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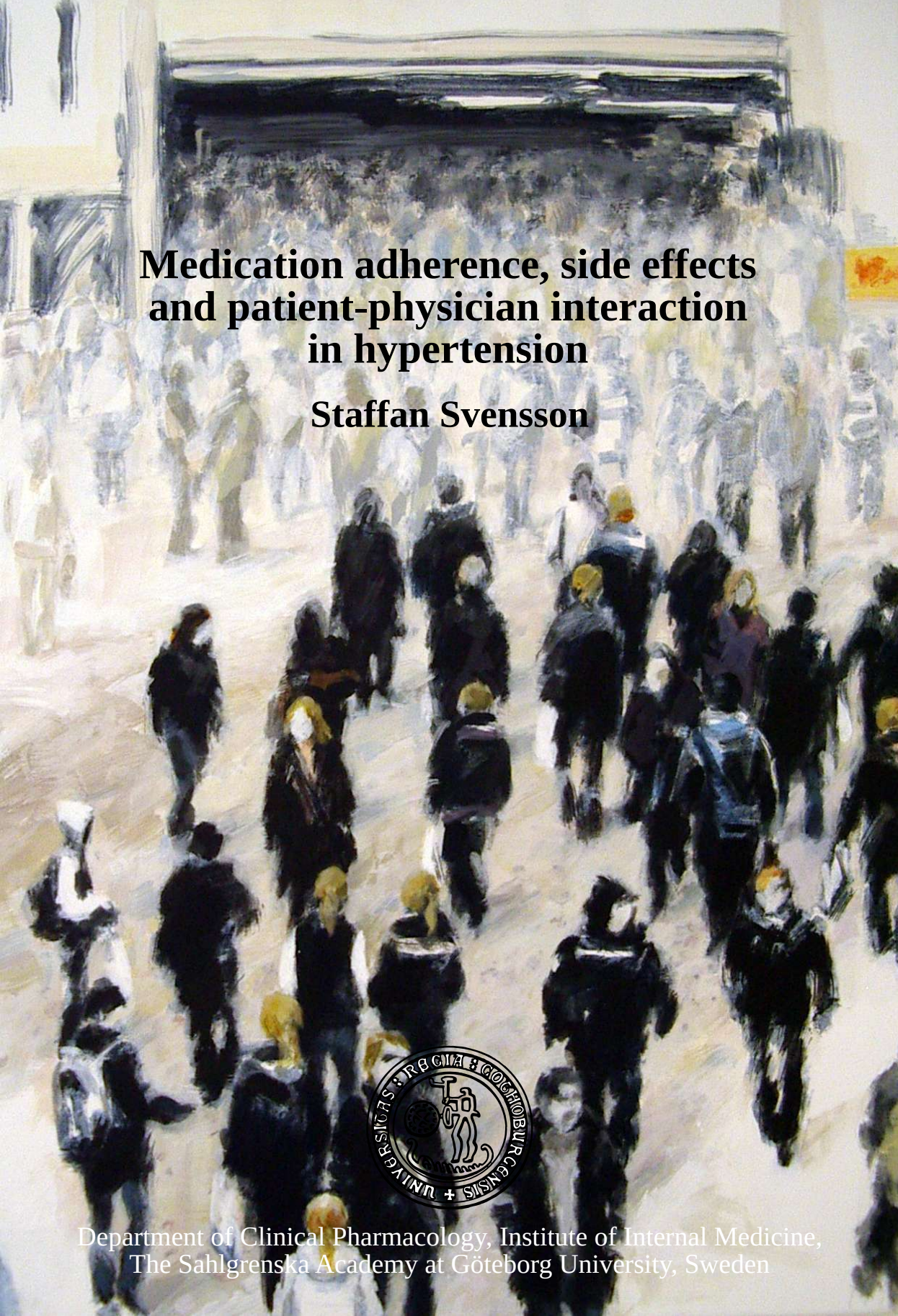

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Abstract

Hypertension is an important risk factor for cardiovascular disease, the incidence of which it is possible to reduce by prophylactic treatment with antihypertensive drugs. In clinical practice, however, only a minority of patients reach target blood pressure levels. The resulting gap between actual and potential health gains has been attributed to the fact that many patients do not take prescribed treatment as recommended, i.e. ”medication non-adherence”. This phenomenon is, however, insufficiently understood.

