FACULTY OF
PHARMACEUTICAL SCIENCES

PARENTS' AND HEALTHCARE PROVIDERS' PERSPECTIVES ON PRIMARY CARE FOR CHILDREN: A COMPARATIVE STUDY

Sigrid Verhelst

A Master dissertation for the study programme Master in Pharmaceutical Care

Academic year: 2017 - 2018

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SUMMARY

Background and aim: As children are usually unable to make health-related decisions, parents play a key role in this process. The first aim of this research was therefore to determine parents' expectations of a healthcare visit for their child with a general practitioner (GP) or a community pharmacist (CP). Additionally, we aimed to assess parents' knowledge about frequently used drugs or drug groups for their child (i.e. paracetamol, ibuprofen and antibiotics). The second aim was to determine (1) the GPs' and CPs' perspectives about treating children and (2) the information provision when prescribing or dispensing paracetamol, ibuprofen or antibiotics. Questioning both groups simultaneously allowed us to compare perspectives.

Methods: An observational cross-sectional study was conducted in April and May 2018. We developed three questionnaires, one for parents, one for GPs and one for CPs. The questionnaire for parents was only available through an online platform. The link to this questionnaire was disseminated through nurseries and elementary schools in the five provincial capitals of Flanders (Antwerp, Bruges, Ghent, Hasselt and Leuven). The healthcare providers were questioned in a face-to-face manner in the same cities, but in order to obtain sufficient data, these questionnaires were also distributed through an online platform.

Results: The study included 380 respondents of which 224 parents, 50 GPs and 106 CPs. Considering the expectations of parents of a healthcare visit for their ill child, "the GP prescribes medication" and "the CP proposes a treatment with medication" were evaluated the least important actions. Considering the expectations of parents about information provision, they expect most information from both GPs and CPs. Regarding knowledge of paracetamol, parents made a correct assessment of the use of this medication in roughly 7 out of 8 situations. For ibuprofen, an approximate correct estimate of when this medication is suitable has been made for all 8 conditions. Regarding knowledge about antibiotics, parents have correctly evaluated the use of antibiotics in 8 out of 11 situations. Only for bronchiolitis, ear inflammation and pharyngitis there is a remarkable proportion (36%, 61% and 52% respectively) that incorrectly expects a prescription for antibiotics. In the questions assessing additional knowledge, answers were spread and parents often pointed out not to know the correct answer. The questionnaire for GPs revealed that prescribing medication is considered the least important action. The questionnaire for CPs showed that providing sufficient privacy is considered least crucial. In practice, for both GPs and CPs, solely a minor proportion provides parents with information about side effects and stopping treatment or provides written information.

Conclusion: Considering parents' expectations for a consultation or dispensation with a GP or CP respectively, there is a substantial resemblance with the healthcare providers' perspective. Regarding parents' knowledge, they are reasonably aware of when paracetamol, ibuprofen and antibiotics can be used. However, healthcare providers should keep parents well informed as some questions revealed a few shortcomings in knowledge.

SAMENVATTING

Achtergrond en doel: Aangezien kinderen meestal niet in staat zijn zelf beslissingen te nemen over hun gezondheid, spelen ouders een sleutelrol in dit proces. Het eerste doel van dit onderzoek was bijgevolg het nagaan van de verwachtingen van ouders betreffende een bezoek aan de huisarts of officina-apotheker voor hun kind. Naast verwachtingen richtte deze studie zich ook op de kennis van ouders omtrent frequent gebruikte geneesmiddelen(groepen) bij kinderen (i.e. paracetamol, ibuprofen en antibiotica). Het tweede doel was om (1) de visie van huisartsen en apothekers na te gaan betreffende het behandelen van kinderen en (2) te evalueren welke informatie zij aan ouders geven bij het voorschrijven of afleveren van paracetamol, ibuprofen en antibiotica. Tot slot werden de visies van deze groepen vergeleken.

Methoden: Een observationeel cross-sectioneel onderzoek werd uitgevoerd in de periode april-mei 2018. We ontwikkelden drie vragenlijsten, één voor ouders, één voor huisartsen en één voor apothekers. De vragenlijst voor ouders was alleen beschikbaar via een online platform. De link naar deze vragenlijst werd verspreid via kinderdagverblijven en basisscholen in de vijf provinciehoofdsteden van Vlaanderen (Antwerpen, Brugge, Gent, Hasselt en Leuven). Zorgverleners werden in dezelfde steden persoonlijk ondervraagd, maar om voldoende gegevens te verkrijgen zijn deze vragenlijsten ook via een online platform verspreid.

Resultaten: De studie omvatte 380 deelnemers, waarvan 224 ouders, 50 huisartsen en 106 apothekers. Volgens de verwachtingen van ouders werden “de huisarts schrijft medicatie voor” en “de apotheker stelt een medicamenteuze behandeling voor” als minst belangrijke acties beschouwd. Het verstrekken van informatie wordt meestal aanzien als de taak van beide zorgverleners. Wat de kennis omtrent paracetamol betreft, maakten ouders in 7 van de 8 situaties een vrijwel correcte inschatting van wanneer deze medicatie geschikt is. Voor ibuprofen is voor alle 8 aandoeningen nagenoeg een correcte evaluatie gemaakt. Met betrekking tot antibiotica maakten ouders in 8 van de 11 situaties een correcte inschatting met uitzondering van bronchiolitis, oor- en keelontsteking, waarvoor een aanzienlijk percentage (respectievelijk 36%, 61% en 52%) ten onrechte een antibioticum verwacht. De aanvullende kennisvragen gaven verdeeldheid aan waarbij ouders er vaak op wezen het antwoord niet te weten. Huisartsen gaven aan het voorschrijven van medicatie als minst belangrijke actie te beschouwen. Apothekers achten voldoende privacy minst cruciaal. Als we beide groepen beschouwen, huisartsen en apothekers, voorziet in praktijk slechts een minderheid informatie voor ouders omtrent bijwerkingen en het stoppen van de behandeling of schriftelijke informatie.

Conclusie: Wat ouders verwachten van een consultatie of aflevering correspondeert overwegend met het perspectief van de zorgverleners. Wat de kennis betreft, zijn ouders behoorlijk goed op de hoogte van wanneer paracetamol, ibuprofen en antibiotica geschikt zijn. Zorgverleners moeten ouders echter goed blijven informeren, aangezien uit een aantal vragen enkele tekortkomingen in kennis naar voren zijn gekomen.

ACKNOWLEDGMENTS

At the beginning of this semester, I started this master dissertation, not knowing what to expect. Today, a few months later, the result which I am proud of, is there. But I could never have done this on my own. For that reason, I would like to thank a few people.

First of all, I would like to thank Prof. Boussery for the opportunity to realize my master dissertation at the Pharmaceutical Care Unit. I greatly appreciate the time and effort invested in bringing this to a successful result.

Next, I would like to thank my greatest support in this process, Eline Tommelein. Eline, thank you for reading my thesis countless times. For all your answers to my questions. To help me on my way when I got a little lost. Thanks to your help and expertise, I have learned a lot during this semester that will undoubtedly be useful for me in the future. And I am so grateful that, thanks to your help, I am able to deliver this result.

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LIST OF ABBREVIATIONS

AAD = Antibiotic-associated diarrhea

APB = Algemene Pharmaceutische Bond

ATC = Anatomical Therapeutic Chemical

BAPCOC = Belgian Antibiotic Policy Coordination Committee

CI = Confidence interval

COX = Cyclo-oxygenase

CP = Community pharmacist

CYP450 = Cytochrome P450

DDD = Defined daily dose

FTE = Full-time equivalents

GFR = Glomerular filtration rate

GP = General practitioner

ICH = International Council for Harmonization

IQR = Interquartile range

MD = Mean difference

MDI = Metered dose inhaler

NHG = Nederlands Huisartsen Genootschap

NSAID = Non-steroidal anti-inflammatory drug

OTC = Over-the-counter

PDCO = Pediatric Committee

PIP = Pediatric investigation plan

PTA = Pharmaceutical technical assistant

PUMA = Pediatric-use marketing authorization

SD = Standard deviation

UK = United Kingdom

WHAM = Who – How (long) – Action – Medication

WHO = World Health Organization

1. INTRODUCTION

1.1. DEFINING PEDIATRIC AGE GROUPS

Within the pediatric population, further subdivisions regarding different age classes are made. Each age class has its own differences, and for this master dissertation, we adhere to the classification of the International Council for Harmonization (ICH) E11[4]. This classification distinguishes five groups, including (1) preterm newborn infants, (2) term newborn infants (0 to 27 days), (3) infants and toddlers (28 days to 23 months), (4) children (2 to 11 years) and (5) adolescents (12 to 16-18 years, dependent on region).

1.2. PREVALENCE OF MEDICATION USE IN CHILDREN

Over the past ten years, the use of medication in children (0-18 years) has increased. In Belgium, the number of pharmaceutical packages dispensed in the pediatric age group increased from 5.4 million packages in 2004 to 6.6 million in 2011[5], which corresponds to an increase of 22,2%. Possible reason for this raise is the Pediatric Regulation (cf. infra) that went into effect on 26 January 2007, which facilitates the development of more safe medication in children.

When examining medication use in children, only small differences were observed depending on the study setting (hospital setting vs. primary care). In 2008-2009, Rashed et al.[6] conducted a study on drug utilization patterns in children (0-18 years). This study was carried out in a hospital setting in five countries (Australia, Germany, China (Hong Kong), Malaysia and the United Kingdom (UK)). According to their findings, the two most frequently used medications, based on the anatomical therapeutic chemical (ATC) classification[1], were anti-infectives for systemic use (J) and medication for the nervous system (N). Considering the study by Sturkenboom et al.[8], carried out in primary care in three European countries (i.e. the Netherlands, UK and Italy), anti-infectives for systemic use were again most commonly used in all age groups (0-18 years). In comparison with the study by Rashed et al. the proportion of medication use for the nervous system (such as paracetamol) was lower. No account was taken of the high over-the-counter (OTC) use of this medication in primary care. The other most commonly used anatomical classes, especially in children under two years of age, were respiratory system drugs (like salbutamol and inhaled steroids) (R), dermatologicals (like fusidic acid) (D) and drugs that act on the alimentary tract and metabolism (like lactulose) (A)[6 8 9].

[1] *"The Anatomical Therapeutic Chemical (ATC) Classification system classified the active substances of medications in five different levels. There are fourteen main anatomical groups which are further subdivided according into pharmacological, therapeutic and chemical subgroups. The fourteen main anatomical groups are: alimentary tract and metabolism (A), blood and blood forming organs (B), cardiovascular system (C), dermatologicals (D), genito-urinary system and sex hormones (G), systemic hormonal preparations (excl. sex hormones and insulins) (H), anti-infectives for systemic use (J), antineoplastic and immunomodulating agents (L), musculo-skeletal system (M), nervous system (N), antiparasitic products, insecticides and repellents (P), respiratory system (R), sensory organs (S) and various (V)" [7](World Health Organization Collaborating Centres (WHOCC). ATC/DDD Index 2018 2018 [Available from: https://www.whocc.no/atc_ddd_index/ accessed March 8, 2018.]).*

For Belgium, the ten drugs or drug groups most often reimbursed in the age group 0-12 years are presented in **Table 1.1.** Examining the top 10 based on dispensed defined daily dose (DDD), it can be observed that 7 out of 10 drugs affect the respiratory system. Evaluating the top 10 by number of dispensations, both anti-infectives for systemic use and respiratory drugs are most prevalent. When we compare this with the findings of the study by Sturkenboom et al.[8] a similar pattern is observed in three other European countries, as mentioned before.

Table 1.1. Representation of the ten drugs or drug groups most often reimbursed in Belgium in the age group 0-12 years *(Algemene Pharmaceutische bond (APB), personal communication, February 27, 2018)*

Top 10 by DDD		Top 10 by number of dispensations	
Name	DDD	Name	Number of dispensations
Ipratropium Bromide	6 009 211	Amoxicillin	689 253
Mometasone	5 702 836	Salbutamol	333 718
Amoxicillin	4 763 584	Amoxicillin and beta-lactamase inhibitor	248 248
Salbutamol	4 555 993	Ipratropium bromide	229 375
Desloratadine	2 883 895	Methylphenidate	211 467
Fluticasone	2 498 638	Anti-infectives, combinations	183 924
Montelukast	2 452 182	Rota virus, live attenuated	179 003
Methylphenidate	2 148 336	Fluticasone	169 876
Omeprazole	1 987 156	Budesonide	160 873
Budesonide	1 600 712	Azithromycin	122 893

1.3. LEGISLATION AND ETHICAL ISSUES

Data about the use of medication in children is often lacking because of exclusion from clinical trials. This knowledge is however essential to set a dosing strategy and to protect children against the risk and harms associated with prescribing medication. Therefore, the European Union Pediatric Regulation was launched to encourage the pharmaceutical industry to perform trials in this population. The Pediatric Regulation is based on the following pillars: (1) the creation of a Pediatric Committee (PDCO)[2] (2) the implementation of a mandatory Pediatric Investigation Plan (PIP)[3] considering all age ranges and (3) awarding rewards and incentives[10] (**Table 1.2.**). For example, when companies complete all studies required by the PIP, a 6-month patent extension or a supplementary protection certificate can be obtained. The PDCO plays a fundamental role in the assessment of these PIPs[11]. Besides strategies to increase knowledge about pediatric dosing for new medication, there are also initiatives to encourage research into already authorized medication. This is guided by the Pediatric-Use Marketing Authorization (PUMA). Applying for a PUMA can yield 10 years of market and data protection for a company[12].

[2] *"The Pediatric Committee (PDCO) is the European Medicines Agency's (EMA) scientific committee responsible for activities on medicines for children and to support the development of such medicines in the European Union by providing scientific expertise and defining pediatric needs."*

[3] A pediatric investigation plan (PIP) is defined as *"a development plan aimed at ensuring that the necessary data are obtained through studies in children, to support the authorization of a medicine for children. All applications for marketing authorization for new medicines have to include the results of studies as described in an agreed PIP, unless the medicine is exempt because of a deferral or waiver. This requirement also applies when a marketing-authorization holder wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized and covered by intellectual property rights"* by the European Medicines Agency.

Table 1.2. Overview of the obligations and incentives in the E.U. Pediatric Regulation		
Type of medical product	Obligation	Incentive
New medicinal product	PIP or waiver	6 months extension of supplementary protection certificate[a]
On patent and authorized medicine	PIP or waiver	6 months extension of supplementary protection certificate[a]
Orphan medicine	PIP or waiver	2 additional years of market exclusivity[a]
Off patent medicine	None (voluntary PIP possible for PUMA)	8+2 years of data protection[a]
PIP: Pediatric Investigation Plan; **PUMA:** Pediatric-Use Marketing Authorization		

[a] If compliance with PIP, the product is authorized in all member states (except for PUMA) and relevant study information is included in the summary of the product characteristics.
Adapted from Zaide Frias, EMA Head of Regulatory Affairs, SME Workshop, 26.04.2013, EMA.

Despite these initiatives, the off-label and unlicensed use of medication in children remains high. One contributing factor is the additional ethical challenge to include children in clinical trials. Children are often unable to understand the risks of clinical trials which results in communication that mainly takes place through parents. Making this decision as a parent is not an easy task as the risks are often unknown[13]. In addition, obtaining an informed consent is more complex and delicate when the decision needs to be made for a child. In this respect, it is important that parents obtain relevant and clear information[14].

1.4. PEDIATRIC DOSING STRATEGY

Currently, data on safety and efficacy are often obtained in adults and extrapolated to children. But growth and physical development (especially for children under the age of twelve) are not linear, so simple extrapolation rarely leads to the desired health effects[13]. In addition, also pharmacology aspects (pharmacodynamics & -kinetics) are different in children from adults. The pharmacodynamics of a medication are defined as *"the effect of the drug on physiological functions and pathological processes"* [15]. Where pharmacokinetics describes how a drug molecule is absorbed, distributed and eliminated by the body[16]. The most significant changes occur during the neonatal period, but likewise, in older children, there are still remarkable differences. A good understanding of these changes in pharmacology is necessary to ensure effective and safe use of medication in the pediatric population[17].

1.4.1. Pharmacodynamics

The knowledge of modified pharmacodynamics in children is rather limited. A few cases of medication in which age-dependent differences are observed, are known[18]. These relate to both the medication-receptor interactions (for example, warfarin[19] and cyclosporine[20]) and the relationship between plasma levels and the observed effect of a medication (for example, the sedation that occurs with midazolam[21 22]). These age-dependent differences in pharmacodynamics must therefore always be considered when, despite a correct dosage, the desired effect is not achieved or when (unexpected) side effects are observed[18 23 24].

1.4.2. Pharmacokinetics

1.4.2.1. Absorption

Absorption is the process through which the medication transfers from the site of administration to the systemic circulation[25]. For oral administration, in general, the differences in gastric pH and the rate of gastric emptying will play a fundamental role.

During the first two years of life, the pH of the stomach decreases as a result of a rise in gastric acid production[26]. This altered pH influences absorption because of changes in dissociation and acid-base ionization. In parallel, the elevated pH in children under two years of age, has an important impact on the stability. For example, acid-labile medications, like penicillin, reaches greater peak concentrations in newborns in comparison with infants and children[27]. Subsequently, also the delay of gastric emptying may change the absorption rate of medication[28]. An example of this was found in a study from Anderson et al.[29] which showed that the absorption rate of paracetamol is decreased significantly during the first days of life.

Also in case of parenteral administration, changes occur in comparison to adults. For example, with topically applied medication, increased systemic exposure is observed due to the higher body surface area/mass ratio, elevated rates of tissue perfusion and a higher degree of skin hydration[1]. Additionally, in some cases rectal administration may be appropriate. Mostly in neonates, bioavailability after rectal administration can be increased in comparison with adults because of their immature hepatic metabolism. Otherwise, faster expulsion of the medication is possible due to the more pulsatile rectum[18]. Thus, bioavailability after rectal administration is variable and not easily predictable[28].

1.4.2.2. Distribution

Distribution is the process by which the medication migrates from one body compartment to another[25]. Two factors are of major importance: the amount of body water and the number of plasma proteins. Compared to adults, the total body water is increased in neonates and very young infants (80-90% of body weight), while the fat content is reduced (10-15% of body weight). In adults, the total body water content decreases to 55-65% and the amount of extracellular water declines to 20% in comparison with 45% in neonates (**Figure 1.1.**). Because of these changes, higher distribution volumes of water-soluble medication are observed in children[18 26].

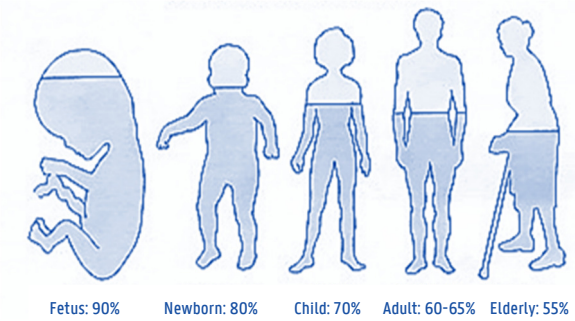

Fig. 1.1. *Proportion of total body water: a decrease in total body water is observed from 90% in the fetus to 80% in newborns and 70% in children. This quantity falls further to 60-65% and 55% in adults and elderly respectively[88].*

In addition, it is generally noted that protein binding capacity in children is reduced. This results in an increase of the free fraction of extensively bound medication[27]. The main reason is the lower amount of circulating plasma proteins such as albumin and α_1-acid glycoprotein, but also the reduced binding affinity and the presence of bilirubin that competes for binding on plasma proteins are involved[18 24 28].

