

# *V*ALORISATION



Most of this thesis is focused on the scientific value of our research into childhood fever in general practice. Nevertheless, in the end one of the most important reasons to perform scientific research is to translate that same research to concrete revenues for actual daily life and practice. This translational process is called valorisation. I hope that readers of this thesis see that this process of valorisation is intertwined in almost every chapter of this dissertation which they have read so far. This chapter will explicitly focus on and summarize that process, first discussing the societal relevance of our research, then zooming in on the concrete revenues of our findings and further on discussing future and innovative perspectives.

### **Societal relevance of childhood fever and translation of this thesis**

Fever is the most common reason for a child to be seen by a GP during out-of-hours care, with one in three contacts for children under the age of 12 years being fever related.<sup>1</sup> If parents consult with a febrile child, it is up to the GP to make sure that their management is as optimal as it can be. This is sometimes challenging for several reasons. First of all, GPs have to consider the safety of the individual child that is sitting in front of them. Things they have to bear in mind which are discussed in chapter 6<sup>2</sup> and the discussion chapter of this thesis are the risk of missing a serious infection, thereby delaying treatment and risking long-term damage to the child versus overtreatment on the other side, leading to side effects, but also possible negative implications of early exposure to antibiotics like a higher risk of developing eczema,<sup>3</sup> asthma,<sup>4</sup> arthritis<sup>5</sup> and even obesity.<sup>6</sup> Second, on a more societal level GPs also have to consider their management decisions taking into account increasing antibiotic resistance as a threat to global health. Many studies have shown that antibiotic resistance is increasing and there is an increasing gap between the burden of infections due to multidrug-resistant bacteria and the development of new antibiotics to tackle the problem.<sup>7</sup> To illustrate, approximately 25 000 people in Europe die every year from antibiotic-resistant bacteria.<sup>7</sup> Furthermore, in the US an estimated 2 million illnesses and 23 000 deaths a year are caused by antibiotic resistance.<sup>8,9</sup> One of the main causes for antibiotic resistance is overuse of antibiotics. It is this overuse that we tried to understand and grasp in the earlier chapters of this thesis,<sup>2,10,11</sup> and tried to improve by development of an interactive booklet as an intervention<sup>12,13</sup> which, if indeed used, can reduce “better safe than sorry” antibiotic prescriptions. In other words, the findings of this thesis are not only relevant for GPs, clinicians working with children, parents and children but for almost every individual in our society. That is to say, the consequences of antibiotic resistance are everyone’s problem. Achievements in modern medicine, such as major surgery, organ transplantation, treatment of preterm babies, and cancer chemotherapy, which we today

take for granted, would not be possible without access to effective treatment for bacterial infections.<sup>9</sup> Though the effect we found was modest, the reduction in antibiotic prescribing found in this thesis of all children seen at out of hours care with fever provide evidence of the likely 'real world' benefits of this intervention, and are therefore highly relevant to the aims of reducing antimicrobial resistance. Extrapolated to the Netherlands, with an average of 1000 children per 6 months per cooperative, 122 cooperatives in total and an average of 1 in 3 to 4 children to receive an antibiotic prescription, around 2000 prescriptions can be prevented in the Netherlands alone by simply providing parents with a booklet for which no special training is required.

The interactive booklet which was studied in this thesis was specifically designed and studied in such a way that it can be implemented tomorrow. As said, it is very low-cost and light-touch and does not require any specific training or instructions. In other words, it could be implemented tomorrow by simply providing GPs with booklets and making sure they use them. Our trial shows that handing out patient information leaflets about childhood fever during routine out-of-hours care is very uncommon, as only 2.8% of parents consulting at control centres reported receiving such information. We believe that this number of 2.8% shows that even in the bread-and-butter condition of childhood fever, uptake and hand-out of available patient information materials (either written or online) is extremely low in routine care, yet crucial for parents to learn about self-management strategies and alarm symptoms. This is something which can be improved by emphasizing the importance of communication and use of written information and referral to reliable websites in medical school and specialists training. Furthermore, it is important to think about other approaches to make sure GPs actually use the booklet and information since merely providing GPs with the booklet did not result in a reduction of antibiotic prescriptions. Strategies to consider are for example using additional platforms, other than printed material, where the booklet can be made available like online or through a smartphone application. Another important strategy on which we are already working is writing articles in national journals and giving lectures at (inter-)national conferences explaining the relevance of the use of the booklet and information in childhood fever to clinicians in everyday practices.