We investigated the topic of adherence by way of a randomised questionnaire material comprising 1013 patients, and audio-recordings of 51 patient-physician consultations and 33 interviews with the patients made after the consultations. All patients came for regular follow-up appointments with their physicians and were under treatment with antihypertensives.

In the questionnaire material, we found that patients who reported side effects of their drugs tended to rate their future risk of cardiovascular complications as being higher. Analysis of the interview data showed that patients had various reasons for sticking to the treatment recommendations: trust in physicians and wanting to avoid sequelae of hypertension were common arguments for doing so, while having side effects and disliking pharmaceuticals in general were reasons against. In the follow-up appointments, we found that the determinants of treatment decisions, i.e. the measured blood pressure values and (suspected) side effects, were defined through negotiation between patients and physicians. On the whole, patients and physicians were more in agreement about the interpretation of blood pressure values than of side effects, and physicians had the last say in the decision-making. We concluded that the antecedents of decisions about using medication are surrounded by uncertainty, and that it is the patient’s interpretation of the ”facts” that, ultimately, determines if and how antihypertensive medications will be taken.

Key words

Patient compliance, Guideline adherence, Hypertension, Adverse effects, Communication, Negotiating.

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List of publications

This thesis is based on the following papers, which will be referred to in the text by their Arabic numerals.

1. Kjellgren KI, Svensson S, Ahlner J, Säljö R. Antihypertensive treatment and patient autonomy – the follow-up appointment as a resource for care. Patient Educ Couns 2000;40(1):39-49.

2. Svensson S, Kjellgren KI, Ahlner J, Säljö R. Reasons for adherence with antihypertensive medication. Int J Cardiol 2000;76(2-3):157-63.

3. Svensson S, Kjellgren KI. Adverse events and patients' perceptions of antihypertensive drug effectiveness. J Hum Hypertens 2003;17(10):671-5.

4. Svensson S, Kjellgren KI, Linell P. Negotiating side effects in follow-up appointments for hypertension. Manuscript, 2005.

5. Svensson S, Linell P, Kjellgren KI. Making sense of blood pressure values in follow-up appointments for hypertension. Manuscript, 2005.

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Contents

Acknowledgements

As this is the only part of a thesis that perhaps 95% of those who get a copy of it will ever read, I decided to put it at the beginning. I want to start out by expressing my gratitude to Karin Kjellgren, my co-author and supervisor, for introducing me to the subject, employing me when I began working on the project as a medical student in Linköping, collecting the data material and allowing me to use it, and generally being very supportive even in times when I was going off in directions she must have known would delay this PhD project for years. Karin has also given my children lots of toys (which they have gratefully destroyed) and introduced me to a number of interesting people, among these Per Linell and Roger Säljö. So, thank you, Karin!

Second in line is Thomas Hedner, co-supervisor and professor at my department. He has always allowed me complete freedom to do what I felt was relevant and has always been ready to infuse me with some of his kamikaze optimism. Next, thanks to the co-authors of the papers in this thesis: the above-mentioned Per Linell, Roger Säljö and also Johan Ahlner (who, together with Karin's other protégé Mikael Hoffmann, aroused my interest in clinical pharmacology). Thanks also to Hans Gill for statistical advice, Elinor Sviberg Carlberg for transcribing the tapes, and Marita Bergström for practical support. I am also grateful to the participants in mock-up disputation exercises: Sverker Jern, Peter Währborg, Inger Ekman, Sven Wallerstedt and Lennart Andrén. To go on, I would like to thank the following people, who are listed either alphabetically or in their order of appearance:

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Preamble

The aim of the project

This thesis is based upon a material gathered between the years 1993 and 1997, with the aim of investigating why patients with high blood pressure do (or do not) take their antihypertensive drugs – a topic called *medication adherence*. So far, the project has spawned ten separate studies, of which the first six were included in a thesis published in 1998 [1] and one of these plus four more are included in the present thesis (Figure 1).

