

**Rapid diagnostic tests for common infection syndromes: less haste, more speed**

PATEL SV<sup>1,2\*</sup>, PULCINI C<sup>3,4</sup>, DEMIRJIAN A<sup>5,6,7</sup> and VAN HECKE O<sup>8</sup>

1. Department of Paediatric Immunology & Infectious Diseases, University Hospital Southampton NHS Foundation Trust, Southampton, UK

2. NIHR Wellcome Trust Clinical Research Facility, University Hospital Southampton NHS Foundation Trust, Southampton, UK.

3. Université de Lorraine, EA 4360 APEMAC, Nancy, France

4. CHRU de Nancy, Service de Maladies Infectieuses et Tropicales, Nancy, France

5. Department of Paediatric Infectious Diseases and Immunology, Evelina London Children's Hospital, London, UK

6. Faculty of Life Sciences & Medicine, King's College London, UK

7. Primary Care and Interventions Unit, Healthcare Associated Infections & Antimicrobial Resistance, Public Health England

8. Nuffield Department of Primary Health Care Sciences, University of Oxford, Oxford, UK

\*Corresponding author. Division of Women and Children. Mailpoint 43. Southampton Children's Hospital. Tremona Road. Southampton, SO16 6YD. +44 23 8120 5360. E-mail: [Sanjay.patel@uhs.nhs.uk](mailto:Sanjay.patel@uhs.nhs.uk)

**Abstract**

Rapid diagnostic tests, which accurately distinguish bacterial from viral infections, are being heralded as the solution to antibiotic overuse, which is a key driver of antimicrobial resistance. We have concerns that this approach is oversimplistic. Rapid diagnostic tests are complex interventions, with clinical context, patient flow, access and timing affecting their

impact. There is little robust evidence that they reduce antibiotic prescribing in real world settings. We suggest that prior to introducing these costly tests, emphasis should be placed on optimising the implementation of efficient evidence-based antimicrobial stewardship interventions, such as increasing the use of proven automated clinical infection syndrome prediction tools by clinicians, supporting patients to self-care by providing them with high quality safety netting resources, providing front-line clinicians with individual prescribing data to facilitate peer benchmarking and setting specific and purposeful antibiotic prescribing targets to improve the quality of antimicrobial prescribing. The stakes are high and time is running out; let's start by getting the basics right.

Rapid diagnostic tests promise to be a central part of the solution to optimise antimicrobial prescribing in ambulatory **healthcare** settings (general practice, outpatient, emergency departments).<sup>1, 2</sup> However, it is uncertain whether the effects of these tests will be realised in the current UK National Health Service (NHS) landscape, especially in primary care.

Before more rapid diagnostic tests for infectious diseases are introduced in the NHS, current antibiotic prescribing practice needs to be optimised through a national rollout of efficient and existing evidence-based interventions. The stakes are high: we risk wasting time and

resources, and potentially increasing antibiotic prescribing in patients with mild bacterial infections who would not benefit from antibiotics.

### *Why is this important*

Antibiotic prescribing is one of the main drivers of bacterial resistance, with most antibiotics prescribed in community based healthcare settings.<sup>3</sup> Antibiotic-resistant infections significantly impact on morbidity, making patients sicker for longer.<sup>4</sup> Yet, the majority of antibiotics do not benefit patients with common infection syndromes and risk harming patients and wasting resources. It is estimated that at least 1 in 3 of all antibiotics prescribed to people in the community do not help people get better any faster.<sup>5, 6</sup>

A recurring theme in national recommendations has been to avoid prescribing antibiotics for 'viral' infections, especially in common respiratory tract infections (e.g. acute cough, sore throat, acute otitis media).<sup>7-9</sup> Yet, on the basis of a clinical history and examination alone, it is extremely challenging for clinicians to distinguish a bacterial from a viral infection with any certainty, resulting in their prescribing of antibiotics just in case the infection is of bacterial aetiology.<sup>10</sup> Rapid diagnostic tests have been heralded as the solution to this, their main focus to distinguish bacterial from viral infections. We have concerns about this oversimplified approach because there is little robust evidence to support relatively costly diagnostics reducing long-term antibiotic prescribing in real world settings.<sup>11-13</sup> In some cases, the use of rapid diagnostic tests has resulted in a stark increase in antibiotic prescribing.<sup>14</sup>

### *What needs to be done*

There are more efficient and less 'costly' evidence-based interventions that should be adopted nationally in order to optimise the landscape before implementing and evaluating rapid diagnostic tests that are fit-for-purpose.