As explained in the discussion of this thesis, the booklet should ideally be combined with other interventions aimed at reducing unwarranted antibiotic prescriptions, such as improved diagnostics, point-of-care tests, interactive workshops<sup>14</sup>, and peer comparison through audit-and-feedback.<sup>15</sup> In addition, in the next paragraph I will discuss why and how

the information used in the booklet and the booklet itself can also be used in different settings, for example before children get sick.

### **Innovativeness and future perspectives of childhood fever management**

We performed one of the largest cluster RCTs ever in general practice and the first one assessing the effectiveness of a booklet for one of the most common reasons for childhood consultations and antibiotic prescriptions. The basis and innovative part of the interactive booklet which was developed and studied in this thesis was a traffic light system aimed at parents. As described in the discussion of this thesis, a traffic light system can also be found in the international NICE guideline for childhood fever<sup>16</sup> and the guideline from Dutch Society of Paediatrics (NVK).<sup>17</sup> The big difference between these traffic lights and the traffic light in the booklet is the fact that they are doctor, or disease-orientated whereas the booklet's traffic light system is parent, or illness-orientated. Parents consulting a GP feel the traffic light has turned to orange, or even red, and it is up to the GP to turn that traffic light back to green in cases of benign (viral) infections thereby empowering parents in their self-management strategies.<sup>18</sup>

As is suggested in the previous chapters, future studies should not only aim at parents of children at the moment they are sick, but also at parents of healthy young children in the general public. By informing them about future illnesses and self-management strategies before children actually get sick, parental self-efficacy and their health care seeking might improve. A potential public health setting to educate parents about fever before their children become sick are well-child clinics.<sup>19</sup> This is a potential setting not only to improve parental knowledge and self-management, but also to reduce illness absenteeism due to fever and common infections among children and parents thereby reducing subsequent societal costs and impact.<sup>19</sup> Another potential setting where there is room for improvement are children's day-care centres. Previous studies have shown that illness absenteeism due to fever and common infections is substantial and mostly driven by unrealistic concerns and negative attitude towards fever of both childcare staff and parents, resulting in illness absenteeism from childcare, work absenteeism among parents and healthcare service use.<sup>20</sup> It is for that reasons that the findings of this thesis resulted in a spin-off project focusing on this setting. We developed a multicomponent intervention consisting of an educational session, a decision tool, the information booklet (as developed in this thesis) and an online video to be used in childcare centers. Results of the cluster randomised trial examining the effects of this multicomponent intervention to optimise decision making among childcare staff on illness absenteeism due to fever and common

infections in 0-4 year-old attending childcare will follow later in 2018.<sup>20</sup> Because of parents' call for one consistent line of information, future studies should also look into the possibility of using a similar intervention by paediatricians in secondary care.<sup>18</sup>

As said, the interactive booklet on childhood fever which was developed and studied throughout this thesis can be implemented tomorrow in general practice thereby improving parental self-management and reducing unwarranted antibiotic prescriptions. The solution to improving antibiotic prescriptions and fever phobia among parents probably does not lie within one simple intervention, but within a combination of different interventions aimed at amongst others surveillance, infection prevention and responsible use of antibiotics before, during and after children get sick.