1.4.2.3. Metabolism

Metabolism is the process by which a drug molecule is made more water-soluble by chemical modification. This is done in order to facilitate biliary and renal excretion[25]. The largest part of metabolism takes place in the liver and is divided into phase 1 and phase 2 reactions. The enzymes necessary for these reactions are still immature at birth[28]. Phase 1 reactions include oxidation, reduction and hydrolysis, where oxidative reactions are the most important. Those reactions are frequently cytochrome P450 (CYP450)-dependent[26]. It should be considered that the ontogeny of these CYP-enzymes is not linear and besides, some CYPs have an increased activity during development, resulting in higher weight-based dose requirements (**Figure 1.2.**).

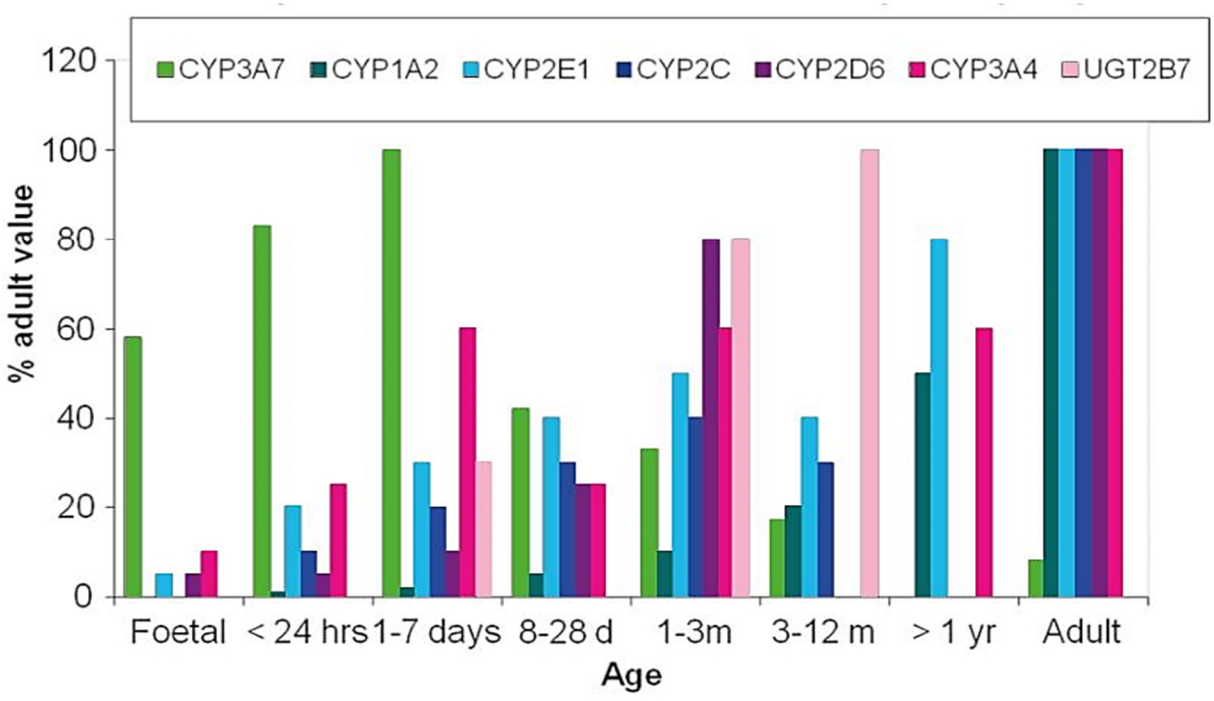

Fig 1.2. *Developmental differences in metabolic enzyme capacity of CYP3A7, CYP1A2, CYP2E1, CYP2C, CYP2D6, CYP3A4 and UGT2B7 according to age, expressed as a percentage of adult capacity[2].*

Analogous to phase 1 reactions, age-dependent differences in enzyme activity are found in phase 2 reactions (conjugation). Phase 1 and phase 2 enzymes that undergo clinical relevant changes during development are summarized in **Table 1.3**.

Table 1.3. Developmental patterns for the ontogeny of important drug-metabolizing enzymes in human[30]

Enzyme	Known developmental pattern
CYP1A2	Not present in appreciable levels in human fetal liver; adult levels reached by approximately 4 months and exceeded in children at 1-2 years of age; adult activity reached after puberty.
CYP2C9, CYP2C19	Apparently absent in fetal liver; low activity in first 2-4 weeks of life, with adult activity reached by approximately 6 months; activity may exceed adult levels during childhood and decline to adult levels after conclusion of puberty.
CYP2D6	Low to absent in fetal liver but present at 1 week of age; activity (i.e., 20% of adult) by 1 month; adult competence by 3-5 years of age.
CYP3A4	Extremely low activity at birth, reaching approximately 30%-40% of adult activity by 1 month and full adult activity by 6 months; may exceed adult activity between 1-4 years of age, decreasing to adult levels after puberty.
CYP3A7	Fetal form of CYP3A that is functionally active (and inducible) during gestation; virtually disappears by 1-4 weeks of postnatal when CYP3A4 activity predominates, but remains present in approximately 5% of individuals.
NAT2	Some fetal activity by 16 weeks' gestation; poor activity between birth and 2 months of age; adult phenotype distribution reached by 4-6 months, with adult activity reached by 1-3 years.
TPMT	Fetal levels approximately 30% of adult values; in newborns, activity is approximately 50% higher than adults with phenotype distribution, which approximates adults; exception is Korean children, where adult activity is seen by 7-9 years of age.
UGT	Ontogeny is isoform specific; in general, adult activity is reached by 6-24 months of age.
ST	Ontogeny is isoform specific and appears more rapid than that for UGT; activity for some isoforms may exceed adult levels during infancy and early childhood.

NAT2: N-acetyltransferase-2**; TPMT:** thiopurine methyltransferase; **UGT:** uridine 5'-diphospho-glucuronosyltransferase; **ST:** sulfotransferase

Adopted from Leeder JS, Kearns GL. Pharmacogenetics in pediatrics: implications for practice. Pediatr Clin North Am 1997; 44:55-77.

1.4.2.4. Excretion

Excretion is defined as *"the process by which waste materials and products of metabolism are eliminated from a body or organism, such as the removal of drugs and their products by the kidney, liver and lungs"*[31]. The major organ involved in the excretion of medication is the kidney. Excretion is achieved through three processes: glomerular filtration (GFR), tubular secretion and tubular reabsorption[26]. GFR and tubular secretion are low in newborns but they reach and exceed adult levels within the first few years of life due to structural and functional maturation of the kidneys (**Figure 1.3.**). Renally eliminated medication therefore shows an inferior clearance in neonates but a superior clearance in infants and preschool children[1 23 26]. Further, reabsorption of weak acids or bases may differ during development due to lower urinary pH in children. As a result, the reabsorption of weakly acidic medication can increase with repercussions on elimination[23 26].

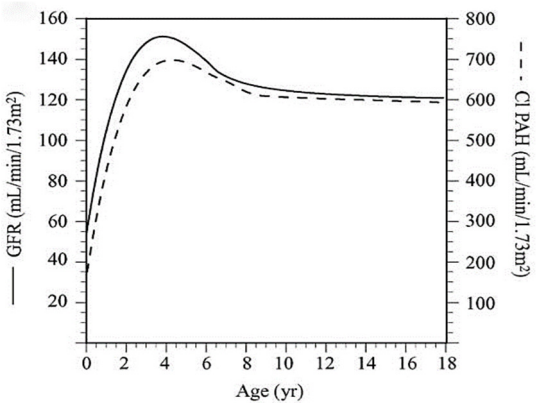

Fig. 1.3. *Age-dependent changes in GFR and p-aminohippurate (PAH) clearance: both levels of GFR and PAH clearance are greatly reduced in newborns, thereafter rise above levels in adults to eventually fall back and reach adult values at the age of 12*[1].

Data concerning changes in biliary excretion are more limited. The hepatic transport proteins, important for biliary medication clearance, would be inefficient in children[1]. The clinical relevance differs according to the transport proteins involved and the proportion of biliary excretion in relation to total excretion[1,28].

1.5. DRUG FORMULATION

If possible, as with adults, oral administration is preferred in children for stability and convenience[32]. However, small children (with an average age limit of six years) are not always able to ingest oral solid medication and consequently, other drug formulations are more important. In addition, not every excipient used in formulations for adults will be safe for use in children (cf. infra) and extra attention to flavors and textures will be necessary to increase compliance[32,33].

1.5.1. Administration route

1.5.1.1. Enteral administration

This includes oral, buccal, sublingual and rectal forms. Studies by Rashed et al.[6] and Kimland et al.[9] showed that almost half of medications administered to children are in oral form. This might still be an underestimation for primary care as these studies were carried out in a hospital setting. Liquid oral forms are often used in pediatrics when ingestion of solid medication is not (yet) possible. Smell and taste appear to be major barriers to (not) accepting the liquid form[32]. The flexibility in dosage offers a great advantage, however attention to dosing errors is necessary[33]. With oromucosal administrations, the organoleptic properties will be important. When the flavor or texture is not accepted, this may lead to premature spit out or ingestion of the medication with repercussion on the dosage. Finally, rectal administration has an important application in young children and offers a solution in case of nausea and vomiting or with swallowing difficulties. When using enemas, small volumes are required (vary from 1-5 ml, depending on age) so that irritation is maximally avoided[32,33].

1.5.1.2. Parenteral administration

Intravenous and intramuscular injections are often challenging because of difficult venous access and low muscle mass respectively[34]. The volumes for injection, especially in neonates, should be limited as much as possible. Use of commercially available ampoules for adults is achievable, with dilution if necessary[33]. Secondly, additional precautions for toxicity are indicated when using transdermal administration in children. Because of the increased body surface/body weight ratio, the chance of systemic side effects is more likely[34]. Besides that, another challenge in pediatrics is a correct inhalation technique. Therefore, it is important to adjust the use of inhaled medication to age by using tools like a spacer or special baby masks. According to

the systematic review of Gillette et al.[35] using a metered-dose inhaler (MDI) without a spacer led to an average number of correct steps ranged from 18% to almost 97%. When a spacer was applied, this range reached 70% to 92,8%. This in turn led to a higher deposition at the level of the lungs. For ocular, nasal and auricular forms of administration, there are no specific implications in children[33].

1.5.2. Excipients

As mentioned earlier, excipients are of major importance to ensure an acceptable taste and stability. To increase the compliance of pediatric formulations, flavorants, colorants and sweeteners are added. In this regard it is important that the color matches the taste, for example, a lemon tasting formulation should have a yellow color[36]. With an increased number of excipients added to the formulation, the potential for medication-excipient and excipient-excipient incompatibility increases likewise. But this is not the only reason why pediatric drug formulation is more complex. Concomitant, not every excipient can be used in children without risks[33]. Examples of "problem" excipients and their potential adverse effect(s) in children are summarized in **Table 1.4.**

1.6. FOCUS ON PARACETAMOL, IBUPROFEN AND ANTIBIOTICS

In 2008-2009, Rashed et al[6]. conducted a prospective multicenter cohort study in five countries i.e. Australia, Germany, Hong Kong, Malaysia and the UK. Over the five countries, 1278 children (0-18 years) who stayed in the pediatric ward for more than 24 hours were included. Based on therapeutic classes, the most frequent medication prescriptions were seen for systemic antibacterials followed by analgesic medications. The anti-inflammatory medications came in fourth place. Based on chemical substance, paracetamol was the most commonly prescribed medication followed by ibuprofen. This study, carried out in a hospital setting, showed that 65% of the pediatric population were given at least one systemic antibacterial during their hospital stay. Almost 61% of the children were given at least one analgesic and 22.1% at least one anti-inflammatory and anti-rheumatic product. If we compare this with primary care[8], antibacterials for systemic use are again most frequently prescribed (<2 years: 435/1000 person years and 2-11 years: 288/1000 person years), with penicillin derivatives and macrolides knowing the largest use. Noteworthy is the less important proportion of paracetamol and ibuprofen. This is probably an underestimation as this medication has a large over-the-counter use while this study only included prescribed medication. Therefore, in this master dissertation, we will focus on these three medications or medication groups.

Table 1.4. Examples of excipients, their role in formulations, potential adverse effect(s) in children, threshold for toxicity and examples of medication containing this excipient

Excipient	Role in formulation	Adverse effect(s)	Threshold for toxicity[37]	Examples of medication containing this excipient
Aspartame	Artificial sweetener	A source of phenylalanine that should be avoided in patients with phenylketonuria.	Zero[a]	Augmentin® (Amoxicillin/clavulanic acid oral suspension)
Benzyl alcohol	Preservative	Gasping syndrome in neonates[b]	Zero[a]	Montelukast (5 mg chewable tablets) Available for children from 6 years old
Benzoic acid	Preservative	Jaundice in neonates	Zero[a]	Comtrex® (paracetamol 325 mg/ phenylephrine hydrochloride 5 mg)
Colorants	Coloring agent	Sensitivity reactions and hyperactive behavior in children	Zero[a]	Perdolan® (50 mg/ml oral suspension) Muco Rhinathiol® (2% syrup)
Ethanol	Solvent	Intoxication (effects of prolonged exposure are not known)	100 mg per dose	PLANTSPRAY® Stodal® (syrup)
Fructose	Sweetener	Should be strongly avoided in children (under the age of two) as diagnosis of hereditary fructose intolerance often has not yet been made. Medications (containing fructose) given intravenously may be life-threatening.	Zero[a]	Emetrol® (Fructose/ Dextrose/ phosphoric acid) Lysox® (Acetylcysteine 200 mg)
Glucose and sucrose	Sweetener	Risk of dental caries and obesity	Zero[a]	Perdolan® (50 mg/ml oral suspension) Muco Rhinathiol® (2% syrup)
Parabens (methyl-, ethyl- and propyl-hydroxybenzoates)	Preservative	Suggestion of estrogenic activity with potential reproductive effects (with propylparaben), hypersensitivity reactions and hyperbilirubinemia in neonates	Zero[a]	Bronchosedal® (dextromethorphan HBr 2 mg/ml syrup) Available for children from 6 years old
Propylene glycol	Solvent	Central nervous system (CNS) effects (seizures, coma, respiratory depression…) especially in neonates and children under the age of four.	Neonates up to 28 days: 1mg/kg/day 1 month-4 years: 50 mg/kg/day 5-17 years: 500 mg/kg/day	Perdolan® (32 mg/ml syrup) Clindamycin (150 mg capsules) Amoxicillin (250 mg/500 mg capsules)
Sodium metabisulfites	Antioxidant	Wheezing, dyspnea and chest tightness in asthmatic children	Zero[a]	Xylocaine (10 mg/ml) + adrenaline (5 µg/ml) solution for injection
Sorbitol	Sweetener	Source of fructose (cf. supra), osmotic diarrhea and gastrointestinal discomfort	Zero[a]	Perdolan® (50 mg/ml oral suspension)

Adapted from Arthur S, Burgess A. How to identify and manage 'problem' excipients in medicines for children 2017 [Available from: https://www.pharmaceutical-journal.com/learning/learning-article/how-to-identify-and-manage-problem-excipients-in-medicines-for-children/20203121.article#fn_1 accessed February 27, 2018.]

[a] A threshold of zero means that the adverse effect(s) may occur from the moment the excipient is present in the preparation.

[b] *"A syndrome in preterm neonates exposed to benzyl alcohol preservative in intravascular solutions that is characterized by unremitting gasping respirations and may include anion gap metabolic acidosis, neurologic deterioration, renal failure, convulsions, intraventricular hemorrhage, and cardiovascular collapse."*[38]

1.6.1. Paracetamol

Paracetamol is a well-tolerated, registered and widely used medication in children. The mechanism of action of paracetamol is complex and not entirely clear but in general, paracetamol is considered to give a weak inhibition of the prostaglandin synthesis[39]. Therefore, it is a strong antipyretic and analgesic (which has a central origin[35]), but it has limited anti-inflammatory effects[40]. According to the guidelines[41,42], it is the first-line treatment in children with fever and pain. Despite the fact that it is a fairly safe medication, attention must be paid to paracetamol-induced liver intoxication[43]. For that reason, paracetamol is contraindicated in children with liver damage. A study by Kominek et al[3]. suggested that paracetamol intoxication is most prevalent in case of intentional poisoning. This was particularly common among adolescents (12-17 years). A real overdose, taken because of severe pain, was much less common (in 9.1% of the cases). In young children (2-4 years) we can conclude that primarily accidental poisoning occurred (**Figure 1.4.**). To avoid this, it is important to respect the maximum dosage of 60 mg/kg/day (with a maximum of 2g/day) in children (3 months to 18 years) with mild pain and fever[44]. Oral administration (solid or liquid) is preferable but when not possible, rectal administration may provide a solution.

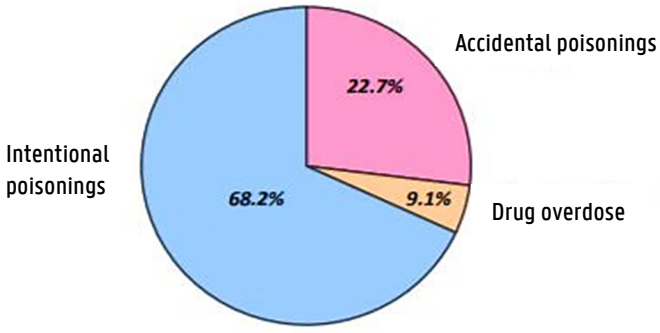

Fig. 1.4. *Percentage distribution of the causes of paracetamol poisonings in patients hospitalized in the Pediatric Clinic during 2004-2012*[3]*.*

1.6.2. Ibuprofen

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) inhibiting the prostaglandin synthesis by inhibition of cyclo-oxygenase (COX) as major mechanism of action. It possesses analgesic, antipyretic and anti-inflammatory effects[45]. Ibuprofen is used in children for various forms of pain (headache, migraine, muscle and joint pain…), juvenile arthritis and fever[46]. In case of fever, ibuprofen has the same (or higher) activity as paracetamol, yet paracetamol remains the first-line therapy because of the superior tolerability[45,47]. With short-term use of ibuprofen, there is generally no increased risk of gastrointestinal bleeding, renal failure or anaphylaxis[48,49]. However, the use of ibuprofen is discouraged in children with known gastric problems and kidney diseases. Other contraindications are children at risk of dehydration (diarrhea/vomiting), children with a known NSAID hypersensitivity and in case of varicella infection. This is due to the association with serious skin complications[50,51]. In the report of Safe Kids Worldwide, ibuprofen is the drug molecule most involved in calls to poison control centers for children aged five and younger[52]. In this

regard, paying attention to the dosage is necessary. When used for treatment of fever and pain (children aged 3 months-12 years) the oral dosage may not exceed 20-30 mg/kg/day in 3-4 doses, with a maximum of 3 days[53]. Similar to paracetamol, oral administration is preferred.