- Firstly, supporting self-care by providing patients with effective safety netting resources, an approach shown to be very effective.<sup>15</sup> For example, following the implementation of an interactive booklet on respiratory tract infections in children, antibiotic prescribing reduced from 40.8% to 19.5% (absolute risk reduction 21.3%, 95% confidence interval 13.7 to 28.9).<sup>16</sup>
- Secondly, improving the implementation of proven automated clinical prediction tools in the management of common infections syndromes.<sup>17-19</sup>
- Thirdly, although aggregate practice-level prescribing data are available e.g. Public Health England's public health profiles ("fingertips") and openprescribing.net, providing general practitioners (GPs) with individual prescribing data provides a more meaningful benchmark of performance.<sup>20</sup> This is key to change prescribing habits which are inherently an individual behaviour in primary care.
- Fourthly, we need to set specific and purposeful antibiotic prescribing targets to improve prescribing quality. While national prescribing targets have aided a quantitative decrease in overall antibiotic prescribing,<sup>21</sup> the goal is to improve the quality of antibiotic prescribing. These quality indicators should focus on the diagnostic process of common infection syndromes, be specific and clinically

meaningful. For example, if we know that the majority of children with acute sore throat do not benefit from antibiotics (but >90% of children receive antibiotics<sup>22</sup>) set an achievable target that only a set proportion of children with acute sore throat receive antibiotics and let practices work towards this target.

- Lastly, the consequences of antimicrobial resistance need to be communicated effectively to the public and healthcare professionals. Public health messages that focus on the future consequences of antibiotic resistance can seem remote and abstract to patients and clinicians when making decisions about treatment.<sup>23</sup> We applaud efforts to reframe public health messages about unnecessary antibiotic use and antibiotic resistance to provide a consistent message that the public and healthcare professionals can relate to.<sup>24</sup> Public understanding of antibiotics and the impact of antimicrobial resistance is vital because consultation expectations are a significant determinant of inappropriate antibiotic use.<sup>25</sup> Patient and public involvement will be key in designing these new public health messages.

Rapid diagnostic tests are complex interventions and clinical context, patient flow, and timing may affect their impact. We accept that rapid diagnostic tests that are fit-for-purpose will eventually transform how clinicians make antimicrobial prescribing decisions. However, diagnostic test evaluations currently fall short because they seldom go on to demonstrate patient benefit or effective implementation.<sup>26</sup> This research gap is being addressed through initiatives such as the VALUE-Dx partnership, which aims to evaluate the impact of rapid diagnostic tests in community setting in order to achieve more personalised, evidence-based antimicrobial prescribing.<sup>27</sup>