## REFERENCES

1. de Bont EG, Lepot JM, Hendrix DA, Loonen N, Guldmond-Hecker Y, Dinant GJ, et al. Workload and management of childhood fever at general practice out-of-hours care: an observational cohort study. *BMJ Open*. 2015;5:e007365.
2. de Bont EG, Peetoom KK, Moser A, Francis NA, Dinant GJ, Cals JW. Childhood fever: a qualitative study on GPs' experiences during out-of-hours care. *Fam Pract*. 2015.
3. Schmitt J, Schmitt NM, Kirch W, Meurer M. Early exposure to antibiotics and infections and the incidence of atopic eczema: a population-based cohort study. *Pediatr Allergy Immunol*. 2010;21:292-300.
4. Droste JH, Wieringa MH, Weyler JJ, Nelen VJ, Vermeire PA, Van Bever HP. Does the use of antibiotics in early childhood increase the risk of asthma and allergic disease? *Clin Exp Allergy*. 2000;30:1547-53.
5. Horton DB, Scott FI, Haynes K, Putt ME, Rose CD, Lewis JD, et al. Antibiotic Exposure and Juvenile Idiopathic Arthritis: A Case-Control Study. *Pediatrics*. 2015;136:e333-43.
6. Scott FI, Horton DB, Mamtani R, Haynes K, Goldberg DS, Lee DY, et al. Administration of Antibiotics to Children Before Age 2 Years Increases Risk for Childhood Obesity. *Gastroenterology*. 2016;151:120-9 e5.
7. ECDC/EMEA. Technical Report. The bacterial challenge: time to react 2009. Available from:  
[https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/0909\\_TER\\_The\\_Bacterial\\_Challenge\\_Time\\_to\\_React.pdf](https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf)
8. US Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States 2013. Available from: <https://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>.
9. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance-the need for global solutions. *Lancet Infect Dis*. 2013;13:1057-98.
10. de Bont EG, Francis NA, Dinant GJ, Cals JW. Parents' knowledge, attitudes, and practice in childhood fever: an internet-based survey. *Br J Gen Pract*. 2014;64:e10-6.
11. de Bont EG, Loonen N, Hendrix DA, Lepot JM, Dinant GJ, Cals JW. Childhood fever: a qualitative study on parents' expectations and experiences during general practice out-of-hours care consultations. *BMC Fam Pract*. 2015;16:131.
12. de Bont EG, Alink M, Falkenberg FC, Dinant GJ, Cals JW. Patient information leaflets to reduce antibiotic use and reconsultation rates in general practice: a systematic review. *BMJ Open*. 2015;5:e007612.

13. de Bont EG, Dinant GJ, Elshout G, van Well G, Francis NA, Winkens B, et al. An illness-focused interactive booklet to optimise management and medication for childhood fever and infections in out-of-hours primary care: study protocol for a cluster randomised trial. *Trials*. 2016;17:547.
14. Little P, Stuart B, Francis N, Douglas E, Tonkin-Crine S, Anthierens S, et al. Effects of internet-based training on antibiotic prescribing rates for acute respiratory-tract infections: a multinational, cluster, randomised, factorial, controlled trial. *Lancet*. 2013;382:1175-82.
15. Meeker D, Linder JA, Fox CR, Friedberg MW, Persell SD, Goldstein NJ, et al. Effect of Behavioral Interventions on Inappropriate Antibiotic Prescribing Among Primary Care Practices: A Randomized Clinical Trial. *JAMA*. 2016;315:562-70.
16. Fields E, Chard J, Murphy MS, Richardson M. Assessment and initial management of feverish illness in children younger than 5 years: summary of updated NICE guidance. *BMJ*. 2013;346.
17. Nijman RG, Oteman N, Oostenbrink R. Guideline for febrile children in the hospital setting; relevance for general practitioners and paediatricians. *Ned Tijdschr Geneeskd*. 2014;158:A7331.
18. de Bont EG, Cals JW. Voor elk kind met koorts een eigen 'stoplicht'? *Ned Tijdschr Geneeskd*. 2014;158.
19. Peetoom KK, Smits JJ, Ploum LJ, Verbakel JY, Dinant GJ, Cals JW. Does well-child care education improve consultations and medication management for childhood fever and common infections? A systematic review. *Arch Dis Child*. 2017;102:261-7.
20. Peetoom KKB, Crutzen R, Bohnen J, Verhoeven R, Nelissen-Vrancken H, Winkens B, et al. Optimising decision making on illness absenteeism due to fever and common infections within childcare centres: development of a multicomponent intervention and study protocol of a cluster randomised controlled trial. *BMC Public Health*. 2017;18:61.