1.6.3. Antibiotics

The use of antibiotics in children is widespread and very useful in case of severe bacterial infections. For example, antibiotics are recommended in case of bacterial meningitis, pneumonia, sepsis etc.[54] The mode of action and usage differs depending on the antibiotic class. Side effects are commonly observed with these powerful medications. Generally, the commensal gut flora can be influenced by all antimicrobial agents resulting in diarrhea and yeast- and fungal infections. According to a study by Wistrom et al.[55] among groups of patients treated with one antibiotic, antibiotic-associated diarrhea (AAD) was most commonly seen in treatment with broad-spectrum penicillins, cephalosporins and clindamycin. Regarding combinations of antibiotics, the combination "cefpodoxime protexil + other" resulted most frequently in AAD, followed by "ceftazidime + other". Another major problem due to the use of antibiotics is the overgrowth of Clostridium difficile with the occurrence of pseudomembranous colitis. This is largely seen with the use of lincomycin and clindamycin[56]. Moreover, during growth and development, two classes of antibiotics are contraindicated i.e. fluoroquinolones (risk of cartilage damage[57]) and tetracyclines (risk of permanent tooth discoloration[58]). Recently, new insights have been gained into the consequences of (extensive) use of antibiotics in the pediatric population. In addition to the general side effects, the long-term consequences are not as innocent as previously thought. Associations were already found between the disruption of the developing microbiome because of antibiotics and the development of asthma[59 60], allergies[61 62], obesity[63-65] and inflammatory bowel disease[66 67].

Additionally, there is a worldwide problem considering antibiotic resistance that needs to be addressed urgently[68]. Therefore, in 2015, the World Health Organization (WHO) created the global action plan on antimicrobial resistance[69]. Also in Belgium, actions have already been taken to limit antibiotic use and resistance through the creation of the BAPCOC[4] guide that includes guidelines on rational use of antibiotics and dosage information for children. This should make clear that, especially in very young children, the use of antibiotics should be limited as the benefits do not always outweigh the disadvantages. This does not detract from the fact that antibiotics can be life-saving medication and therefore also appropriate in some situations.

[4] Belgian Antibiotic Policy Coordination Committee (BAPCOC) is a federal agency with a strong scientific base that aims to promote responsible antibiotic use in Belgium and to combat increasing antibiotic resistance.

1.7. PATIENT PERSPECTIVES

When it comes to medication use in children, parents play a central role. Therefore, parental expectations are important and need to be addressed. As (young) children are usually unable to make health-related decisions themselves, parents need to be well informed. Therefore, insight into the perspectives of patients and parents are necessary to improve the quality of pediatric care. Unfortunately, today's focus on improving the quality of care is too often on what professionals think while patient perspectives are usually forgotten. This implies a change in our thinking pattern in which patients and parents will be (actively) involved in improving pediatric care instead of being only (passive) recipients of care[70].

Patient experiences have already proven their worth and recent research has established that there is a positive relationship between patient experience, effectiveness and safety[71]. For example, an improved and more timely diagnosis can be supported when transparent information and an empathic, two-way communication is applied. This leads to less unnecessary diagnostic testing and an increase in participation in personal care. Moreover, by involving the patient, the value of the medication will become clearer which in turn leads to an increased adherence to therapy. Accordingly, transparent communication and monitoring of patient expectations is an added value to increase effectiveness[71]. Other studies showed positive associations between patient perspectives and safety. For example, Isaac et al.[72] found a positive correlation between measures of patient experiences of care and six safety indicators (decubitus ulcer; failure to rescue; infections due to medical care; postoperative hemorrhage, respiratory failure, pulmonary embolism and sepsis).

But there are also a few difficulties that should be considered when assessing patients' experiences. Attention should be given to the fact that patients are a heterogeneous group with varying expectations, experiences and different levels of knowledge. Consequently, the problems of selection and reporting bias will have to be considered[70]. Therefore, patient experiences are all too often regarded as subjective and separate from the "real" clinical work. In this regard, it is important that this attitude is abandoned and the usefulness of such studies, both in terms of safety and effectiveness, is recognized.

2. OBJECTIVES

In scientific research, focus is often on the point of view of healthcare providers. However, patient perspectives are becoming increasingly important. When we consider the pediatric population, the latter is the responsibility of the parents. Therefore, we wanted to involve both parents and healthcare providers (specifically GPs and CPs) in this research. The goal was to map expectations and knowledge of parents on the one hand and perspectives of healthcare providers on the other.

- First, we aimed to assess the general expectations of parents when consulting GPs or CPs with an ill child. Subsequently, we intended to assess the knowledge of parents about three commonly used medications or medication groups in children, i.e. paracetamol, ibuprofen and antibiotics. Finally, we wanted to determine which healthcare provider parents consult for which indication.
- We aimed to simultaneously investigate the perspectives of GPs and CPs about treating children. Our first objective was to evaluate general aspects which healthcare providers consider important when treating a child. Secondly, we aimed to determine which actions concerning information provision healthcare providers carry out when prescribing or dispensing paracetamol, ibuprofen or antibiotics.

Finally, we intended to evaluate to what extent parents' expectations correspond to healthcare providers practices. In addition, we wanted to determine the areas in which parents do not have sufficient knowledge of the medication used for their child. By examining the expectations and knowledge of parents, we believe to improve primary care for the pediatric population by a more adequate response of healthcare providers.

3. METHODS

3.1. STUDY DESIGN AND SETTING

During April and May 2018, an observational, cross-sectional study was performed, set in the five provincial capitals of Flanders (Antwerp, Bruges, Ghent, Hasselt and Leuven). In this study, parents of young children and primary healthcare providers (GPs and CPs) were questioned about their perspectives on primary care and medication use in children through (online) questionnaires. The study was collaboratively developed by a pharmacist and a pediatrician and approved by the Ethics Committee of the Ghent University Hospital (B670201836025). All participants gave their consent when starting the questionnaire.

3.2. PARTICIPANTS

The survey for parents was solely conducted through online questionnaires. Parents with at least one child between the age of zero and twelve were eligible. Parents were contacted through a selection of nurseries, kindergartens and elementary schools in the five provincial capitals. A list of 10 nurseries and 10 elementary schools was drawn up for each city using Google Maps[73]. First, we searched the name of the city. Subsequently, "nursery" or "elementary school" was used as a search term. In each city, the first 10 nurseries and schools that appeared were called. When a nursery or school agreed to participate in the research, they disseminated the URL link to the parents by e-mail. The online survey was available from April 16 to May 7. We aimed to include 200 parents.

Simultaneously, two slightly different questionnaires were developed for GPs and CPs. We aimed to visit five pharmacies and one GP group practice in person in every city to include a minimum of 25 CPs and 25 GPs. In order to reach a wider target population, the questionnaire was spread online as well. For this purpose, social media channels were used. The selection of pharmacies to contact was also carried out through Google Maps[73]. In the five provincial capitals of Flanders, we searched for "pharmacy". Based on the first pharmacies to appear, a list was created for every city. Subsequently, they were called in order of appearance. In each city, the pharmacies that agreed to participate were included. The recruitment of physicians was done in a slightly different way. Because of feasibility, GP practices were selected based on the number of GPs active in the office. A list of three group practices was established for each city. These were subsequently contacted by phone. In every city, the first GP group practice that agreed to participate was included. The pharmacies and GP practices that agreed to collaborate were visited in April 2018. The objective was to include 100 healthcare providers (divided over the two groups). An overview of the method of recruitment is given in **Figure 3.1**.

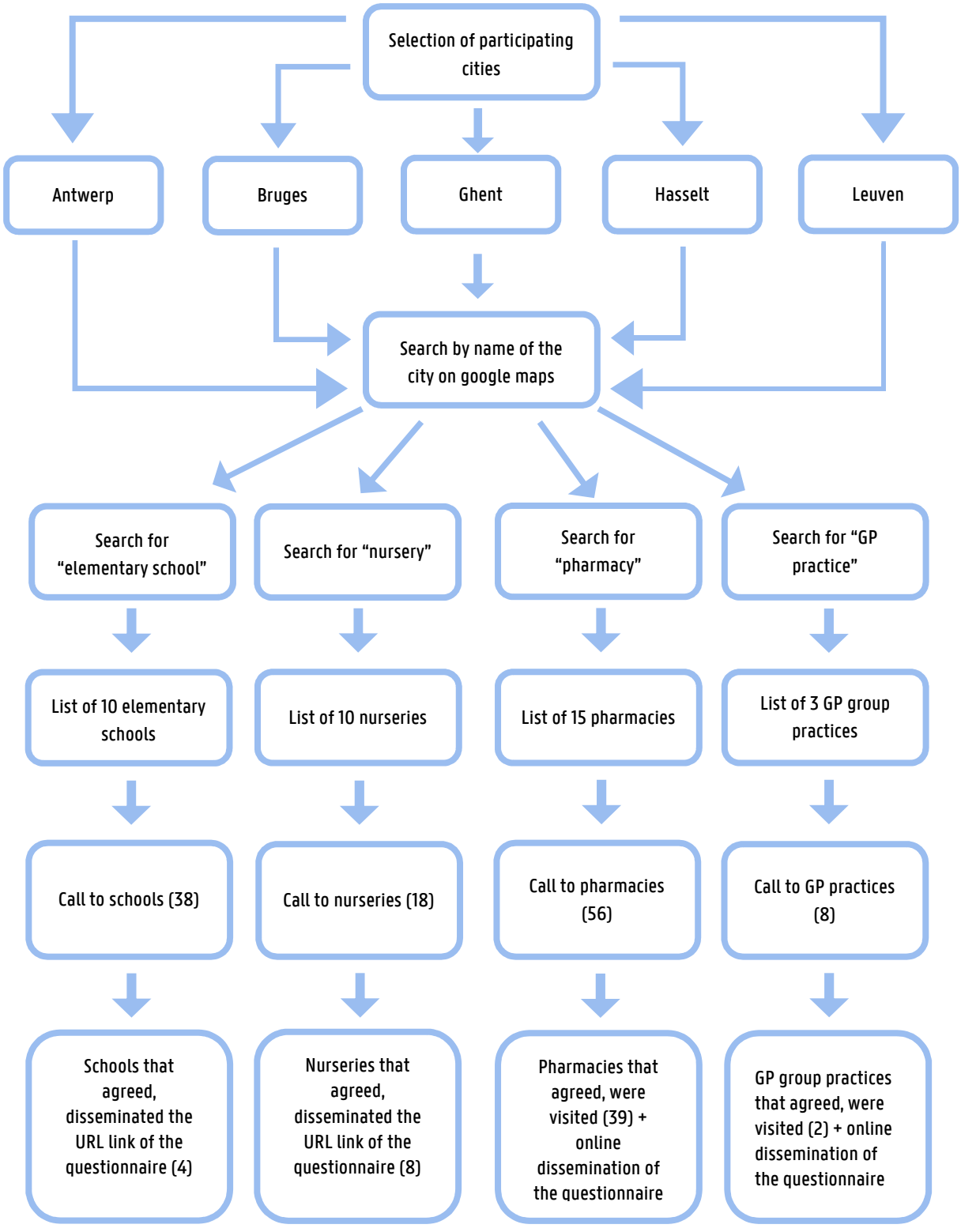

Fig. 3.1. *Overview of the applied method of recruitment of parents, CPs and GPs. Numbers in parentheses represent the corresponding quantities.*

3.3. QUESTIONNAIRES AND OUTCOMES

The survey for parents was divided into seven sections: (1) demographics, (2) expectations towards a GPs consultation and CPs dispensation, (3) expected source of information, (4) knowledge about paracetamol, (5) knowledge about ibuprofen, (6) knowledge about antibiotics and (7) practical cases. The survey can be consulted in appendix (**Annex A**). The questionnaires for healthcare providers contained the following five sections: (1) demographics, (2) scoring of actions relating to a consultation/dispensation for an ill child, (3) actions taken when prescribing/dispensing paracetamol, (4) actions taken when prescribing/dispensing ibuprofen and (5) actions taken when prescribing/dispensing antibiotics. Both questionnaires can be consulted in appendix (**Annex B & C**).

3.3.1. Parents' survey

Considering their expectations when consulting GPs or CPs when their child is ill, parents were asked to score statements on a 5-point Likert scale (1 indicating "not at all important" and 5 indicating "very important"). Subsequently, parents were asked from which healthcare provider they expect what information. Also, the perceived level of language use of their GP and CP was assessed on a 10-point scale (1 indicating parents do not understand anything of what the healthcare provider is telling them and 10 indicating everything is fully understood). The following three sections evaluated parents' knowledge about paracetamol, ibuprofen and antibiotics. First, it was investigated whether parents make a correct assessment of when this medication is recommended. Subsequently, a series of statements were submitted with the aim of indicating to what extent they agree with the statement. For this purpose, again, a 5-point Likert scale was used (1 indicating "strongly disagree" and 5 indicating "strongly agree"). Parents were also asked if their child had experienced any side effects in case they had already used antibiotics. This was followed by the question whether they had already heard of antibiotic resistance and, if so, what it is affected by in their opinion. In the last section, we presented three cases in which the parents had to indicate whom they would consult or where they would look for information. In first instance they were asked to do this in case the situation affected their child. This was followed by the question to repeat the evaluation when they themselves where the subject.

3.3.2. Healthcare providers' survey

First, general aspects to which GPs and CPs give attention when they are consulted by a parent with an ill child (0-12 years) were questioned. To this end, similar to the parents' questionnaire, healthcare providers had to assign scores, by using a 5-point Likert scale (1 indicating "not at all important" and 5 indicating "very important") to the listed statements. Supplementary, the GPs and CPs had to make an estimate of their own language use on a 10-point scale (1 indicating their patients do not understand anything that is being said, 10 indicating their patients understand everything). In the last three sections we investigated the information GPs and CPs provide when prescribing or dispensing paracetamol, ibuprofen and antibiotics. For this purpose, the healthcare providers were asked to recall their last consultation for/dispensation of paracetamol, ibuprofen and antibiotics for a child. Subsequently, they had to indicate the steps they had taken at that time. The healthcare providers were also asked to estimate how long a mean consultation or dispensation for paracetamol, ibuprofen and antibiotics lasts. To conclude the questionnaire, GPs and CPs were requested to estimate to what extent parents are aware of the problem regarding antibiotic resistance. GPs were specifically asked how many times they experience pressure from parents to prescribe antibiotics when they do not consider it necessary. Finally, the healthcare providers had the opportunity to write down remarks on antibiotic resistance.

3.4. STATISTICAL ANALYSIS

For the processing of the results, Excel® 2016 (Microsoft Corporation, Redmond, WA, USA) and SPSS statistics 25 (IBM Corp., Armonk, NY, USA) were used. First, the answers were coded in Excel® 2016. Descriptive statistics were applied for the calculation of numbers with percentages, medians with interquartile range and means with standard deviations as appropriate. Independent Samples T-tests were performed to compare means.

4. RESULTS

4.1. DEMOGRAPHICS

The study included a total of 380 respondents of which 224 were parents, 50 were GPs and 106 were CPs. Parents were reached through eight nurseries and four elementary schools that disseminated the questionnaire (**Annex D**). Of the responding GPs, 11 were personally interviewed (in two group practices) and 39 completed the questionnaire online. Only a limited number of GPs were interviewed personally because Bruges and Hasselt were the only provincial capitals where a group practice was found willing to cooperate within the time limit. Considering the 106 CPs, 46 were personally interviewed and 60 completed the questionnaire through the online form. Demographic data of included parents and healthcare providers are summarized in **Table 4.1**. and **Table 4.2.** respectively.

Table 4.1. Demographic data of included parents	
Parents (n = 224)	
Male gender, n (%)	31 (14%)
Age, mean ± SD (range)	35,3 ± 5,4 (24-57)
Origin, n (%)	
North African	3 (1%)
Other African	2 (1%)
Latin American	2 (1%)
Asian	2 (1%)
Caucasian	214 (96%)
Middle-East	1 (0%)
Participants with one child, n (%)	85 (38%)
Participants with two children, n (%)	107 (48%)
Participants with three children, n (%)	30 (13%)
Participants with four children, n (%)	2 (1%)
Age of participants' children, mean ± SD (range)	4,8 ± 4,1 (0-23)
Number of children per participant, median (IQR)	2 (1-2)
Distribution of participants by province, n (%)	
Antwerp	50 (22%)
East Flanders	43 (19%)
Flemish Brabant and Limburg	125 (56%)
West Flanders	6 (3%)
Education, n (%)	
Primary education	2 (1%)
Secondary education	29 (13%)
Higher education	193 (86%)
Job sector, n (%)	
Healthcare sector	52 (23%)
Education	42 (19%)
Government	24 (11%)
Independent entrepreneur	26 (12%)
Construction sector	7 (3%)
Food industry	21 (9%)
Banking and insurance	3 (1%)
Other	49 (22%)

Table 4.2. Demographic data of healthcare providers	
GPs (n = 50)	
Male gender, n (%)	18 (36%)
Age, mean ± SD (range)	36,5 ± 12,1 (25-72)
Number of GPs with (grand)children, n (%)	27 (54%)
Distribution of GPs by province, n (%)	
Antwerp	7 (14%)
East Flanders	17 (34%)
Flemish Brabant and Limburg	12 (24%)
West Flanders	14 (28%)
Years of experience, mean ± SD (range)	10,4 ± 12,4 (0-47)
Number of GPs in training, n (%)	13 (26%)
Number of FTEs in the GP practice, mean ± SD (range)[a]	3,7 ± 2,4 (1-10)
Mean number of patients a day, mean ± SD (range)[b]	21,8 ± 9,4 (10-60)
CPs (n = 106)	
Male gender, n (%)	20 (19%)
Age, mean ± SD (range)	33,9 ± 11,0 (22-70)
Number of CPs with (grand)children, n (%)	49 (46%)
Distribution of CPs by province, n (%)	
Antwerp	28 (26%)
East Flanders	32 (30%)
Flemish Brabant and Limburg	27 (25%)
West Flanders	19 (18%)
Years of experience, mean ± SD (range)	10,2 ± 10,3 (0-45)
Number of FTEs, mean ± SD (range)[c]	2,8 ± 1,5 (1-9)
Position, n (%)	
Number of responsible pharmacists	47 (44%)
Number of deputy pharmacists	49 (48%)
Number of PTAs	3 (3%)
Number of pharmacist interns	7 (7%)
Mean number of patients a day, mean ± SD (range)[d]	119,7 ± 55,2 (40-400)

CP: Community Pharmacist; **FTE:** Full-Time Equivalents; **GP:** General Practitioner; **PTA:** Pharmaceutical Technical Assistant

[a] Calculated based on the response of 49 GPs
[b] 2 GPs answered this question with "varies significantly"
[c] Calculated based on the response of 100 CPs
[d] 24 CPs answered this question with "varies significantly"

4.2. PARENTS' SURVEY

The parents' assessment of the expectations when visiting GPs and CPs with their ill child is illustrated in **Figure 4.1** and **Figure 4.2.** Only those parents indicating that they had already consulted a pharmacist when their child was ill (without prior consultation of a physician) were presented the statements concerning CPs (n=146). **Figure 4.3.** gives an overview of which healthcare provider should provide what information according to parents.

