis: Communicating care management decisions, factors that influence decision to prescribe and antibiotic prescribing training for staff in primary care OOH services. The findings suggest that antibiotic prescribing in primary care OOH is influenced by OOH factors including consultation time, working contracts and access to patient records.

Respondent's report that patients within this setting are more acutely ill, therefore suggesting that more antibiotics may be required than within in-hour general practice. Participant response to potential training was positive provided it is varied in its delivery and provides regular updates on national and local guidelines.

Conclusions

The study findings will describe participant experiences of and views on prescribing antibiotics for RTI in primary care OOH services, including similarities and differences between NPs and GPs. The team will describe how findings compare with existing evidence on ‘in hour' antibiotic prescribing for RTIs. The study will also explore NP and GP views on the need for a training intervention. If warranted, data generated from this project will be used to develop a training intervention to help improve prescribing behaviour in OOH services.

4. Analysis of recruitment in a pragmatic observational study on C-reactive protein point-of-care testing in primary care

Margaretha Minnaard[1], Janna van der Zand[1], Alma van de Pol[1], Niek de Wit[1], Alwin Schierenberg[1], Rogier Hopstaken[2], Sanne van Delft[2], Theo Verheij[1], Berna Broekhuizen[1]
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Objectives

Failure to recruit all eligible study patients can lead to biased results. Little is known on selective patient recruitment in studies on implementation of diagnostic devices. The aim of this observational study was to measure recruitment of patients in an implementation study in primary care on use of point-of-care (POC) C-reactive protein (CRP) and to evaluate recruitment bias and its impact on the study endpoint.

Method

In a cross sectional observational study on POC CRP implementation and related antibiotics prescribing we compared included patients with all eligible patients to assess representativeness of the included subjects. Eligible patients were adults presenting with acute cough in primary care between March and September 2012. The frequency of POC CRP testing and the proportion of prescribed antibiotics were compared between recruited and non-recruited patients. As measure of bias odds ratios (ORs) with accompanying 95% confidence intervals (CIs) for the association between CRP level (< 20 mg/L or not) and antibiotic prescribing were computed.

Results

Of all 1473 eligible patients 348 (24%) were recruited. In recruited patients POC CRP tests were conducted and antibiotics prescribed more frequently as compared to non-recruited patients (81% vs. 6% and 44% vs. 29%, respectively). The ORs were 18.2 (95% CI 9.6-34.3), 30.5 (95% CI 13.2-70.3) and 3.8 (95% CI 0.9-14.8) in respectively all eligible patients, the recruited and the non-recruited patients.

Conclusions

Selective recruitment resulted in an overestimation of POC CRP test use and antibiotic prescribing.

5. Effectiveness and safety of seasonal influenza vaccination in asthma: a systematic review and meta-analysis

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Objectives

To evaluate the protective and adverse effects of seasonal influenza vaccines in people with asthma

Method

A systematic review and meta-analysis was conducted and assessed the overall quality of evidence using the GRADE methodology. Electronic medical databases were searched from Jan 1970 to Jan 2016 for observational and experimental studies on vaccine effectiveness and safety in people with asthma. Identification of additional studies was performed by searching references, citations, and contacting vaccine companies for unpublished or ongoing studies. The screening of studies, data extraction, and quality appraisal was performed independently by two reviewers. Separate meta-analyses were undertaken for observational and experimental studies using random-effects models.

Results

We included 35 eligible studies, and four to meta-analyses. Most studies included children and inactivated vaccines. Pooled vaccine effectiveness (VE) was 45% (OR: 0.55; 95% CI: 0.44 to 0.69) for influenza. Pooled effectiveness of live vaccines was 81% (RR: 0.19; 95% CI: 0.06 to 0.67) for influenza and 72% (RR: 0.28; 95% CI: 0.10 to 0.80) for influenza-like illness. The protective effect of vaccination was also observed against asthma exacerbations. No increased risk of vaccine-related asthma symptoms and attacks was identified. The quality of the body of evidence was considered very low for all outcomes based on GRADE methodology.

Conclusions

Evidence regarding the protection provided by seasonal influenza vaccines in people with asthma against influenza, asthma exacerbations, and other clinical outcomes is limited and of very low quality. Thus, better quality evidence is required, particularly in adults with asthma. Influenza vaccines were safe and well tolerated in children and adults with asthma. However, the safety of live vaccines should keep being monitored in asthma due to limited available evidence.