Introduction
The term placebo has been used since the 1950s. A placebo can be seen as an inert substance and the placebo effect follows after the dose.[1] When prescribing a placebo, the practitioner records the agent as a drug, but it isn’t. Patients think they are taking a drug to treat their illness/pain, assuming that the drug will have a beneficial effect. We can see this process as the positive energy we draw from ourselves. Evidence is increasing that the placebo effect is a genuine psychobiological event, attributable to the therapeutic context in which the patient is being treated at that moment.[1] However, this raises an important issue: can doctors ethically prescribe placebos to patients? Patients assume that the drug will make them better or will alleviate their symptoms, but in fact the efficacy of placebos has not been effectively proven in practice. We can see this process as the positive energy we draw from ourselves. Evidence is increasing that the placebo effect is a genuine psychobiological event, attributable to the therapeutic context in which the patient is being treated at that moment.[1] However, this raises an important issue: can doctors ethically prescribe placebos to patients? Patients assume that the drug will make them better or will alleviate their symptoms, but in fact the efficacy of placebos has not been effectively proven in practice. Some Randomized Controlled Trials (RCTs) have indicated that placebos are effective. However in most of these RCTs a treatment group is compared to a group receiving placebo. This means that both groups know that there is a chance they will receive a placebo. This is much different from a doctor prescribing a placebo in practice and patients not being aware of it. If patients discover that they have been tricked, they may feel cheated and may no longer have any confidence in the practitioner.

As more and more people become aware of the prescription of placebos, this could cause major changes within our health care system. The population could lose confidence in doctors and other caregivers. The doctor-patient relationship could be in danger. At this time I think it’s unethical that the autonomy of the patients is taken from them this way. It can be seen as a form of paternalism where decisions that affect patients are taken – without their knowledge – by someone else. In this essay I focus mainly on the dilemma of prescribing placebos to patients who have unexplained somatic symptoms. Is it ethical to give placebos to such patients? Is there a difference if patients are informed that they have a chance of getting a placebo? And what is the influence of a positive or negative context in which the “placebo” is prescribed?

Medical scientific progress
In 2006 “The American Medical Association’s Council on Ethical and Judicial Affairs” took a position against the use of placebos in clinical practice.[2] To ethically defend the use of placebos, their effectiveness must be proven first.[3]

It has been shown that only a small number of doctors in the USA prescribe inert pills and injections (that comply with the formal definition of a placebo). However, 50% of the doctors prescribe medications which they expect will have no effect on the condition of the patient and thus essentially serve as a placebo.[4] If we look at the improvement in the subjective symptoms it is therefore important to find a way to make use of this placebo effect and avoid patient-deception.

Previous research has shown that the placebo effect is clinically significant in Irritable Bowel Syndrome (IBS).[1] No diagnostic tests and no effective treatments are available for IBS.[3] One study showed that the use of an “open-label”- placebo, which were defined as openly described inert interventions delivered with a plausible rational, is an effective treatment in IBS. In comparison to patients who received no treatment, patients with an open-label placebo scored much better with respect to symptom improvement. This study ran from 2009 until April 2010. However, it is debatable whether open-label placebo is a real form of placebo treatment.[4]

In a recent meta-analysis, all 73 RCTs that were eligible for the study (a total of 8364 patients with IBS) found a placebo response rate of 37.5%.[5] In a Randomized Controlled Trial, researchers compare treatment groups with control groups not receiving treatment (as in a placebo-controlled study). The placebo effect reported in RCTs is controversial, because the positive effect in the placebo group is not necessarily a psychosocial effect. It may be that this is the natural course of the disease, the extent to which the symptoms fluctuate, regression to the mean or response bias because the patient shows subjective symptoms. Sometimes it’s impossible to exclude that the effect is not caused by other concomitant therapies.[1] This has to do with the assumption of ceteris paribus, it’s not always possible to guarantee that the other parameters remain the same.

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Another question we must ask is whether a placebo has side effects, called the nocebo phenomenon. Here we should distinguish between events occurring in getting the drug (regardless of cause), and side effects that can be directly attributed to the drug (the cause is the drug itself).[6] It is a distinction between the expected negative effect and side effects of placebo. The nocebo effect is getting diseases or symptoms, in combination with negative expectations and associated with a particular emotional state.[7]

From a psychological standpoint many mechanisms contribute to the placebo effect. Patients who receive a placebo have certain expectations of the response in the future. It has been shown that if a positive expectation is aroused in a patient, the patient responds better to the placebo.[1][8][9] [10] Another mechanism is due to classical conditioning [11]. Repeated associations between a neutral stimulus and an active drug may result in the ability to induce an effect through a neutral stimulus, similar to that of the active drug. In addition, previous experiences and social observations also affect the potential placebo effect.[12]

Another study looked at patient and therapist influences on the operation of the placebo effect in IBS. The study focused on the characteristics of patients and therapists and their personal interaction. The conclusion was that gender (female) and personality of the patients (outgoing, pleasant and open to new experiences) had an influence on the placebo effect, but only in the group where there was a warm and empathic interaction between patients and therapists.[13] Besides IBS a possible beneficial placebo effect has been reported for a number of symptoms/conditions.(table 1).