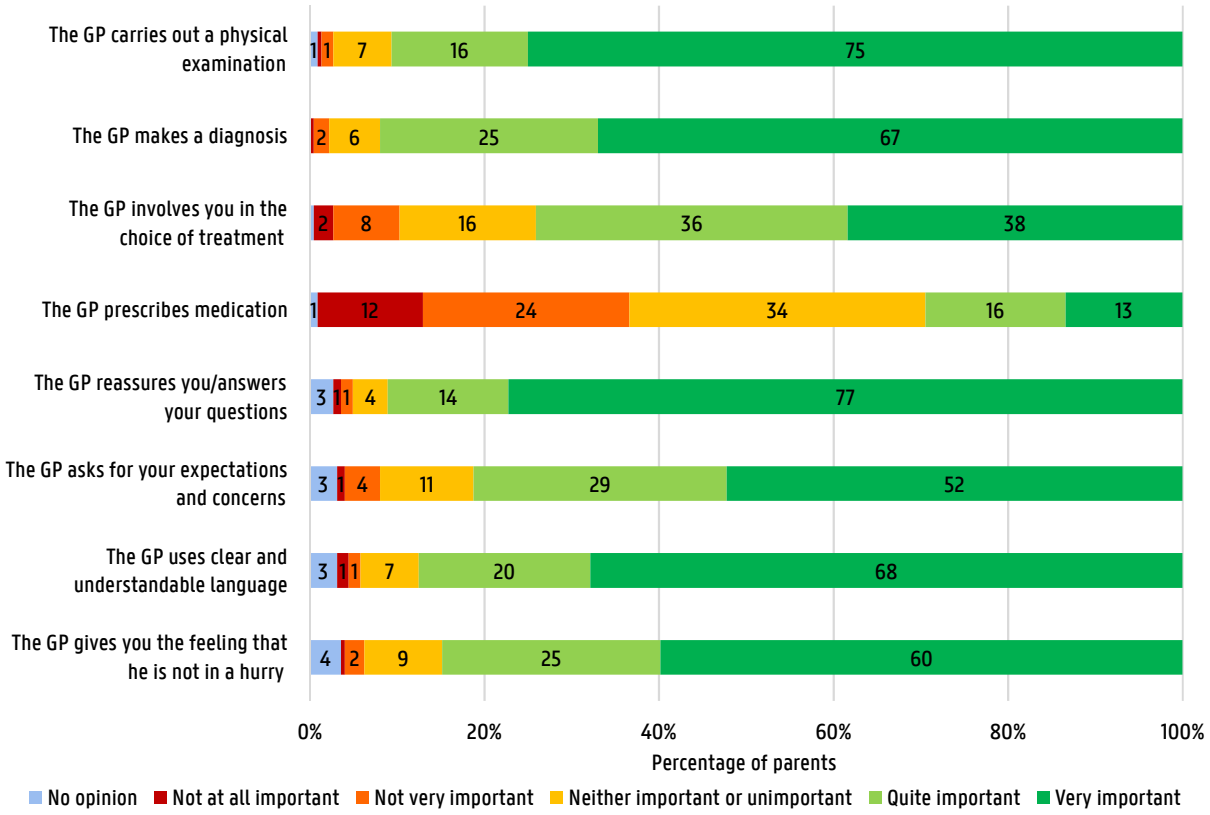

Fig. 4.1. *Representation in percentage of parents' expectations when visiting a GP with their ill child (n=224).*

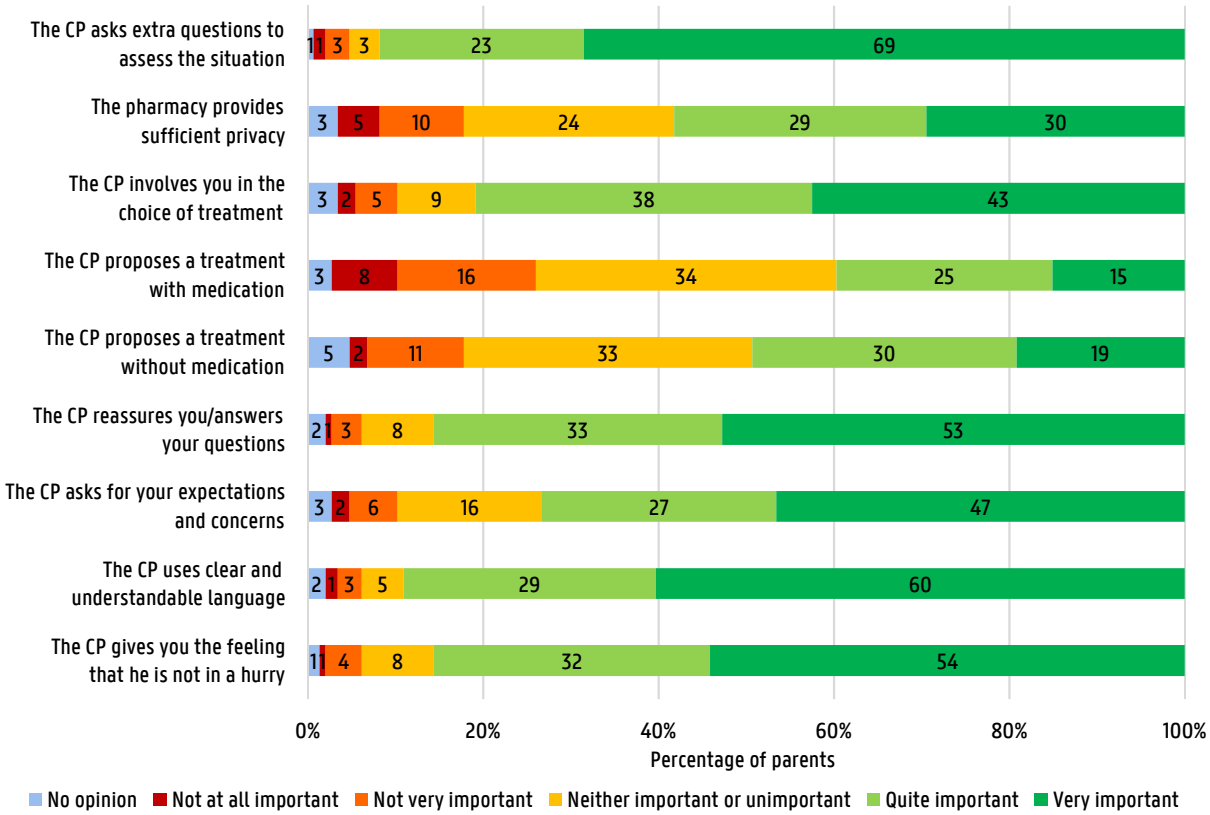

Fig. 4.2. *Representation in percentage of parents' expectations when visiting a CP with their ill child (n=146).*

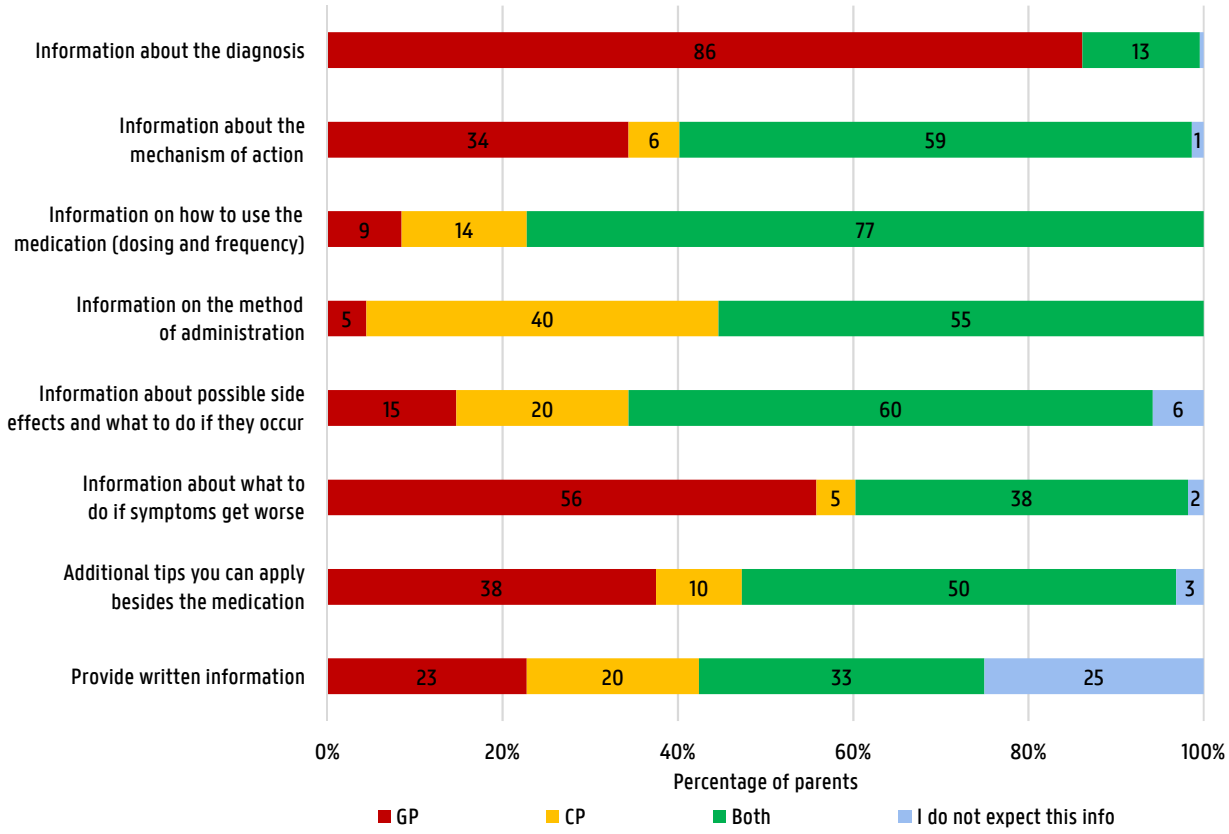

Fig 4.3. *Representation in percentage of which healthcare provider should provide what information according to parents (n=224).*

Of the 224 included parents, 222 (99%) indicated to know paracetamol, 219 (98%) ibuprofen and 222 (99%) antibiotics. Only parents who indicated to know the specific medication were provided with the questions about the subject. When asked in which situations parents administer paracetamol to their child(ren), the majority of the parents answered (high) fever and pain. The answer “pain when the teeth come in” was frequently given. Three parents (1,3%) indicated to give paracetamol for inflammation. When examining the answers about ibuprofen, parents give ibuprofen mainly in case of fever and pain. However, it was often noted they prefer paracetamol. Parents also alternate ibuprofen with paracetamol (whether or not on physicians' advice). Twenty parents (8,9%) never used ibuprofen or only if the physician recommended it.

Table 4.3. represents the proportion of parents that deem the use of paracetamol, ibuprofen or antibiotics appropriate in certain situations. **Table 4.4** shows the (non-)medical choice of parents in case of different symptoms/diseases in their child.

Table 4.3. Representation of the proportion of parents that deemed paracetamol, ibuprofen and antibiotics appropriate in case of different symptoms/diseases				
Symptom/disease	N (%)[a]		Symptom/disease	N (%)
	Paracetamol	Ibuprofen		Antibiotics
Fever (>38°C) and your child does not feel ill	73 (33%)	39 (18%)	Influenza	4 (2%)
Fever (>38°C) and your child feels ill	210 (95%)	153 (70%)	Cold	0 (0%)
Influenza	88 (40%)	53 (24%)	Pneumonia	187 (84%)
Headache	97 (44%)	52 (24%)	Varicella (chicken pox)	8 (4%)
Inflammatory pain (e.g. ear inflammation or pharyngitis)	119 (54%)	160 (73%)	Sore throat	2 (1%)
Muscle pain	22 (10%)	37 (17%)	Bronchiolitis (RSV)	79 (36%)
Abdominal pain	15 (7%)	8 (4%)	Meningitis	163 (73%)
Sprained ankle	20 (9%)	30 (14%)	Ear inflammation	136 (61%)
			Pharyngitis	116 (52%)
			Diarrhea	4 (2%)
			Fever	1 (1%)

[a] Parents were not asked to choose between paracetamol or ibuprofen, so both answers could be indicated.

Table 4.4. Representation of (non-)medical choice of parents in case of symptoms/diseases in their child				
Symptom/disease	N (%)			
	I would not give any medication	Paracetamol	Ibuprofen	I give what I have at home
Fever	3 (1%)	**145 (66%)**	34 (16%)	37 (17%)
Headache	85 (39%)	**89 (41%)**	18 (8%)	27 (12%)
Influenza	64 (29%)	**100 (46%)**	22 (10%)	33 (15%)
Ear inflammation	20 (9%)	56 (26%)	**116 (53%)**	27 (12%)

The parents' assessment of the statements to review their knowledge about paracetamol, ibuprofen and antibiotics are summarized in **Figure 4.4., 4.5.** and **4.6.**

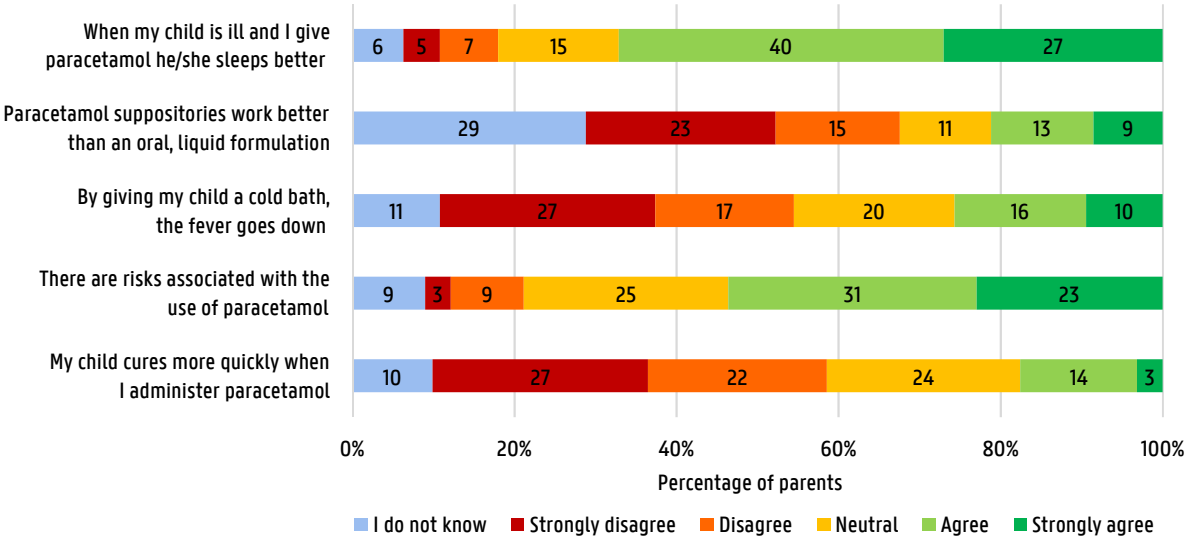

Fig. 4.4. *Parents' assessment in percentage of the statements examining knowledge about paracetamol (n=222).*

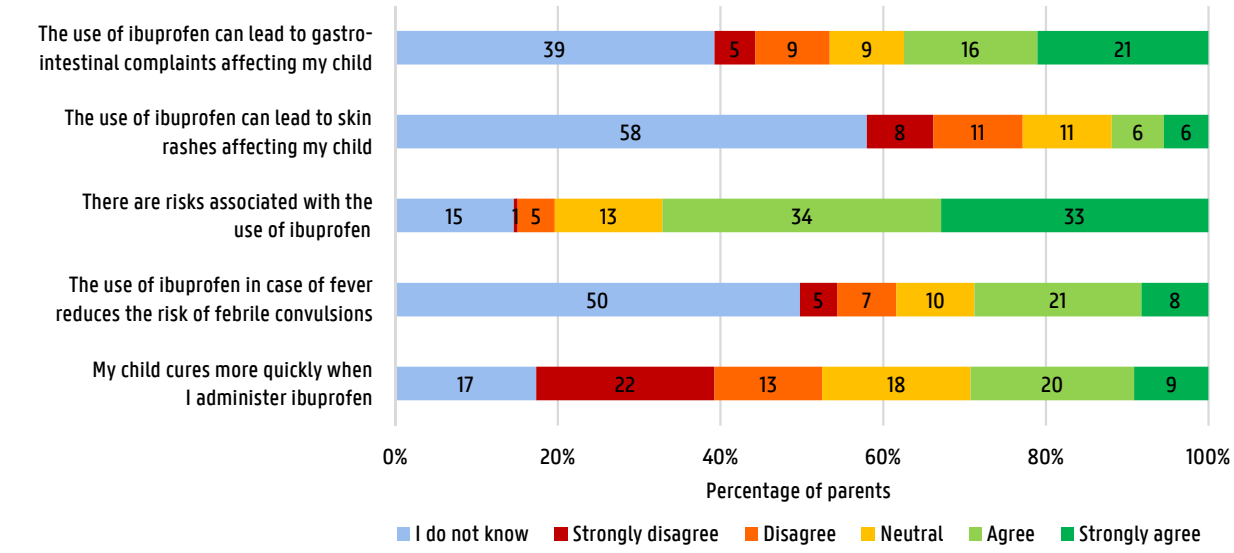

Fig. 4.5. *Parents' assessment in percentage of the statements examining knowledge about ibuprofen (n=219).*

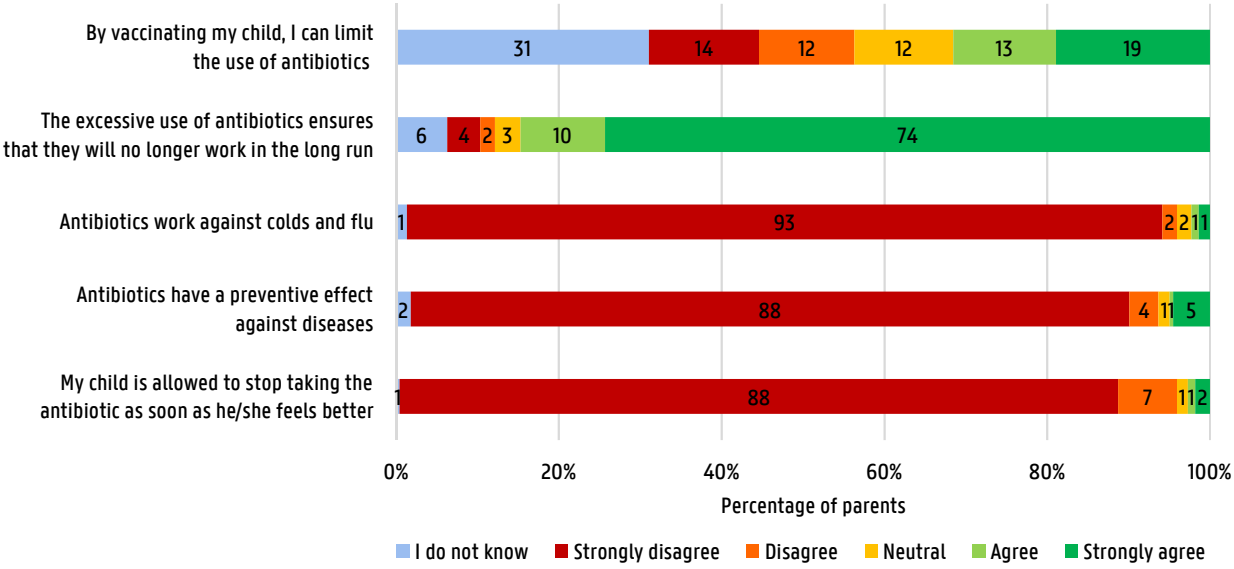

Fig. 4.6. *Parents' assessment in percentage of the statements examining knowledge about antibiotics (n=222).*

When asked what side effects their child(ren) have experienced in case of antibiotic use, the most frequent answer was "gastrointestinal complaints" and in particular "diarrhea". "Skin rashes" and "allergic reactions" were also mentioned. Some parents indicated that their child(ren) did not experience any side effects. Furthermore, 182 (82%, n=222) parents indicated to already have heard about antibiotic resistance. In their opinion, excessive and incorrect use encourages this. Examples were cited, such as "not finishing the entire course" and "prescribing and using antibiotics for conditions for which this is not actually indicated".

Figures 4.7., 4.8. and **4.9.** show which healthcare provider(s) parents would consult or where they would look for information regarding case 1, 2 and 3 respectively (choosing more than one option was allowed).