**Transparency declarations:** none to declare

## REFERENCES

1. Kozel TR, Burnham-Marusich AR. Point-of-Care Testing for Infectious Diseases: Past, Present, and Future. *J Clin Microbiol* 2017; **55**: 2313-20.
2. Rapid Diagnostics: Stopping Unnecessary Use of Antibiotics. The Review On Antimicrobial Resistance. <https://amr-review.org/sites/default/files/Paper-Rapid-Diagnostics-Stopping-Unnecessary-Prescription-Low-Res.pdf> (accessed 08/11/2019).
3. PHE. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR). London, 2018.
4. van Hecke O, Wang K, Lee JJ et al. Implications of Antibiotic Resistance for Patients' Recovery From Common Infections in the Community: A Systematic Review and Meta-analysis. *Clin Infect Dis* 2017; **65**: 371-82.
5. Fleming-Dutra KE, Hersh AL, Shapiro DJ et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. *JAMA* 2016; **315**: 1864-73.
6. Pouwels KB, Dolk FCK, Smith DRM et al. Actual versus 'ideal' antibiotic prescribing for common conditions in English primary care. *J Antimicrob Chemother* 2018; **73**: 19-26.
7. Standing Medical Advisory Committee (SMAC), Sub-Group on Antimicrobial resistance. The path of least resistance. Department of Health, 1998.
8. Health Protection Agency (HPA): Management of Infection Guidance for Primary Care (2000).
9. National Institute for Health and Care Excellence (NICE) antimicrobial prescribing guidelines <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines> (accessed 26/12/2019).
10. Horwood J, Cabral C, Hay AD et al. Primary care clinician antibiotic prescribing decisions in consultations for children with RTIs: a qualitative interview study. *Br J Gen Pract* 2016; **66**: e207-13.
11. Brendish NJ, Malachira AK, Armstrong L et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. *Lancet Respir Med* 2017; **5**: 401-11.
12. Lee JJ, Verbakel JY, Goyder CR et al. The Clinical Utility of Point-of-Care Tests for Influenza in Ambulatory Care: A Systematic Review and Meta-analysis. *Clin Infect Dis* 2019; **69**: 24-33.
13. Little P, Stuart B, Francis N et al. Antibiotic Prescribing for Acute Respiratory Tract Infections 12 Months After Communication and CRP Training: A Randomized Trial. *Ann Fam Med* 2019; **17**: 125-32.
14. Hopkins H, Bruxvoort KJ, Cairns ME et al. Impact of introduction of rapid diagnostic tests for malaria on antibiotic prescribing: analysis of observational and randomised studies in public and private healthcare settings. *BMJ* 2017; **356**: j1054.
15. Spoelman WA, Bonten TN, de Waal MW et al. Effect of an evidence-based website on healthcare usage: an interrupted time-series study. *BMJ Open* 2016; **6**: e013166.
16. Francis NA, Butler CC, Hood K et al. Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial. *BMJ* 2009; **339**: b2885.
17. Hay AD, Redmond NM, Turnbull S et al. Development and internal validation of a clinical rule to improve antibiotic use in children presenting to primary care with acute respiratory tract infection and cough: a prognostic cohort study. *Lancet Respir Med* 2016; **4**: 902-10.

18. Gulliford MC, van Staa T, Dregan A et al. Electronic health records for intervention research: a cluster randomized trial to reduce antibiotic prescribing in primary care (eCRT study). *Ann Fam Med* 2014; **12**: 344-51.
19. Little P, Hobbs FD, Moore M et al. Clinical score and rapid antigen detection test to guide antibiotic use for sore throats: randomised controlled trial of PRISM (primary care streptococcal management). *BMJ* 2013; **347**: f5806.
20. Gerber JS, Prasad PA, Fiks AG et al. Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: a randomized trial. *JAMA* 2013; **309**: 2345-52.
21. Bou-Antoun S, Costelloe C, Honeyford K et al. Age-related decline in antibiotic prescribing for uncomplicated respiratory tract infections in primary care in England following the introduction of a national financial incentive (the Quality Premium) for health commissioners to reduce use of antibiotics in the community: an interrupted time series analysis. *J Antimicrob Chemother* 2018; **73**: 2883-92.
22. O'Brien K, Bellis TW, Kelson M et al. Clinical predictors of antibiotic prescribing for acutely ill children in primary care: an observational study. *Br J Gen Pract* 2015; **65**: e585-92.
23. Van Hecke O, Butler CC, Wang K et al. Parents' perceptions of antibiotic use and antibiotic resistance (PAUSE): a qualitative interview study. *J Antimicrob Chemother* 2019; **74**: 1741-7.
24. Wellcome Trust. Reframing Resistance report: <https://wellcome.ac.uk/reports/reframing-antimicrobial-resistance-antibiotic-resistance> (accessed 26/12/2019).
25. McNulty CA, Nichols T, French DP et al. Expectations for consultations and antibiotics for respiratory tract infection in primary care: the RTI clinical iceberg. *Br J Gen Pract* 2013; **63**: e429-36.
26. Verbakel JY, Turner PJ, Thompson MJ et al. Common evidence gaps in point-of-care diagnostic test evaluation: a review of horizon scan reports. *BMJ Open* 2017; **7**: e015760.
27. <https://www.imi.europa.eu/projects-results/project-factsheets/value-dx> (accessed 08/11/2019).