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Chapter 1
General introduction
GENERAL INTRODUCTION

Impact of migraine
Migraine is a headache disorder with a major impact on the daily life of the patient. During migraine attacks, that last for 4 to 72 hours, most patients have to interrupt their activities and lie down. Some patients can continue their activities after having taken medication but are still unable to function normally. Also, between attacks, the physical, mental and social functioning of patients is highly influenced by the unpredictability of migraine attacks. In the Netherlands, every year about 25% of women and 7.5% of men experience one or more migraine attacks and about 25% of migraine patients experience at least two attacks per month.

Migraine treatment
Over time, different types of therapies for migraine have been investigated and various medications have been studied. At this moment, four possible groups of attack medications are available: paracetamol, acetylsalicylic acid, nonsteroidal anti-inflammatory drugs (NSAIDs) and triptans. Sometimes a combination of these medications is used. When patients experience two or more attacks per month, guidelines advise to discuss the possibility of starting preventive treatment. Preventive treatment for migraine implies that patients have to take medication on a daily basis to prevent the occurrence of migraine attacks. Several different medications are used for the prevention of migraine attacks, including antiepileptic drugs, beta blockers and calcium channel blockers, and subtypes of antidepressants. Behavioural treatment (i.e. relaxation therapy, biofeedback or cognitive behavioural therapy) is considered when treatment with medication does not lead to a substantial decrease in migraine attacks.

Effectiveness of migraine treatment
Despite the various options available for the treatment of migraine, it remains a highly disabling disorder. In the Global Burden of Disease analysis 2010, migraine was the disorder with the eighth highest number of years lived with disability (YLD), directly after chronic obstructive pulmonary disease (COPD) and anxiety disorders. In 2011, the World Health Organization (WHO) performed a survey among neurologists, general practitioners (GPs) and patients’ representatives from 101 countries and concluded that headache disorders are under-recognized, under-diagnosed and under-treated. It was concluded that many patients are unnecessarily seen by a specialist instead of a GP, that management guidelines are used routinely in only 55% of responding countries, that no appropriate medication is available, and that education on headache disorders in medical training is lacking. Therefore we can conclude that both the organisation of care as well as treatment possibilities are suboptimal.
Migraine treatment in the Netherlands

The Netherlands has advantages with regards to migraine treatment. For example, evidence-based management guidelines are available for the treatment of headache in both primary care and secondary care. Also, about 50% of migraine patients visit their GP and referrals to secondary care are relatively scarce. However, when looking at data on the use of medication for migraine, we have to conclude that also in the Netherlands the treatment of migraine is not optimal. Over 25% of migraine patients are eligible for preventive treatment as they suffer from two or more attacks each month. However, only 8-12% of all migraine patients actually uses it. Remarkably, when asked, more than half (55%) of the Dutch migraine patients who experience two or more attacks per month wants to try preventive treatment. Furthermore, in the Netherlands, about 3% of triptan users consume ≥12 triptan doses each month and are probably suffering from medication induced headache. Hence, there is room for improvement in the different aspects of the treatment of migraine in Dutch primary care.

Aim of this thesis

The aim of this thesis is to study how improvement can be achieved in the treatment of migraine in the primary care setting. The main assumptions underlying this thesis are that many patients with migraine suffer unnecessarily because of undertreatment, and that a proactive approach towards migraine patients in primary care would lead to a decrease in headache complaints and associated costs.

In the second chapter we evaluate whether a proactive approach towards migraine patients in primary care is effective in diminishing headache complaints. In the subsequent three chapters, we study migraine treatment in primary care from various viewpoints and using different study designs. In the last two chapters we evaluate two methodological issues that confronted us during our research and are important for research in primary care. The content of the work in this thesis is summarised below.

CHAPTER 2. Many patients with migraine suffer unnecessarily because they are not using their medications appropriately, or they are unaware of the possibility of prophylactic treatment. We conducted a pragmatic cluster-randomised controlled trial in general practice to study whether a proactive approach to patients with migraine, including an educational intervention for GPs, would lead to a decrease in occurrence of headache and associated costs.

CHAPTER 3. The number of migraine patients eligible for preventive treatment is considerably higher than the number of patients actually using it. We performed an explorative survey among Dutch patients and their GPs participating in the trial on
preventive medication (Chapter 2). We asked GPs and patients who did not start preventive treatment whether they had discussed the possibility of preventive treatment and, if so, why they decided not to start it.

CHAPTER 4. Clinical trials on the prophylactic effect of propranolol and metoprolol for migraine show that starting these medications leads to a decrease in the use of attack medication of 1.5 to 8.9 doses per month. However, no studies are available on the effectiveness of these medications in daily practice. We performed a retrospective cohort study in a large Dutch representative general practice database in which we examined the effect of starting preventive treatment with propranolol or metoprolol.

CHAPTER 5. The most frequently used outcomes in studies on the effectiveness of migraine treatment are whether the patient is free of pain, nausea, and photophobia and phonophobia within 2 hours. These regularly used outcomes and related outcome measures are based on consensus among migraine specialists. However, migraine patients have not been asked in a systematic manner what they consider important themselves. Therefore, we performed an online Delphi procedure to construct a short list of outcome measures that are considered most important by the migraine patients themselves.

CHAPTER 6. Pragmatic trials often have a control group receiving ‘usual care’, because they are generally performed to determine whether an intervention can improve current practice. Ideally, the behaviour of caregivers and patients in this control group should be influenced as little as possible by the actions of researchers. We performed a review of 73 pragmatic trials published in three leading medical journals relevant to primary care to 1) explore the variety of approaches to the usual care concept in pragmatic trials and 2) to provide insight into the influence of the study design on the behaviour of caregivers and patients in a ‘usual care’ control group.

CHAPTER 7. To interpret questionnaire scores in daily practice and evaluation studies, clinicians and researchers need to know what change in score reflects a meaningful change in the condition of an individual patient, and what difference reflects a meaningful difference between groups. Therefore, we determined the within-person minimally important change (MIC) and the between-group minimally important difference (MID) of the Headache Impact Test-6 (HIT-6) questionnaire, which we used in our trial (Chapter 2).

CHAPTER 8. This chapter summarizes and discusses the main findings of the work presented in this thesis. Finally, a description is given of the the added value of this thesis for daily (primary) care and suggestions are made for future research.
REFERENCES