"When your child (7 years old) came home from school last night, he/she felt completely in order. After dinner he/she suddenly complained about headaches and muscular pain. You decided to measure temperature, which was 39.5°C. Subsequently, your son/daughter went to bed early, but this night he/she felt very unwell with cold shivers and severe headache. This morning it was a challenge to eat or drink."

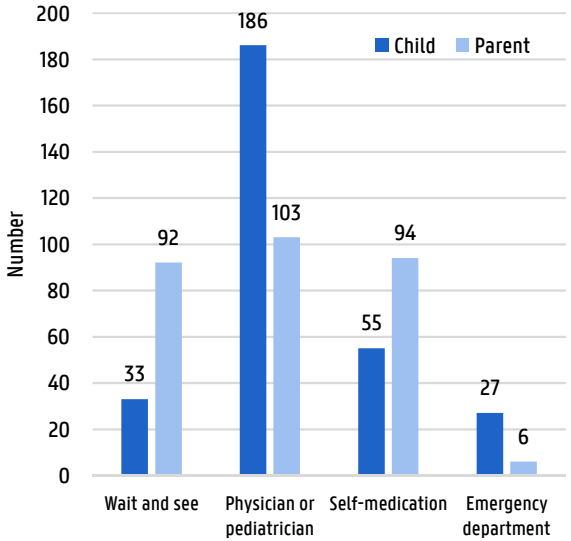

Fig. 4.7. *Comparison of which healthcare provider parents (n=224) would consult/where they would look for information when case 1 affects their child versus when the situation affects themselves. The options chosen by less than 10% of the parents are not shown.*

"You pick up your 6-month-old baby from the nursery. He has been coughing for two days and also suffers from a stuffy nose. He does not have a fever but he is very weepy. Sleeping is difficult because of this, for both the baby and you."

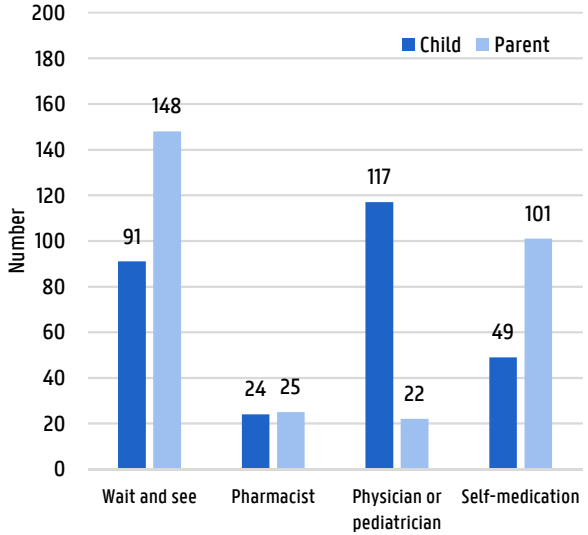

Fig. 4.8. *Comparison of which healthcare provider parents (n=224) would consult/where they would look for information when case 2 affects their child versus when the situation affects themselves. The options chosen by less than 10% of the parents are not shown.*

"When your child (10 years old) came home from a school trip last night, he/she complained of abdominal pain and therefore did not want to eat. This morning he/she got up with diarrhea and had to go to the toilet four times in two hours. It is now lunchtime and the abdominal pain is still not better, moreover he/she currently feels a bit nauseous."

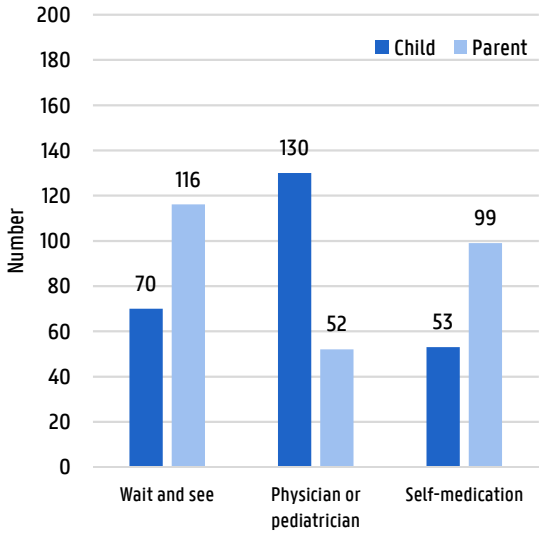

Fig. 4.9. *Comparison of which healthcare provider parents (n=224) would consult/where they would look for information when case 3 affects their child versus when the situation affects themselves. The options chosen by less than 10% of the parents are not shown.*

4.3. HEALTHCARE PROVIDERS' SURVEY

Figure 4.10. shows the importance GPs attach to certain actions during a consultation for an ill child. Results of level of language use of GPs are shown in **Figure 4.11.** An Independent Samples T-test for comparing the mean scores assigned to the language use by parents versus GPs (MD = 0,8 [95% CI: 0,53 - 1,07]; p < 0,001) was performed.

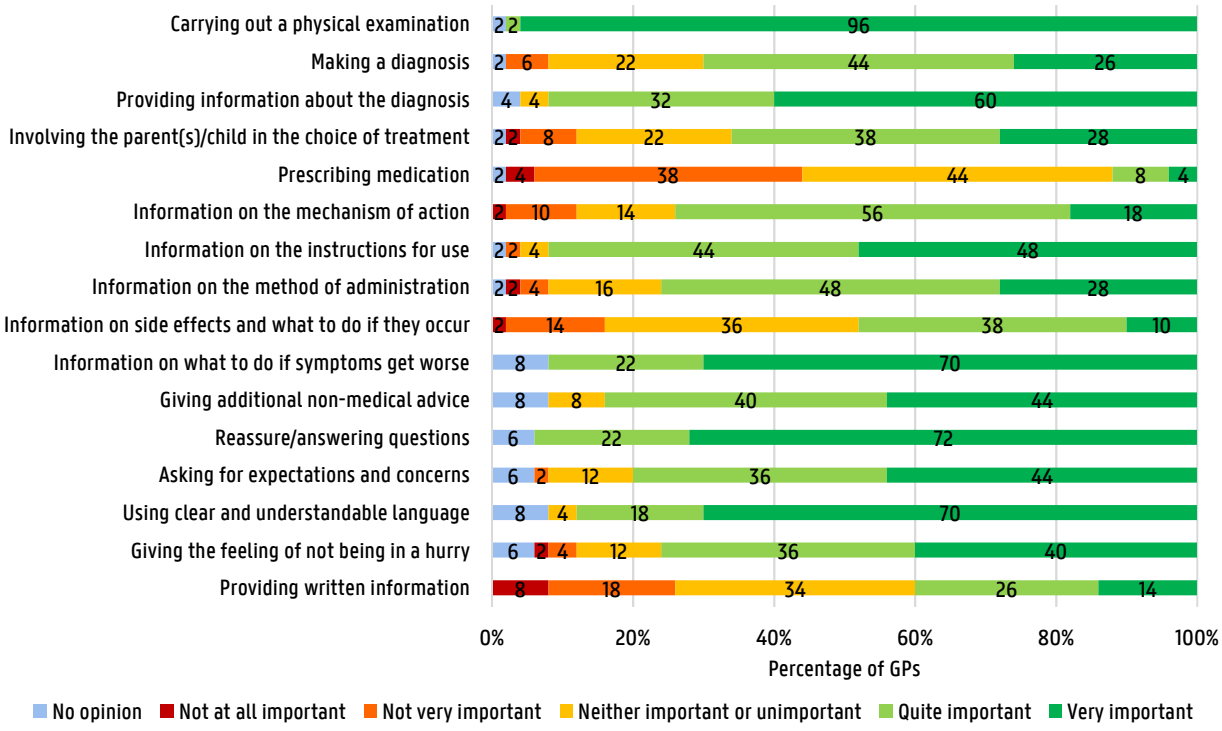

Fig. 4.10. *Representation in percentage of the importance attached to certain actions during a consultation for an ill child by GPs (n=50).*

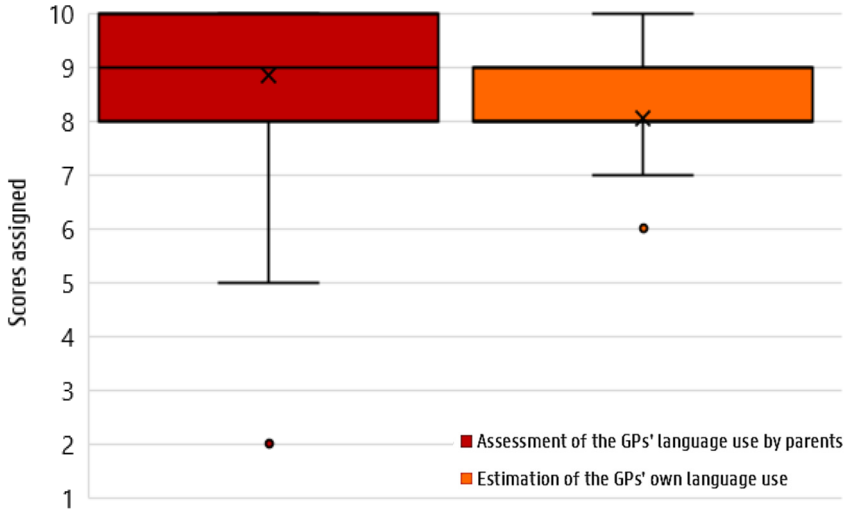

Fig. 4.11. *Comparison of how parents (n=224) assess the GPs' language use on a scale from 1 to 10, where 1 means they do not understand anything and 10 indicating everything is fully understood (mean ± SD: 8,9 ± 1,1; range: 2-10), with GPs' (n=50) estimation of their own language use (mean ± SD: 8,1 ± 0,8; range: 6-10).*

Figure 4.12. shows the importance CPs attach to certain actions during a consultation/dispensation for an ill child. Results of level of language use of CPs are shown in **Figure 4.13.** An Independent Samples T-test for comparing the mean scores assigned to the language use by parents versus CPs (MD = 0,9 [95% CI: 0,65 - 1,15]; p < 0,001) was performed. **Table 4.5.** provides an overview of the different actions GPs and CPs indicated to carry out when recalling their last consultation for/dispensation of paracetamol, ibuprofen and antibiotics.

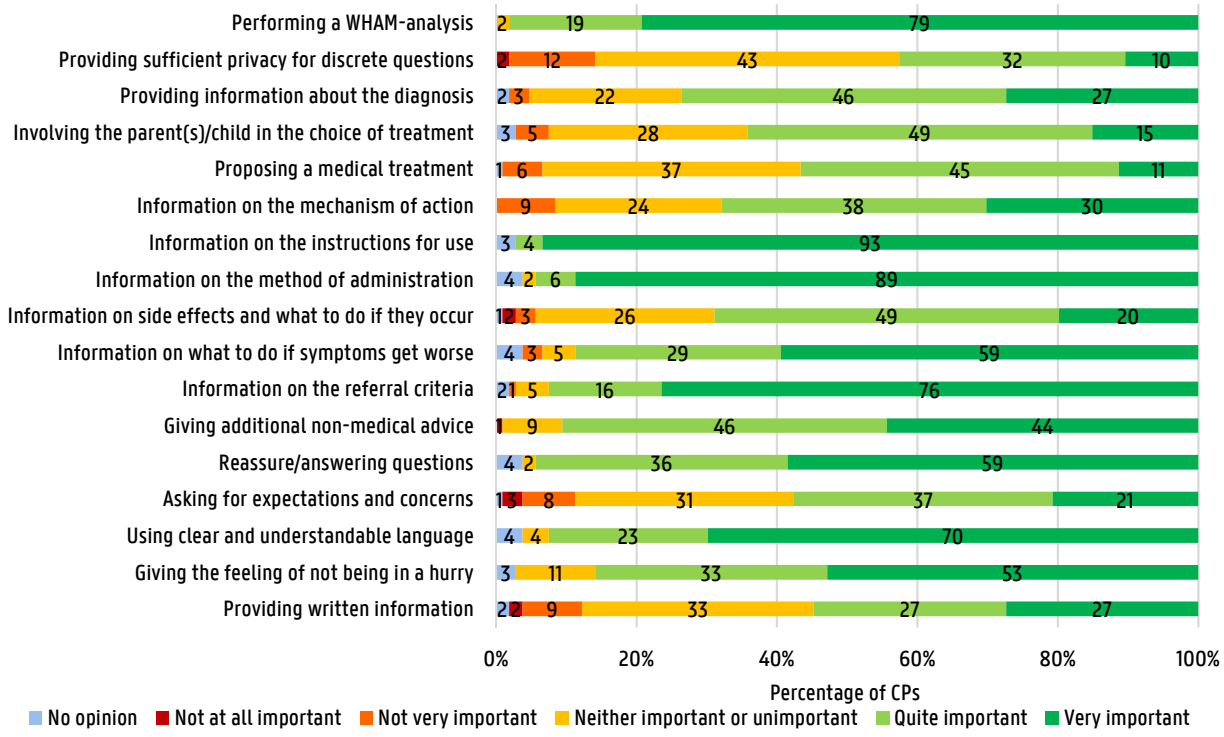

Fig. 4.12. Representation in percentage of the importance attached to certain actions during a consultation/dispensation of medication for an ill child by CPs (n=106).

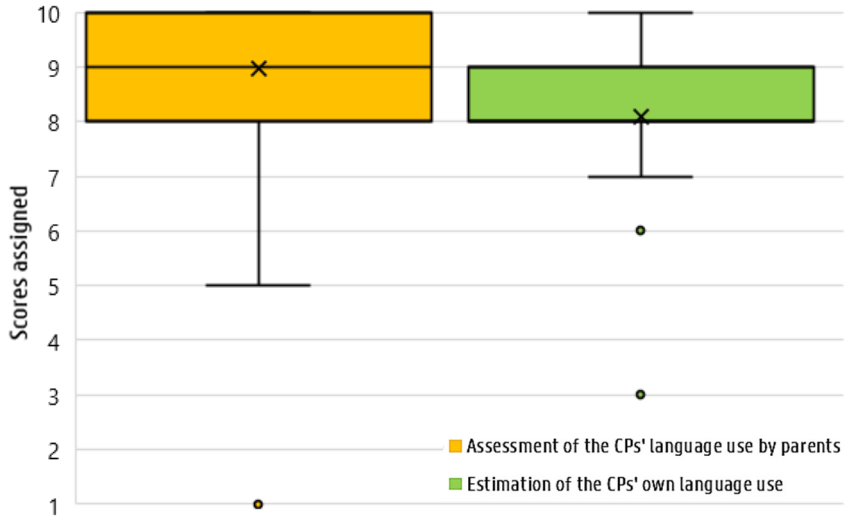

Fig. 4.13. Comparison of how parents (n=224) assess the CPs' language use on a scale from 1 to 10, where 1 means they do not understand anything and 10 indicating everything is fully understood (mean ± SD: 9,0 ± 1,1; range: 1-10), with CPs' (n=106) estimation of their own language use (mean ± SD: 8,1 ± 1,0; range: 3-10).

Table 4.5. Overview of the different actions carried out by GPs and CPs when recalling their last consultation for/dispensation of paracetamol, ibuprofen and antibiotics and for each action the number and percentage of GPs and CPs that performed them

Submitted action	N (%)	
Paracetamol	**GPs (n=50)**	**CPs (n=106)**
To perform a verbal anamnesis[a]	50 (100%)	NA
To perform a physical examination[a]	50 (100%)	NA
To perform a WHAM-analysis[b]	NA	102 (96%)
To discuss possible treatment options with parents	40 (80%)	65 (61%)
To provide information on the underlying condition *(in the case of paracetamol: pain and fever)*	49 (98%)	64 (60%)
To provide dosage information *(quantity and frequency)*	43 (86%)	106 (100%)
To provide information on the instructions for use *(e.g. how to use a dosing syringe)*[b]	NA	103 (97%)
To provide information on side effects/hazards of paracetamol	8 (16%)	26 (25%)
To provide information about stopping treatment	19 (38%)	37 (35%)
To provide information on referral criteria[b]	NA	82 (77%)
To provide information about returning to the GP[a]	45 (90%)	NA
To provide non-medical advice *(e.g. lifestyle adjustments and nutritional advice)*	42 (84%)	52 (49%)
To provide written information	7 (14%)	38 (36%)
Ibuprofen	**GPs (n=50)**	**CPs (n =105)**
To perform a verbal anamnesis[a]	50 (100%)	NA
To perform a physical examination[a]	50 (100%)	NA
To perform a WHAM-analysis[b]	NA	101 (96%)
To discuss possible treatment options with parents	42 (84%)	84 (80%)
To provide information on the underlying condition *(in case of ibuprofen: pain, fever or inflammation)*	50 (100%)	79 (75%)
To provide dosage information *(quantity and frequency)*	44 (88%)	105 (100%)
To provide information on the instructions for use *(e.g. how to use a dosing syringe)*[b]	NA	103 (98%)
To provide information on side effects/hazards of ibuprofen	32 (64%)	84 (80%)
To provide information about stopping treatment	28 (56%)	41 (39%)
To provide information on the referral criteria[b]	NA	84 (80%)
To provide information about returning to the GP[a]	48 (96%)	NA
To provide non-medical advice *(e.g. lifestyle adjustments and nutritional advice)*	40 (80%)	47 (45%)
To provide written information	9 (18%)	38 (36%)
Antibiotics	**GPs (n=50)**	**CPs (n=106)**
To perform a verbal anamnesis[a]	49 (98%)	NA
To perform a physical examination[a]	50 (100%)	NA
To discuss possible treatment options with parents[a]	46 (92%)	NA
To provide information on the underlying condition *(in the case of antibiotics: the bacterial infection for example, providing information about what a pneumonia is)*	48 (96%)	49 (46%)
To provide information on the dosage *(quantity and frequency)*	49 (98%)	105 (99%)
To provide information on the instructions for use *(e.g. how to use a dosing syringe)*[b]	NA	105 (99%)
To provide information on side effects/hazards of antibiotics	28 (56%)	65 (61%)
To provide information about (not prematurely) stopping the treatment	41 (82%)	101 (95%)
To provide information on the referral criteria[b]	NA	46 (43%)
To provide information about returning to the GP[a]	48 (96%)	NA
To provide non-medical advice *(e.g. lifestyle adjustments and nutritional advice)*	41 (82%)	50 (47%)
To provide written information	16 (32%)	41 (39%)

GP: General Practitioner; **NA:** Not Assessed; **WHAM:** Who - How (long) - Action - Medication

[a] This statement was only provided to GPs

[b] This statement was only provided to CPs

In addition, GPs (n=50) indicated that a consultation for paracetamol lasted a mean 16,7 ± 4,1 minutes (range: 10 min – 35 min). For ibuprofen and antibiotics, this considered respectively 16,5 ± 3,4 minutes (range: 12 min – 30 min) and 16,8 ± 3,8 minutes (range: 12 min – 30 min). CPs, on the other hand, reported that a dispensation of paracetamol (n=105) lasted a mean 5,3 ± 2,7 minutes (range: 1 min – 15 min), for ibuprofen (n=104) 5,7 ± 3,1 minutes (range: 1 min – 20 min) and for antibiotics (n=105) this considered 6,3 ± 2,7 minutes (range: 2 min – 15 min).

Out of 100 antibiotic consultations, GPs experience in 21,6 ± 20,5 (range: 0 – 90) cases pressure from parents to prescribe antibiotics when they do not consider it necessary. Out of 100 patients, GPs (n=50) believe that 38,4 ± 27,8 patients are knowledgeable about the antibiotic resistance problem (range: 0 - 90). CPs (n=105) think that 42,2 ± 20,0 patients are aware of this problem (range: 1 – 90).