<table>
<thead>
<tr>
<th><strong>Table 1 - Complaints whereby placebo could be useful.</strong></th>
<th>A. Hróbjartsson and P.C. Gotzsche (14)</th>
<th>W. Hauser et al. (15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pain</td>
<td>fibromyalgia syndrome (FMS)</td>
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<tr>
<td>nausea</td>
<td>peripheral diabetic neuropathy (DPN)</td>
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<td>asthma</td>
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<td>phobia</td>
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**Ethical aspects**

Patients think they feel better when they take a pill (which is prescribed by someone with extensive knowledge and experience), but in fact, its efficacy is not known. Regardless of whether patients feel better from taking a placebo, the ethical dilemma to deal with is deception. Doctors want the best for their patients, with a positive outcome, but this does not justify "cheating". In principle, lying and not telling the whole truth can be seen as two separate things. For example, doctors don’t tell patients all the possible symptoms of a specific disease, but provide only the most important ones and omit the others. However, this omission is probably unconscious; it is information that is in the background and not directly of the utmost importance. Doctors have good intentions and will come back to this aspect later on. They can justify why they did not tell everything immediately. Therefore, this is totally different than prescribing a placebo. The principles of beneficence and doing no harm also play a part. If a doctor prescribes a placebo to a patient, he/she intends to do the best for the patient. Yet no one has the right to determine that do well, and not harm are beyond the responsibility not to keep the patient in state of deception; leaving the patient in state of deception is worse than not offering the opportunity of placebo treatment. In addition, at the time that the patient finds out that he/she is getting a placebo, there is no longer any good: it’s more harm. This is because the patient has lost confidence in the practitioner, which is often to the detriment of the patient because the treatment relationship is damaged.[16]

Another problem is that patients can’t give informed consent if they are not aware of what they get. They didn’t receive the information that allows them to make a rational decision. In this way patients have no influence in their treatment.[16] Besides, by giving a placebo, practitioners violate the right to autonomy. In fact patients are not aware of their options. Autonomy means that patients are informed of their condition, that their questions are answered and that the treatment options, including risks and benefits, are discussed.[17] However, the patients may also prefer to remain in state of deception in this way (with a placebo) instead of knowing the truth. Of course we can’t estimate this beforehand. It’s clear that through deception they couldn’t make their own choice.
Opinion

Conclusions
On the first look, placebo prescription seems to be a good treatment for certain groups of people. It’s possible that placebo has a positive effect, that there’s a reduction of symptoms and the patients feel better. If we’re ever going to see placebo as a real treatment, we must take some factors into account. The most important is to inform the patient very well.

The first option is not to tell patients that they have a somatically unexplained physical symptom; instead tell them a treatment is available. Doctors prescribe a drug, but they tell them that the effect of the drug is not known. What do you put at the box (containing the so-called drug) that the patient will get at the pharmacy? They can invent a name for the drug, but an internet search will reveal that this drug does not exist. In addition, the name of this placebo will at least be known by healthcare workers. In this way, if it’s impossible to prevent patients from finding out that they have received a placebo, to what extent is the effect of placebo still guaranteed?

The second option is to proceed as outlined above, but then explain that they largely concern a psychosocial effect and related physical changes and possible improvement of somatic complaints. It may be that patients in this way do not make a connection with a placebo. However, the effects of a placebo (positive and negative) are not always predictable or known. We are unable, as with many other medicines, display the exact effect and side effects.

A third option is to tell patients who have unexplained physical symptoms that they can choose a placebo treatment. The placebo is discussed in a positive context. It is mentioned that a positive effect is not guaranteed, but that many positive results are known (“open-label placebo”). This possible effect, however, depends on several factors, but it should be emphasized that it can have a positive impact on individual patients. However, the question remains of whether an open-label placebo can be seen as having a placebo effect.

In my opinion we are not ready to prescribe placebos in clinical practice. There are still too many drawbacks for prescribing placebos and the evidence is not unequivocal. A study has demonstrated that patients with IBS with an “open-label” placebo had better outcomes than no treatment, but also many people with “open label” placebos experienced no effect. I think the second of the above options is best. Doctors do not lie to patients, but in fact withhold a little information. I believe that option three is impossible to apply. Supposing that we would apply the second option in the Netherlands, then we should have a clear policy with respect to this form of placebo. I think we should offer this option to all patients with an unexplained somatic disorder. Then we can give patients the opportunity to choose freely. For me, confidence in the healthcare system is essential. The doctor-patient relationship is crucial.
References