Regarding antibiotic resistance, GPs reported the following concerns: *"This is a major problem which will cause that antibiotics will no longer work. Patients live too much in the present and do not think of the future. They are often aware of this problem, but they have the feeling it does not apply to them, this leads to frustration. Additionally, there is still excessive and incorrect use of antibiotics, which is partly due to over-prescription. But GPs are blamed too often. As example, whether it is a viral or bacterial infection is not always known (for example, the difference between bronchiolitis and pneumonia). In this situation, we should weigh up the advantages and disadvantages of prescribing antibiotics."*

CPs, on the other hand, mentioned the following: *"This is a growing problem, a threat to public health and will eventually lead to untreatable infections which causes anxiety. Antibiotic resistance is encouraged by a few factors. For example, patients still have insufficient knowledge about the correct use of antibiotics (e.g. an antibiotic course is still not always finished) and they are still prescribed too quickly or incorrectly by physicians. But in recent years we observe a strong decline in prescription behavior, especially among young physicians. Additionally, antibiotic resistance is a global problem maintained by the free availability of antibiotics abroad. As a consequence, parents and healthcare providers should still be informed even more about this subject."*

5. DISCUSSION

5.1. MAIN FINDINGS OF THIS STUDY

This was a cross-sectional study, conducted in the five provincial capitals of Flanders (Antwerp, Bruges, Ghent, Hasselt and Leuven). Parents of young children and primary healthcare providers (GPs and CPs) were questioned about their perspectives on primary care and medication use in children through (online) questionnaires. In total, there were 380 participants of which 224 parents, 50 GPs and 106 CPs.

Considering the expectations of parents about actions carried out during a consultation, "the GP prescribes medication" and "the CP proposes a treatment with medication" were evaluated the least important actions. In the opinion of parents, providing information is usually the responsibility of both GPs and CPs. Considering language use of healthcare providers, parents scored this significantly higher than GPs and CPs themselves. Regarding parental knowledge, paracetamol is generally used in case of fever and pain while inflammatory pain is considered the most important indication for ibuprofen. Considering knowledge about antibiotics, parents have correctly evaluated the use of antibiotics in 8 out of 11 situations. Only for bronchiolitis, ear inflammation and pharyngitis there is a remarkable proportion (36%, 61% and 52% respectively) that incorrectly expects a prescription for antibiotics. In the questions assessing additional knowledge of this medication, answers were spread and parents often pointed out not to know the correct answer. Regarding GPs' and CPs' perspectives, prescribing medication and providing sufficient privacy are respectively considered of minor importance. Finally, in practice, three actions regarding information given to parents are carried out solely by a minor proportion of GPs and CPs i.e. information about (1) side effects, (2) stopping treatment and (3) providing written information.

5.2. WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

Several studies that focus on parents' perspectives have been conducted previously. The majority of these studies were carried out in a hospital setting or concern a specific disorder[74] [75] [76]. In contrast, studies that assess general expectations of parents in primary care are scarce. In comparison with the current study however, a few concordances are found. For example, the study by Halls et al.[75] showed that most parents considered reassurance and advice from their GP to be very important. Additionally, carrying out a physical examination was indicated by these parents as one of the most essential expectations. This is both in line with our findings. Subsequently, the study by Halls et al. sought parents' views on antibiotics, specifically in the case of lower respiratory tract infections. Similar to our study, parents were knowledgeable about the fact that antibiotics are often prescribed too quickly which will create problems in the future and indicated awareness of antibiotic resistance.

Furthermore, some studies have been carried out that aimed at parental practices and knowledge of medication use for their children. Some of these studies focused on paracetamol[77], ibuprofen[78] or antibiotics[79]. Considering our study, parents appear to be quite aware of when paracetamol and ibuprofen are appropriate. Nevertheless, there are a few aspects on which knowledge is insufficient. For example, the study by de Bont et al.[77] and this one show that parents tend to give paracetamol or ibuprofen for fever, even if the child does not feel ill. Also, the study by Kelly et al.[78] showed that paracetamol and ibuprofen are often alternated by parents. This is also reflected in the results of our study. However due to the higher risk of dosage errors, this is not recommended[80]. Our current research also shows that a significant proportion of parents (54%) would administer paracetamol in case of inflammatory pain. It is not clear whether this is a well-considered choice of parents because of the safety profile of paracetamol or whether parents are unaware of the fact that paracetamol does not have anti-inflammatory activity. Considering antibiotics, the findings of our study are far more positive than those of the study by Zyoud et al.[79] In the latter study there was a considerable lack of knowledge. For example, 70% of the parents (strongly) agreed that children with flu-like symptoms would recover more quickly by using antibiotics. By contrast, in our study, the estimation of when the GP should prescribe antibiotics has largely evaluated correctly. Nevertheless, some parents in this current research still expect the GP to prescribe antibiotics against viral infections. Also, ear inflammation and pharyngitis are two conditions where a significant proportion of the parents (i.e. 61% and 52% respectively) indicated to expect the GP to prescribe antibiotics. In theory, this is rarely necessary, especially in primary care.

Considering the statements assessing knowledge about paracetamol, ibuprofen and antibiotics, the answers were spread and parents often point out not to know the correct answer. Especially for paracetamol and ibuprofen there are shortcomings in knowledge. A similar pattern was found in the studies of Kelly et al.[78] and Chiappini et al.[81] where knowledge about suppositories and febrile convulsions was also surveyed. For antibiotics, according to the results of our study, it seems that parents have a fairly good knowledge.

Concerning the source of information, a study by Holappa et al[82]. investigated which source parents use to obtain information about medications they use for their child(ren). In our study parents were asked whom they would consult or where they would look for information according to different situations affecting their child. The current responses were comparable with the findings of Holappa et al. For example, parents are most inclined to consult a physician (or pediatrician). The role of the pharmacist, internet or friends/family was limited in both in our study, as in the study of Holappa et al. Additionally, we compared whether parents would do the same in case the situation affects themselves. In this regard, parents indicated to have much more a wait-and-see attitude or to treat themselves with medication.

5.3. WHAT THIS STUDY ADDS

In contrast to previous research, this is the first study that gives an overview of the general expectations of parents and healthcare providers in primary pediatric care. It is the first time that three groups involved in primary care (parents, GPs and CPs), were questioned simultaneously. This implies that it becomes clear where opinions are similar and aspects emerge on which the opinions differ. For that reason, this study shows the areas in which, according to the parents, primary care is still inadequate. This enables us to make a few recommendations for healthcare providers to adjust the information they provide parents with. This will lead, in our opinion, to an improvement in primary care for children.

The first focus of this study was on the general expectations of parents. They considered for both, GPs and CPs, the statements related to the provision of a treatment as least important. Conversely, reassuring and answering questions were considered as very important. This might show that parents do not prioritize the treatment, but mainly want to be reassured. Also, involvement in the choice of treatment was not considered crucial to all parents. Regarding the provision of information, parents expect most information of both healthcare providers. But in general, they estimate the role of the CP slightly less important than the GPs' role when it concerns the provision of information. Notable is that opinions on obtaining written information are very divided, with about a quarter of the parents not expecting this information at all. However, studies have shown that written information is better remembered and leads to better compliance[83]. Focusing on language use, more than 90% of parents scored both healthcare providers an eight or more. In comparison, the included healthcare providers scored themselves slightly lower (statistically significant difference), but still with a mean value of eight. Parents and healthcare providers both indicated to consider the use of a clear and understandable language as very important.

Second focus was on the perspectives of healthcare providers. Regarding GPs, prescribing medication and providing written information are of minor importance. Similarities are observed for CPs, but they additionally indicated providing sufficient privacy as less important. Comparing the aspects healthcare providers consider important with the actions they carry out in practice, there is a strong resemblance for GPs. Topics they considered important were the actions carried out by most GPs and vice versa. This is less applicable for CPs, but the actions carried out by 95% or more of all CPs correspond to the statements that were identified as most important. It is noteworthy that more than half of the CPs do not give non-medical advice despite having indicated that they consider this to be very important. Providing information about side effects and stopping treatment are actions that are carried out less frequently by both GPs and CPs.

Generally, the results indicate that healthcare providers' information given to parents when prescribing or dispensing medication is to a large extent in accordance with the expectations of parents. Also, the expectations of the different groups (parents in relation to healthcare providers but also the healthcare providers interpersonal) have a great resemblance.

5.4. LIMITATIONS OF THIS STUDY

First, the cross-sectional study design implicates a disadvantage because it is only possible to establish a correlation at population level. This type of study design is therefore only hypothesis-generating and is not able to establish a causal relationship. However, this type of study gives a good first indication.

Secondly, the respondents may behave differently when participating in research. Especially, GPs and CPs can act differently towards a student than towards a real patient. Therefore, social desirability bias cannot be excluded which may lead to a more positive presentation of the results than in reality. However, by guaranteeing anonymity of participants this was limited as much as possible. This is also reflected in the fact that the results of our study are comparable to those of previous studies.

The third and largest limitation is the low generalizability. The method of recruitment implicates that mainly motivated or interested parents, GPs and CPs took part in this research, leading to a participation bias. Indeed, almost a quarter of the participating parents in this research work in the healthcare sector, compared to about 5% in the total Flemish population[84]. Subsequently, the surveys where disseminated predominantly in cities. Participants from cities may respond differently to those from villages. For example, there are generally more highly educated people in an urban environment compared to a rural environment[85]. In this respect, the proportion of the highly educated in this study was fairly large (86%). Indeed, data from Statbel indicated that in 2016, 30% of the Belgian population finished higher education[86]. This may have affected our results, such as the questions about language use and antibiotic resistance. Furthermore, the gradations in health skills must be considered, as there are a significant number of people with reduced health skills. First, the participants must be able to read the health information. These are called functional health skills. Understanding scientific terms and processes are called the scientific health skills. These are often overestimated. Examples from this survey include words such as bronchiolitis (RSV) and febrile convulsions. The questions assumed that parents are familiar with these terms, which is not always the case in practice. Finally, cultural health skills also play a role. Patients from a different culture are often unfamiliar with the Western disease concept. This can result in a different view of medication use[87]. To take account for this, the origin (ethnic background) was verified in the demographic data. As expected, the majority of the respondents (96%) was Caucasian.

5.5. IMPLICATIONS FOR PRACTICE

The results of this study enable us to make provide some recommendations. First, parents expect information about the condition and the use of medication almost always from both healthcare providers. Consequently, it is the responsibility of both GPs and CPs to pay attention to this topic. Considering parents' knowledge about paracetamol, ibuprofen and antibiotics, it is the task of healthcare providers to inform parents properly because a few shortcomings in knowledge were revealed. Some recommendations for healthcare providers are presented in **Box 1**.

Box 1: Aspects healthcare providers should emphasize about paracetamol, ibuprofen and antibiotics

- Paracetamol is the first-line treatment for fever and pain and has no anti-inflammatory activity.
- Medication is not recommended when a child has a fever but does not feel ill.
- Alternating paracetamol and ibuprofen is not encouraged, due to the higher risk of dosage errors.
- Antibiotics are not recommended for viral infections such as influenza, varicella and bronchiolitis.
- Ear inflammation or pharyngitis are rarely a reason to use antibiotics.
- Suppositories are not the first choice as method of administration.
- The use of external cooling methods to reduce fever, such as giving a cold bath, are not recommended.
- The administration of medication like paracetamol or ibuprofen, does not address the underlying cause and therefore the child will not cure more quickly.
- Side effects of paracetamol are virtually non-existent if the prescribed dose is respected.
- The use of ibuprofen could lead to skin rashes and gastro-intestinal complaints.
- Medications like ibuprofen or paracetamol do not affect the risk of febrile convulsions.
- By vaccinating children, we can lower the use of antibiotics in the future.

When we consider healthcare providers' actions regarding information provision carried out in practice, there are a few aspects with potential for improvement. These are summarized in **Box 2**.

Box 2: Recommendations for actions that require specific attention by healthcare providers

- Providing information about side effects (as 95% of the parents expect this information).
- Providing information about stopping treatment.
- Providing non-medical advice (mainly a focus for CPs).
- Providing written information.

5.6. IMPLICATIONS FOR FUTURE RESEARCH

Due to the low generalizability, it would be useful to carry out a study in which a significant number of participants are of different ethnic origin. A better distribution in terms of educational attainment would also give a more accurate picture. Furthermore, we decided to limit this study to three drugs or drug groups. These were chosen because of their frequent use in the age group studied. However, there are other drugs, such as those affecting the respiratory system (for example, salbutamol) and those affecting the alimentary tract and metabolism (for example, omeprazole and ranitidine), which also have a significant use in children. It may be useful to involve them as well. Additionally, the inclusion of secondary healthcare providers such as pediatricians could also be of added value for this research.

6. CONCLUSION

In general, parents do not necessarily expect healthcare providers to propose any treatment, whether with or without medication. Their main reason to consult a healthcare provider is to obtain answers to their questions and to be reassured. When it concerns the provision of information, parents usually expect this from both healthcare providers, although the GPs' role is considered slightly more important. Furthermore, the language use of GPs and CPs was considered exceptionally good by parents. Regarding parenteral knowledge, the questions about paracetamol, ibuprofen and antibiotics have shown that parents are approximately aware of when these are appropriate. However, it should be stressed that paracetamol is the first choice for pain and fever and has no anti-inflammatory activity. Parents should also be better informed about the fact that medication is not recommended when a child has a fever but does not feel ill. As for antibiotics, it remains important to emphasize that they do not help in case of a viral infection such as bronchiolitis, varicella or influenza. Also, the use of antibiotics is rarely necessary for ear infections or pharyngitis. Additionally, the statements that assessed parents' knowledge about paracetamol, ibuprofen and antibiotics revealed a few shortcomings, especially for paracetamol and ibuprofen. The knowledge about antibiotics is rather good, although there is still potential for improvement. And because of the growing problem of antibiotic resistance, it remains up to the healthcare provider to inform patients properly. As most important finding from the practical cases can be decided that parents are more inclined to consult the physician/pediatrician or the emergency department for their child(ren). For themselves, they have much more a wait-and-see attitude or are more inclined to treat themselves with medication. It is also notable that this question has shown the rather limited role of the pharmacist, internet and friends or family.

By examining the general aspects healthcare providers consider important, we notice that GPs attach least importance to prescribing medication. For CPs, providing sufficient privacy is regarded less critical. Additionally, both healthcare providers considered the provision of written information as less important. In conclusion, the opinions of both groups of healthcare providers coincide to a large extent. Subsequently, it was investigated which actions, relating to information given to parents, the healthcare providers carry out when prescribing or dispensing paracetamol, ibuprofen and antibiotics. Mainly, we can conclude that the actions taken by GPs correspond to what they have indicated to be important. This is less applicable to CPs, where more division is observed. In fact, the CPs indicated a few aspects as very important, but which they do not implement in practice. Most important example is the provision of non-medical advice. Moreover, both groups give little information about possible side effects and stopping treatment.

Comparing both study groups (parents and healthcare providers), there is a strong convergence between them. The results indicate that healthcare providers' information given to parents is to a large extent in accordance with their expectations. Comparing their expectations, all three groups considered the treatment less important. This also applies to the provision of written information. However, this definitely can be of added value. Finally, we can mention that healthcare providers should discuss more frequently on side effects, as 95% of the parents expect this information.

In the future, it would be useful to repeat this study with a more representative group of participants. Including a larger proportion of parents of a different ethnic origin and a better distribution of education levels may lead to fundamentally different results. Also, it was decided to limit this study to three drugs or drug groups because of their extensive use in children. However, there are still other drugs with frequent use in the pediatric population that would be interesting to investigate. Proposals include drugs that affect the respiratory system (for example, salbutamol) and those that affect the alimentary tract and metabolism (for example, omeprazole and ranitidine). Finally, including secondary healthcare providers, like pediatricians, can also be useful for this research.

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8. APPENDIX

Annex A: *Questionnaire provided to the parents*

Beste ouder,

Wetenschappelijk onderzoek hecht meer en meer belang aan verwachtingen en bevindingen van patiënten. Wanneer dit gaat over ziekte of medicatiegebruik bij kinderen spelen de ouders een centrale rol. Daarom onderzoek ik het standpunt, de verwachtingen en de kennis van ouders rond medicatiegebruik bij hun kind. Ook vragen we naar de verwachtingen ten opzichte van huisartsen en apothekers. Deze enquête duurt ongeveer 10 à 15 minuten. Na deelname ontvangt u een fiche over het gebruik van paracetamol, ibuprofen en antibiotica.

Alle antwoorden worden anoniem (hierbij is er totaal geen terugkoppeling meer mogelijk naar uw persoonlijk dossier) verwerkt en enkel gebruikt in het kader van dit onderzoek. Bij vragen of opmerkingen kan u mailen naar Sigrid.Verhelst@UGent.be.

Alvast hartelijk bedankt voor uw medewerking!
Sigrid Verhelst
1ste masterstudent farmaceutische zorg (Universiteit Gent)

"Ik verklaar mij akkoord dat deze vragenlijst volledig vrijwillig is, dat steeds kan onderbroken worden, en dat alle gegevens anoniem zullen verwerkt worden."
☐ Ik ga akkoord en ga verder met de vragenlijst

Deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan het UZ Gent, en zal worden uitgevoerd volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki opgesteld ter bescherming van mensen deelnemend aan klinische studies. In overeenstemming met de Belgische wet van 8 december 1992 en de Belgische wet van 22 augustus 2002, zal uw persoonlijke levenssfeer worden gerespecteerd. De experimentenwet van 7/05/2004 verplicht ons om deelnemers aan wetenschappelijke projecten te verzekeren voor de deelname en het risico (hoe klein ook) dat men loopt. De waarschijnlijkheid dat u door deelname aan deze studie enige schade ondervindt, is extreem laag. Indien dit toch zou voorkomen, wat echter zeer zeldzaam is, werd een verzekering afgesloten conform de Belgische wet van 7 mei 2004, die deze mogelijkheid dekt.

Demografische gegevens

1. Wat is uw geslacht? ☐ Man ☐ Vrouw

2. Hoe oud bent u? .....

3. Welke afkomst heeft u? ☐ Noord-Afrikaans ☐ Overig Afrikaans ☐ Latijns-Amerikaans ☐ Aziatisch ☐ Blanke oorsprong ☐ Andere: .....

4. Wat is de leeftijd van uw oudste kind? .....
   Wat is de leeftijd van uw tweede kind? (Indien u maar 1 kind heeft mag u hier 0 invullen) .....
   Wat is de leeftijd van uw derde kind? (Indien u maar 1 kind heeft mag u hier 0 invullen) .....
   Wat is de leeftijd van uw vierde kind? (Indien u maar 1 kind heeft mag u hier 0 invullen) .....
   Wat is de leeftijd van uw vijfde kind? (Indien u maar 1 kind heeft mag u hier 0 invullen) .....

5. Wat is uw postcode? .....

6. Wat is de hoogste opleiding die u volgt of heeft gevolgd?
   - ☐ Lager onderwijs
   - ☐ Middelbaar onderwijs (evt. met 7e jaar)
   - ☐ Hogeschool
   - ☐ Universiteit
   - ☐ Andere: .....

7. In welke sector werkt u? (Specificeer indien mogelijk)
   - ☐ Zorgsector .....
   - ☐ Onderwijs .....
   - ☐ Overheid.....
   - ☐ Zelfstandige.....
   - ☐ Bouw.....
   - ☐ Voedingsindustrie .....
   - ☐ Horeca .....
   - ☐ Bank en verzekeringen .....
   - ☐ Andere: .....

Deel 1: verwachtingen ten opzichte van de zorgverlener

In dit deel vragen we u na te denken over wat u verwacht van uw huisarts of apotheker indien u hen raadpleegt. Eerst komt een consult bij de huisarts aan bod. Vervolgens een bezoek bij de apotheker.

8. Indien u een **huisarts** raadpleegt wanneer uw kind ziek is, in welke mate hecht u dan belang aan onderstaande stellingen. Het cijfer 1 geeft aan dat u dit helemaal niet belangrijk vindt. Het cijfer 5 geeft aan dat u dit zeer belangrijk vindt. Indien u geen mening heeft kan u dat ook aanduiden.

Stelling	1	2	3	4	5	Geen Mening
De huisarts voert een lichamelijk onderzoek uit						
De huisarts stelt een diagnose						
De huisarts betrekt u bij het kiezen van een behandeling						
De huisarts schrijft medicatie voor						
De huisarts stelt u gerust/ beantwoordt uw vragen						
De huisarts peilt naar uw verwachtingen en bezorgdheden						
De huisarts gebruikt duidelijke en begrijpelijke taal						
De huisarts geeft u het gevoel niet gehaast te zijn						

9. Raadpleegde u al eens een apotheker rechtstreeks wanneer uw kind ziek was (met andere woorden: zonder eerst contact op te nemen met bijvoorbeeld een huisarts, specialist, vroedvrouw…)?
   ☐ Ja ☐ Nee
   Indien u op deze vraag "nee" antwoordde, ga dan meteen door naar vraag 11.

10. Indien u een **apotheker** rechtstreeks (= zonder voorafgaand bezoek aan een arts) raadpleegt wanneer uw kind ziek is, in welke mate hecht u dan belang aan onderstaande stellingen. Het cijfer 1 geeft aan dat u dit helemaal niet belangrijk vindt. Het cijfer 5 geeft aan dat u dit zeer belangrijk vindt. Indien u geen mening heeft kan u dat ook aanduiden.

Stelling	1	2	3	4	5	Geen Mening
De apotheker stelt bijkomende vragen om de situatie in te schatten						
De apotheek voorziet in voldoende privacy om eventueel discrete vragen te stellen						
De apotheker betrekt u bij het kiezen van een behandeling						
De apotheker stelt een behandeling met medicatie voor						
De apotheker stelt een behandeling zonder medicatie voor (bv. levensstijlaanpassingen of voedingsadvies)						
De apotheker stelt u gerust/beantwoordt uw vragen						
De apotheker peilt naar uw verwachtingen en bezorgdheden						
De apotheker gebruikt duidelijke en begrijpelijke taal						
De apotheker geeft u het gevoel niet gehaast te zijn						

Deel 2: Informatiebron

11. Van welke zorgverlener verwacht u de volgende informatie?

Stelling	Apotheker	Arts	Beide	Ik verwacht deze info niet
Informatie over de diagnose (bv. wat de oorzaak is en hoelang de symptomen aanhouden)				
Informatie over hoe de medicatie ervoor zorgt dat uw kind zich beter voelt				
Informatie over hoe de medicatie gebruikt moet worden (hoeveel, wanneer en hoelang de medicatie innemen)				
Informatie over de manier van toedienen (bv. uitleg over gebruik puffer, doseerspuitje, suppo…)				
Informatie over mogelijke bijwerkingen van de medicatie en wat te doen indien deze optreden				
Informatie over wat te doen indien de symptomen erger worden				
Extra tips die u kan toepassen naast medicatie				
Schriftelijke informatie meegeven				

12. Op een schaal van 1-10, hoe begrijpelijk vindt u de taal die uw **huisarts** gebruikt? Het cijfer 1 betekent dat u helemaal niets begrijpt van wat uw huisarts u vertelt. Het cijfer 10 betekent dat u alles helemaal begrijpt. .....
13. Op een schaal van 1-10, hoe begrijpelijk vindt u de taal die uw **apotheker** gebruikt? Het cijfer 1 betekent dat u helemaal niets begrijpt van wat uw apotheker u vertelt. Het cijfer 10 betekent dat u alles helemaal begrijpt. .....

Deel 3: kennis over paracetamol

14. Kent u het geneesmiddel paracetamol (Dafalgan®, Perdolan®...) ☐Ja ☐ Nee
Indien u op deze vraag "nee" antwoordde, ga dan meteen door naar vraag 18.

15. In welke situatie(s) geeft u paracetamol (Dafalgan®, Perdolan®) aan uw kind(eren)?

.....

.....

16. In welk van volgende situaties is paracetamol, voor uw kind(eren), aangewezen volgens u? (Zet een kruisje in de geschikte kolom)

Symptoom/ziekte	Aangewezen	Niet aangewezen
Koorts (>38°C) en uw kind voelt zich niet ziek		
Koorts (>38°C) en uw kind voelt zich ziek		
Griep		
Hoofdpijn		
Ontstekingspijn (oor of keelontsteking)		
Spierpijn		
Buikpijn		
Verzwikte enkel		

17. In welke mate gaat u akkoord met volgende stellingen? (1 = helemaal niet akkoord en 5 = helemaal akkoord)

Stelling	1	2	3	4	5	Ik weet het niet
Mijn kind geneest sneller wanneer ik paracetamol toedien						
Er zijn risico's verbonden aan het gebruik van paracetamol						
Door mijn kind een koud bad te laten nemen daalt de koorts						
Paracetamol suppo's werken beter dan paracetamol siroop						
Wanneer mijn kind ziek is en ik geef paracetamol slaapt hij/zij beter						

Deel 4: kennis over ibuprofen

18. Kent u het geneesmiddel ibuprofen (Nurofen®, Brufen®...) ☐ Ja ☐ Nee
Indien u op deze vraag "nee" antwoordde, ga dan meteen door naar vraag 23.

19. In welke situatie(s) geeft u ibuprofen (Nurofen®) aan uw kind(eren)?

.....

.....

20. In welk van volgende situaties is ibuprofen, voor uw kind(eren), aangewezen volgens u? (Zet een kruisje in de geschikte kolom)

Symptoom/ziekte	Aangewezen	Niet aangewezen
Koorts (>38°C) en uw kind voelt zich niet ziek		
Koorts (>38°C) en uw kind voelt zich ziek		
Griep		
Hoofdpijn		
Ontstekingspijn (oor of keelontsteking)		
Spierpijn		
Buikpijn		
Verzwikte enkel		

21. In welke mate gaat u akkoord met volgende stellingen? (1 = helemaal niet akkoord en 5 = helemaal akkoord)

Stelling	1	2	3	4	5	Ik weet het niet
Mijn kind geneest sneller als ik ibuprofen toedien						
Het gebruik van ibuprofen bij koorts doet het risico op koortsstuipen dalen						
Er zijn risico's verbonden aan het gebruik van Ibuprofen						
Het gebruik van ibuprofen kan leiden tot huiduitslag bij mijn kind						
Het gebruik van ibuprofen kan leiden tot maag-darm klachten bij mijn kind						

22. Geeft u in volgende situaties, voor uw kind(eren), de voorkeur aan paracetamol, ibuprofen of geeft u gewoon wat u in huis heeft? (Zet een kruisje in de geschikte kolom)

Symptoom/ziekte	Ik geef niets	Paracetamol	Ibuprofen	Ik geef wat ik in huis heb
Koorts				
Hoofdpijn				
Griep				
Oorontsteking				

Deel 5: kennis over antibiotica

23. Weet u wat een antibioticum is? ☐ Ja ☐ Nee

Indien u op deze vraag "nee" antwoordde, ga dan meteen door naar vraag 29.

24. Bij welk van volgende aandoeningen verwacht u dat de arts antibiotica voorschrijft voor uw kind(eren)?

Symptoom/ziekte	Ik verwacht dat de arts antibiotica voorschrijft	Ik verwacht niet dat de arts antibiotica voorschrijft
Griep		
Verkoudheid		
Longontsteking		
Varicella (Waterpokken)		
Keelpijn		
Bronchiolitis (RSV)		
Hersenvliesontsteking		
Oorontsteking		
Keelontsteking		
Diarree		
Koorts		

25. In welke mate gaat u akkoord met volgende stellingen? (1 = helemaal niet akkoord en 5 = helemaal akkoord)

Stelling	1	2	3	4	5	Ik weet het niet
Mijn kind mag stoppen met het innemen van het antibioticum vanaf hij/zij zich beter voelt						
Antibiotica werken preventief tegen ziekten						
Antibiotica werken tegen verkoudheid en griep						
Het overmatig gebruik van antibiotica zorgt ervoor dat ze op termijn niet meer werken						
Door mijn kind te vaccineren kan ik het gebruik van antibiotica beperken						

26. Indien uw kind reeds een antibioticakuur kreeg, welke bijwerkingen ondervond uw kind toen?

.....

.....

27. Heeft u al gehoord van antibiotica resistentie? ☐ Ja ☐ Nee
28. Zo ja, wat beïnvloedt antibiotica resistentie volgens u?

.....

.....

Deel 6: praktische casussen

Indien volgende situatie zich voordoet, wie zou u raadplegen of waar zou u informatie opzoeken? **Meerdere opties aanduiden is toegelaten.**

29. Toen uw kind (7 jaar) gisteravond thuiskwam van school voelde hij/zij zich nog helemaal in orde. Na het avondeten klaagde hij/zij plots over hoofd- en spierpijn. U besloot de temperatuur te meten en deze bedroeg 39,5°C. Uw zoon/dochter ging vervolgens vroeg naar bed maar deze nacht voelde hij/zij zich zeer onwel met koude rillingen en hevige hoofdpijn. Eten en drinken ging deze ochtend ook zeer moeizaam. Wie zou u raadplegen of waar zou u informatie opzoeken?

    ☐ Ik zou nog even afwachten
    ☐ Apotheker
    ☐ Arts
    ☐ Ik behandel zelf met een geneesmiddel
    ☐ Internet
    ☐ Pediater
    ☐ Spoeddienst
    ☐ Tijdschriften/boeken
    ☐ Vrienden/familie
    ☐ Andere: .....

    Indien dezelfde situatie zich voordoet, maar nu niet bij uw kind maar bij u zelf, met andere woorden: Toen u gisteravond thuiskwam van u werk voelde u zich nog helemaal in orde. Na het avondeten kreeg u plots last van hoofd- en spierpijn. U besloot de temperatuur te meten en deze bedroeg 39,5°C. Daarom besloot u vroeg naar bed te gaan maar deze nacht voelde u zich zeer onwel met koude rillingen en hevige hoofdpijn. Eten en drinken ging deze ochtend ook zeer moeizaam. Wie zou u raadplegen of waar zou u informatie opzoeken?

    ☐ Ik zou nog even afwachten
    ☐ Apotheker
    ☐ Arts
    ☐ Ik behandel mezelf met een geneesmiddel
    ☐ Internet
    ☐ Spoeddienst
    ☐ Tijdschriften/boeken
    ☐ Vrienden/familie
    ☐ Andere: .....

30. U haalt uw baby van 6 maanden op van de crèche. Hij moet sinds twee dagen veel hoesten en heeft ook last van een verstopte neus. Hij heeft geen koorts maar is wel heel huilerig. Slapen gaat hierdoor moeizaam, zowel voor de baby als voor u. Wie zou u raadplegen of waar zou u informatie opzoeken?

    ☐ Ik zou nog even afwachten
    ☐ Apotheker
    ☐ Arts
    ☐ Ik behandel zelf met een geneesmiddel
    ☐ Internet
    ☐ Pediater
    ☐ Spoeddienst
    ☐ Tijdschriften/boeken
    ☐ Vroedvrouw
    ☐ Vrienden/familie
    ☐ Andere: .....

Indien dezelfde situatie zich voordoet, maar nu niet bij uw kind maar bij u zelf, met andere woorden: U heeft sinds twee dagen een zware hoest te pakken en heeft ook last van een verstopte neus. Overdag valt dit mee maar 's nachts heeft u hierdoor veel moeite met slapen waardoor u overdag vermoeid bent. U heeft geen last van koorts. Wie zou u raadplegen of waar zou u informatie opzoeken?

☐ Ik zou nog even afwachten
☐ Apotheker
☐ Arts
☐ Ik behandel mezelf met een geneesmiddel
☐ Internet
☐ Spoeddienst
☐ Tijdschriften/boeken
☐ Vrienden/familie
☐ Andere: .....

31. Toen uw kind (10 jaar) gisteravond thuiskwam van een schoolreis klaagde hij/zij van buikpijn en wou bijgevolg niets eten. Deze ochtend is hij/zij opgestaan met diarree en is in 2 uur tijd al 4 keer naar het toilet moeten gaan. Het is ondertussen middag en de buikpijn is nog steeds niet beter, hij/zij voelt zich nu ook wat misselijk. Wie zou u raadplegen of waar zou u informatie opzoeken?

☐ Ik zou nog even afwachten
☐ Apotheker
☐ Arts
☐ Ik behandel zelf met een geneesmiddel
☐ Internet
☐ Pediater
☐ Spoeddienst
☐ Tijdschriften/boeken
☐ Vrienden/familie
☐ Andere: .....

Indien dezelfde situatie zich voordoet, maar nu niet bij uw kind maar bij u zelf, met andere woorden: Toen u gisteravond thuiskwam van een weekendje in de Ardennen had u last van buikpijn waardoor u 's avonds geen trek had. Deze ochtend stond u op met diarree die de laatste uren alleen maar is toegenomen. U bent op 2 uur tijd al 4 keer naar het toilet moeten gaan. Het is ondertussen middag en de buikpijn is nog steeds niet beter, u voelt zich ondertussen ook wat misselijk. Wie zou u raadplegen of waar zou u informatie opzoeken?

☐ Ik zou nog even afwachten
☐ Apotheker
☐ Arts
☐ Ik behandel mezelf met een geneesmiddel
☐ Internet
☐ Spoeddienst
☐ Tijdschriften/boeken
☐ Vrienden/familie
☐ Andere: .....

Wenst u een fiche te ontvangen over het gebruik van paracetamol, ibuprofen en antibiotica? Gelieve dan hier uw e-mailadres in te vullen (dit zal niet voor andere doeleinden gebruikt worden).

.....

Annex B: *Questionnaire provided to the GPs*

Beste huisarts,

Wetenschappelijk onderzoek hecht meer en meer belang aan verwachtingen en bevindingen van patiënten. Wanneer dit gaat over ziekte of medicatiegebruik bij kinderen spelen de ouders een centrale rol. Daarom onderzoek ik het standpunt en de kennis van ouders rond medicatiegebruik bij hun kind evenals hun verwachtingen ten opzichte van huisartsen en apothekers. Deze vragenlijst wordt via scholen en crèches verspreid. Vervolgens worden de resultaten vergeleken met de visie van zorgverleners. Deze enquête zal slechts enkele minuten van uw tijd vragen. Na deelname ontvangt u een fiche over het gebruik van paracetamol, ibuprofen en antibiotica.

Alle antwoorden zullen anoniem (hierbij is er totaal geen terugkoppeling meer mogelijk naar uw persoonlijk dossier) verwerkt worden en enkel gebruikt worden in het kader van dit onderzoek. Gelieve de enquête dus in alle eerlijkheid in te vullen. Bij vragen of opmerkingen kan u steeds mailen naar Sigrid.Verhelst@UGent.be.

Alvast hartelijk bedankt voor uw medewerking!
Sigrid Verhelst
1ste masterstudent farmaceutische zorg (Universiteit Gent)

"Ik verklaar mij akkoord dat deze vragenlijst volledig vrijwillig is, dat steeds kan onderbroken worden, en dat alle gegevens anoniem zullen verwerkt worden."
☐ Ik ga akkoord en ga verder met de vragenlijst

Deze studie werd goedgekeurd door een onafhankelijke Commissie voor Medische Ethiek verbonden aan het UZ Gent, en zal worden uitgevoerd volgens de richtlijnen voor de goede klinische praktijk (ICH/GCP) en de verklaring van Helsinki opgesteld ter bescherming van mensen deelnemend aan klinische studies. In overeenstemming met de Belgische wet van 8 december 1992 en de Belgische wet van 22 augustus 2002, zal uw persoonlijke levenssfeer worden gerespecteerd. De experimentenwet van 7/05/2004 verplicht ons om deelnemers aan wetenschappelijke projecten te verzekeren voor de deelname en het risico (hoe klein ook) dat men loopt. De waarschijnlijkheid dat u door deelname aan deze studie enige schade ondervindt, is extreem laag. Indien dit toch zou voorkomen, wat echter zeer zeldzaam is, werd een verzekering afgesloten conform de Belgische wet van 7 mei 2004, die deze mogelijkheid dekt.

Demografische gegevens

1. Wat is uw geslacht? ☐ Man ☐ Vrouw
2. Hoe oud bent u? .....
3. Heeft u kinderen/kleinkinderen? ☐ Ja ☐ Nee
4. Aantal jaren ervaring als huisarts: ..... / ☐ Ik ben HAIO
5. Postcode dokterspraktijk: .....
6. Aantal full-time equivalenten in de dokterspraktijk: .....
7. Gemiddeld aantal patiënten per dag: ..... / ☐ Dit varieert sterk

Deel 1: scoren van handelingen met betrekking tot een consultatie voor een ziek kind

8. Indien u een ouder met een ziek kind (0-12 jaar) op consultatie krijgt, in welke mate hecht u belang aan onderstaande stellingen tijdens het consult? (1 = hier hecht ik helemaal geen belang aan en 5 = dit vind ik uitermate belangrijk)

Stelling	1	2	3	4	5	Geen mening
Uitvoeren van een lichamelijk onderzoek						
Stellen van een diagnose						
Informatie geven over de diagnose (bv. wat de oorzaak is en hoelang de symptomen aanhouden)						
De ouder en het kind betrekken bij het kiezen van een behandeling						
Voorschrijven van medicatie						
Informatie geven over hoe de medicatie ervoor zorgt dat het kind zich beter voelt (= het werkingsmechanisme van het geneesmiddel)						
Informatie geven over de gebruiksinstructies (hoeveel, wanneer en hoelang de medicatie innemen)						
Informatie geven over de manier van toedienen (bv. uitleg over gebruik puffer, doseerspuitje, suppo…)						
Informatie geven over mogelijke bijwerkingen van de medicatie en wat te doen indien deze optreden						
Informatie geven over wat te doen indien de symptomen erger worden						
Geven van extra tips die kunnen toegepast worden naast de medicatie (= niet-medicamenteus advies zoals levensstijlaanpassingen en voedingsadvies)						
Geruststellen/beantwoorden van vragen						
Peilen naar verwachtingen en bezorgdheden						
Gebruiken van duidelijke en begrijpelijke taal						
De patiënt het gevoel geven niet gehaast te zijn						
Schriftelijke informatie meegeven						

9. Op een schaal van 1-10, hoe schat u uw eigen taalgebruik in tijdens een consult? Het cijfer 1 betekent dat de patiënt er helemaal niets van begrijpt. Het cijfer 10 betekent dat de patiënt alles begrijpt. .....

Deel 2: handelingen bij het voorschrijven van paracetamol

10. Probeer uw laatste consult voor pijn/koorts voor een kind jonger dan 12 jaar, waar u paracetamol aanraadde, voor de geest te halen. Welke van volgende stappen voerde u allemaal uit? (Kruis aan)

    ☐ Mondelinge anamnese
    ☐ Lichamelijk onderzoek
    ☐ Overleg met ouders over de mogelijke behandelopties
    ☐ Informatie geven over de onderliggende aandoening (in het geval van paracetamol: pijn en koorts)
    ☐ Informatie geven over de dosering (hoeveelheid en frequentie)
    ☐ Informatie geven over bijwerkingen/gevaren van paracetamol
    ☐ Informatie geven over het stoppen van de behandeling
    ☐ Informatie geven over terugkeren naar de arts
    ☐ Niet-medicamenteus advies geven
    ☐ Schriftelijke informatie meegeven

11. Hoelang duurde het consult ongeveer in minuten? .....

Deel 3: handelingen bij het voorschrijven van ibuprofen

12. Probeer uw laatste consult voor pijn/koorts/ontsteking voor een kind jonger dan 12 jaar, waar u ibuprofen aanraadde, voor de geest te halen. Welke van volgende stappen voerde u allemaal uit? (Kruis aan)

    ☐ Mondelinge anamnese
    ☐ Lichamelijk onderzoek
    ☐ Overleg met ouders over de mogelijke behandelopties
    ☐ Informatie geven over de onderliggende aandoening (in het geval van ibuprofen: pijn, koorts en ontsteking)
    ☐ Informatie geven over de dosering (hoeveelheid en frequentie)
    ☐ Informatie geven over bijwerkingen/gevaren van ibuprofen
    ☐ Informatie geven over het stoppen van de behandeling
    ☐ Informatie geven over terugkeren naar de arts
    ☐ Niet-medicamenteus advies geven
    ☐ Schriftelijke informatie meegeven

13. Hoelang duurde het consult ongeveer in minuten? .....

Deel 4: handelingen bij het voorschrijven van antibiotica

14. Probeer uw laatste consult voor een bacteriële infectie waarvoor antibiotica was aangewezen voor een kind jonger dan 12 jaar voor de geest te halen. Welke van volgende stappen voerde u allemaal uit? (Kruis aan)

    ☐ Mondelinge anamnese
    ☐ Lichamelijk onderzoek
    ☐ Overleg met ouders over de mogelijke behandelopties
    ☐ Informatie geven over de onderliggende aandoening (in het geval van antibiotica: de bacteriële infectie bv. informatie geven over wat een longontsteking is)
    ☐ Informatie geven over de dosering (hoeveelheid en frequentie)
    ☐ Informatie geven over bijwerkingen/gevaren van antibiotica
    ☐ Informatie geven over het (niet vroegtijdig) stoppen van de behandeling
    ☐ Informatie geven over terugkeren naar de arts
    ☐ Niet-medicamenteus advies geven
    ☐ Schriftelijke informatie meegeven

15. Hoelang duurde het consult ongeveer in minuten? .....

16. Op 100 antibiotica consultaties, in hoeveel gevallen ervaart u druk vanuit ouders om antibiotica voor te schrijven wanneer u dit zelf niet nodig acht? ..... /100

17. Op 100 patiënten, van hoeveel schat u in dat ze op de hoogte zijn van antibiotica resistentie? ...../100

18. Wat roept antibioticaresistentie bij u op?

.....

.....

Wenst u een fiche te ontvangen over het gebruik van paracetamol, ibuprofen en antibiotica? Gelieve dan hier uw e-mailadres in te vullen (dit zal niet voor andere doeleinden gebruikt worden).

.....

Annex C: *Questionnaire provided to the CPs*

Beste apotheker,

Wetenschappelijk onderzoek hecht meer en meer belang aan verwachtingen en bevindingen van patiënten. Wanneer dit gaat over ziekte of medicatiegebruik bij kinderen spelen de ouders een centrale rol. Daarom onderzoek ik het standpunt en de kennis van ouders rond medicatiegebruik bij hun kind evenals hun verwachtingen ten opzichte van huisartsen en apothekers. Deze vragenlijst wordt via scholen en crèches verspreid. Vervolgens worden de resultaten vergeleken met de visie van zorgverleners. Deze enquête zal slechts enkele minuten van uw tijd vragen. Na deelname ontvangt u een fiche over het gebruik van paracetamol, ibuprofen en antibiotica.

Alle antwoorden zullen anoniem (hierbij is er totaal geen terugkoppeling meer mogelijk naar uw persoonlijk dossier) verwerkt worden en enkel gebruikt worden in het kader van dit onderzoek. Gelieve de enquête dus in alle eerlijkheid in te vullen. Bij vragen of opmerkingen kan u steeds mailen naar Sigrid.Verhelst@UGent.be.

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Demografische gegevens

1. Wat is uw geslacht? ☐ Man ☐ Vrouw
2. Hoe oud bent u? .....
3. Heeft u kinderen/kleinkinderen? ☐ Ja ☐ Nee
4. Aantal jaren ervaring in de officina-apotheek: .....
5. Postcode apotheek: .....
6. Aantal full-time equivalenten in de apotheek: ..... Apothekers, ...Farmaceutisch-Technisch Assistenten
7. Uw functie: ☐ Apotheektitularis ☐ Adjunct-apotheker ☐ Apotheker-vervanger ☐ FTA ☐ Stagiair
8. Gemiddeld aantal patiënten per dag: ..... / ☐ Dit varieert sterk

Deel 1: scoren van handelingen met betrekking tot een consultatie/aflevering voor een ziek kind

9. Indien een ouder met een ziek kind (0-12 jaar) langskomt in de apotheek, zonder voorafgaand een arts te raadplegen, in welke mate hecht u belang aan onderstaande stellingen? (1 = hier hecht ik helemaal geen belang aan en 5 = dit vind ik uitermate belangrijk)

Stelling	1	2	3	4	5	Geen mening
Uitvoeren van een WHAM-analyse (voor **w**ie, **h**oe manifesteren de symptomen zich, wat is er **a**nders reeds geprobeerd en wordt er nog andere **m**edicatie genomen door het kind?)						
Voorzien in voldoende privacy voor eventueel discrete vragen						
Informatie geven over de diagnose (bv. wat de oorzaak is en hoelang de symptomen aanhouden)						
De ouder en het kind betrekken bij het kiezen van een behandeling						
Een medicamenteuze behandeling voorstellen						
Informatie geven over hoe de medicatie ervoor zorgt dat het kind zich beter voelt (= het werkingsmechanisme van het geneesmiddel)						
Informatie geven over de gebruiksinstructies (hoeveel, wanneer en hoelang de medicatie innemen)						
Informatie geven over de manier van toedienen (bv. uitleg over gebruik puffer, doseerspuitje, suppo…)						
Informatie geven over mogelijke bijwerkingen van de medicatie en wat te doen indien deze optreden						
Informatie geven over wat te doen indien de symptomen erger worden						
Informatie geven over wanneer de arts moet worden geraadpleegd (= de doorverwijscriteria)						
Geven van extra tips die kunnen toegepast worden naast de medicatie (= niet-medicamenteus advies zoals levensstijlaanpassingen en voedingsadvies)						
Geruststellen/beantwoorden van vragen						
Peilen naar verwachtingen en bezorgdheden						
Gebruiken van duidelijke en begrijpelijke taal						
De patiënt het gevoel geven niet gehaast te zijn						
Schriftelijke informatie meegeven						

10. Op een schaal van 1-10, hoe schat u uw eigen taalgebruik in tijdens een aflevering? Het cijfer 1 betekent dat de patiënt er helemaal niets van begrijpt. Het cijfer 10 betekent dat de patiënt alles begrijpt. .....

Deel 2: handelingen bij het afleveren van paracetamol

11. Probeer uw laatste aflevering van paracetamol voor een kind jonger dan 12 jaar voor de geest te halen, waarbij de ouder niet specifiek om paracetamol vroeg maar u raadpleegde omwille van pijn en koorts bij zijn/haar kind. Welke van de volgende stappen voerde u allemaal uit? (Kruis aan)

    ☐ WHAM-analyse (voor **w**ie, **h**oe manifesteren de symptomen zich, wat is er **a**nders reeds geprobeerd en neemt het kind nog andere **m**edicatie?)
    ☐ Overleg met ouders over de mogelijke behandelingsopties
    ☐ Informatie geven over de onderliggende aandoening (in het geval van paracetamol: pijn en koorts)
    ☐ Informatie geven over de dosering (hoeveelheid en frequentie)
    ☐ Informatie geven over de gebruiksinstructies (bv. hoe een doseerspuitje te gebruiken)
    ☐ Informatie geven over bijwerkingen/gevaren van paracetamol
    ☐ Informatie geven over het stoppen van de behandeling
    ☐ Informatie geven over de doorverwijscriteria
    ☐ Niet-medicamenteus advies geven
    ☐ Schriftelijke informatie meegeven

12. Hoelang duurde de aflevering ongeveer in minuten? .....

Deel 3: handelingen bij het afleveren van ibuprofen

13. Probeer uw laatste aflevering van ibuprofen voor een kind jonger dan 12 jaar voor de geest te halen, waarbij de ouder niet specifiek om ibuprofen vroeg maar u raadpleegde omwille van pijn/koorts/ontsteking bij zijn/haar kind. Welke van de volgende stappen voerde u allemaal uit? (Kruis aan)

    ☐ WHAM-analyse (voor **w**ie, **h**oe manifesteren de symptomen zich, wat is er **a**nders reeds geprobeerd en neemt het kind nog andere **m**edicatie?)
    ☐ Overleg met ouders over de mogelijke behandelingsopties
    ☐ Informatie geven over de onderliggende aandoening (in het geval van ibuprofen: pijn, koorts en ontsteking)
    ☐ Informatie geven over de dosering (hoeveelheid en frequentie)
    ☐ Informatie geven over de gebruiksinstructies (bv. hoe een doseerspuitje te gebruiken)
    ☐ Informatie geven over bijwerkingen/gevaren van ibuprofen
    ☐ Informatie geven over het stoppen van de behandeling
    ☐ Informatie geven over de doorverwijscriteria
    ☐ Niet-medicamenteus advies geven
    ☐ Schriftelijke informatie meegeven

14. Hoelang duurde de aflevering ongeveer in minuten? .....

Deel 4: handelingen bij het afleveren van antibiotica

15. Probeer uw laatste aflevering van een antibioticum voor een kind jonger dan 12 jaar voor de geest te halen. Welke van de volgende stappen voerde u allemaal uit? (Kruis aan)

    ☐ Informatie geven over de onderliggende aandoening (in het geval van antibiotica: de bacteriële infectie bv. informatie geven over wat een longontsteking is)
    ☐ Informatie geven over de dosering (hoeveelheid en frequentie)
    ☐ Informatie geven over de gebruiksinstructies (bv. hoe een doseerspuitje te gebruiken)
    ☐ Informatie geven over bijwerkingen/gevaren van antibiotica
    ☐ Informatie geven over het (niet vroegtijdig) stoppen van de behandeling
    ☐ Informatie geven over de doorverwijscriteria
    ☐ Niet-medicamenteus advies geven
    ☐ Schriftelijke informatie meegeven

16. Hoelang duurde de aflevering ongeveer in minuten? .....

17. Op 100 patiënten, van hoeveel schat u in dat ze op de hoogte zijn van antibiotica resistentie? ...../100

18. Wat roept antibiotica resistentie bij u op?

.....

.....

Wenst u een fiche te ontvangen over het gebruik van paracetamol, ibuprofen en antibiotica? Gelieve dan hier uw e-mailadres in te vullen (dit zal niet voor andere doeleinden gebruikt worden).

.....

Annex D: *Number of elementary schools/nurseries in every provincial capital that disseminated the questionnaire and number of pharmacies/GP practices visited in every city*

Provincial capital	Number of schools called	Number of schools that disseminated the questionnaire	Number of nurseries called	Number of nurseries that disseminated the questionnaire	Remarks
Antwerp	5	1	1	1	When a school or nursery refused, the main reason was the frequent demand for this type of surveys they are overwhelmed with.
Bruges	12	0	8	3	In Bruges no school was found that wanted to participate. When a school or nursery refused, the main reason was the frequent demand for this type of surveys they are overwhelmed with.
Ghent	6	1	1	1	When a school or nursery refused, the main reason was the frequent demand for this type of surveys they are overwhelmed with.
Hasselt	5	2	3	2	When a school or nursery refused, the main reason was the frequent demand for this type of surveys they are overwhelmed with.
Leuven	12	0	5	1	All schools refused because of the frequent demand for such surveys. Because it is not possible to participate in all studies, they limit themselves to students of the KU Leuven. Eventually, contact was made with "het loket kinderopvang" so that the survey in Leuven was still disseminated through all Leuven nurseries and "Het huis van het Kind".
Total	38	4	18	8	

Provincial capital	Number of pharmacies called	Number of pharmacies visited	Number of GP practices called	Number of GP practices visited
Antwerp	11	8	3	0
Bruges	11	7	1	1
Ghent	8	8	1	0
Hasselt	14	7	1	1
Leuven	12	9	2	0
Total	56	39	8	2

Annex E: *Internationalization@Home*

1. The Pharmacist is a key stakeholder in measuring and managing patients' adherence to medications – Bernard Vrijens

Non-adherentie is binnen de gezondheidszorg een veel gezien fenomeen. Dit is geen zwart-wit concept en kent bovendien een dynamisch aspect, wat tot zeer uiteenlopende klinische consequenties leidt. Drie grote processen spelen een belangrijke rol wanneer we spreken over adherentie en tijdens elk van deze processen kan het fout lopen namelijk tijdens de initiatie (Start de patiënt met het nemen van de medicatie?), de implementatie (Neemt de patiënt de medicatie in zoals aanbevolen?) en de persistentie (Houdt de patiënt de behandeling vol?). Dit leidt ertoe dat non-adherentie op zeer verschillende manieren tot uiting komt waardoor een geïndividualiseerde aanpak cruciaal is. Het is een opmerkelijke vaststelling dat 30% van de patiënten niet eens start met het innemen van de medicatie en dit omwille van diverse redenen. Wanneer we spreken over adherentie is "drug forgiveness" een belangrijk en nog veel te weinig in rekening genomen concept. Zo zal de "drug forgiveness" in sterke mate bepalen welk level van adherentie aanvaardbaar is voor welk type medicatie. Verder worden geïndividualiseerde behandelingen vandaag de dag steeds belangrijker en zal hier naar de toekomst toe veel meer op ingezet moeten worden. Als we willen dat het beroep van de zorgverlener niet vervangen wordt door algoritmes zal onze manier van werken moeten wijzigen. Er bestaat echter geen magische pil die de non-adherentie kan aanpakken maar we zullen hier zelf inspanningen voor moeten leveren. Zo zijn er bijvoorbeeld tools ter beschikking die tot verbetering kunnen leiden maar deze moeten verder uitgewerkt worden. Ook zal dit meer samenwerking vereisen van verschillende zorgverleners (zowel apothekers, artsen, sociale werkers etc.). Maar voor de apotheker blijft hierin een sleutelrol weggelegd. Het is dan ook onze taak hieraan te blijven werken. Tot slot zal deze non-adherentie aanpakken niet alleen de patiënt ten goede komen, maar ook de maatschappij omwille van de enorm hoge kost die hiermee gepaard gaat.

2. Nanomedicine(s): where do we come from, where do we go? – Patrick Couvreur

Het veld van de nanotechnologie werd slechts enkele decennia geleden geïntroduceerd en is inmiddels reeds uitgegroeid tot een belangrijk domein dat op grote interesse kan rekenen. Toepassing van deze nanotechnologie heeft geleid tot de ontwikkeling van nanomedicijnen, het onderwerp van deze lezing. Conventionele geneesmiddelen kennen een aantal nadelen, bijvoorbeeld de onmogelijkheid tot het passeren van membranen en het vertonen van een niet-specifieke distributie. Sommige problemen kunnen aangepakt worden door de formulatie aan te passen maar dit is vaak onvoldoende. Daaruit groeide de nood aan andere oplossingen wat heeft geleid tot de ontwikkeling van nanomedicijnen. Zo zullen nanopartikels een

geneesmiddel inkapselen met een aantal voordelen tot gevolg. In eerste instantie wordt het geneesmiddel op deze manier beschermd tegen degradatie. Ten tweede is door middel van nanomedicijnen een zeer specifieke targetting van bepaalde cellen mogelijk. Dit is bijvoorbeeld het geval voor bepaalde borstkanker cellijnen die een overexpressie vertonen van biotinereceptoren. Hiertoe worden nanomedicijnen ontwikkeld die beschikken over biotine op hun oppervlak waardoor specifiek binding met deze biotinereceptoren mogelijk wordt. Bovendien zullen nanopartikels een betere intracellulaire diffusie mogelijk maken. Een ander significant probleem dat omzeild kan worden met behulp van nanomedicijnen is het toenemend aantal cellijnen die multidrug-resistentie vertonen. Door het inkapselen van onder meer cytostatica worden deze efflux processen vermeden. Dit is een enorm interessante techniek aangezien dit geen aanpassing van de molecule vereist, maar enkel een wijziging in de manier van toedienen. Tot slot maakt het gebruik van nanopartikels het mogelijk om bijvoorbeeld twee verschillende geneesmiddelen te combineren in één partikel. Maar ook de combinatie van een diagnosticum en een therapeuticum, een zogenaamd "theragnostic particle", is reeds ontwikkeld. Dit maakt duidelijk dat nanomedicijnen een enorme verscheidenheid aan mogelijkheden bieden, waar we in de komende jaren ongetwijfeld nog veel meer van zullen horen.

3. The uses of Hippocratic epidemiology – Albert Hofman

Epidemiologie is een tak van de wetenschap die zich bezighoudt met het bestuderen van de frequentie van ziekten en factoren die deze beïnvloeden. Hippocrates, de grondlegger van de Westerse geneeskunde, introduceerde vier grote vraagstukken binnen de epidemiologie i.e. (1) etiologie, (2) diagnose, (3) prognose en (4) behandeling. Deze werden vervolgens doorheen de lezing toegepast door Hofman. Hierbij werd gestart vanuit de "big picture" (≈diagnose). Zo zien we sinds de 17de eeuw een drievoudige toename in levensverwachting. Maar uit verschillende studies blijkt ook dat levensverwachting een zeer plastisch concept is en snel kan wijzigen over de tijd. Vervolgens werd dieper ingegaan op "de oorzaken" (≈etiologie). In deze context werd dementie aangehaald, een typisch voorbeeld van een ziekte waarvan de prevalentie toeneemt met de leeftijd. In dit verband haalde Hofman aan dat hij de stelling "there is no such thing as ageing" ondersteunde. Vanuit dit standpunt worden ziekten niet veroorzaakt door het verouderingsproces maar door een accumulatie van allerlei risico's. Zo werden als oorzaken van alzheimer drie redenen aangehaald i.e. (1) genen, (2) omgevingsfactoren en (3) interacties tussen genen en omgeving. Om de rol van genetica op alzheimer te bestuderen kan gebruik gemaakt worden van genome wide association studies en genomics. Deze nieuwere technieken in combinatie met cohortstudies zijn van enorm belang in epidemiologisch onderzoek. Maar ook niet-genetische factoren spelen een rol zoals traumatische, endocriene, inflammatoire en vasculaire factoren. Zo stelde Kraeplin dat atherosclerose aan de basis ligt van alzheimer. Wanneer we tot slot de epidemiologie van Hippocrates toepassen, is de laatste stap het ondernemen van actie (≈interventie).

In dit opzicht hebben studies reeds aangetoond dat de incidentie van dementie de afgelopen jaren is afgenomen. Om dit in kaart te brengen speelt epidemiologisch onderzoek een cruciale rol. Als besluit kan hierbij worden geconcludeerd dat epidemiologie de brug vormt tussen de klinische wereld en de preventieve geneeskunde, waarbij het potentieel voor preventie van chronische ziekten groot is.

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