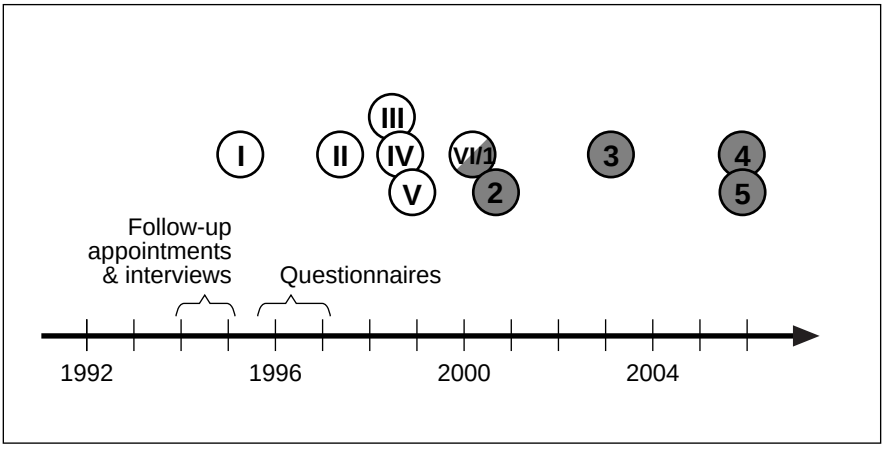

Figure 1: Timeline of the project. Circles with roman numerals: studies included in first thesis based on project data. Circles with arabic numerals: studies included in this thesis. Study VI/1 was included in both.

The overall aim of the project was, at its inception, specified as ”To document and analyse prerequisites of patient adherence to anti-hypertensive medication in routine clinical practice” [1]. At the time of specifying this overall aim I was not yet involved, but I am nevertheless happy to subscribe to it in retrospect. The overall aim was accompanied by a number of specific aims, parts of which I contributed to investigating, but at the stage when I started doing independent analyses, what was originally planned had pretty much already been done. On the other hand, various observations and ideas had come up underway, spawning new approaches to the data. It was therefore not, for my part at least, a matter of first having a number of specific aims and then, in an orderly fashion,

ticking them off one by one as I proceeded through the project. But I will return to this topic later on.

Treating hypertension with drugs involves striking the best balance between prevention of cardiovascular complications and avoidance of side effects of treatment [2, 3]. A lot of this thesis deals with the question of how this balance between these ”pros” and ”cons” is struck. This question largely boils down to, we will claim, how the pros and cons are defined, which is, in turn, something settled through interpretation of the ”facts” that guide decision-making.

There were no interventions

Research on the topic of medication adherence tends to be of two types: attempts to understand its reasons (observational studies) and attempts to do something about it (interventional studies). Of course, if an intervention is successful you may also learn a lot about the source of the problem. In any case, we performed no interventions but instead focussed on trying to understand the nature of medication adherence. Thus, whatever emerges from these studies has no immediate applicability, as we have in no way manipulated patients, health care staff or their environments with the aim of increasing adherence. On the other hand, the interventions to increase adherence that have been tested so far have not met with any great success [4], so in order to come up with more promising interventions, ventures directed at gaining a fuller insight into the problem are needed. In the words of Haynes et al:

> ”As low adherence affects all self-administered treatments, and as the numbers of efficacious, self-administered treatments continue to grow, investment in fundamental and applied adherence research is likely to pay large dividends.” [4]

Or, as pointed out by Machiavelli, in order to manipulate people[1], you first need to understand them [5].

1 Whether it is fair and proper to manipulate people at all is another question.

Introduction

Hypertension

Hypertension is a sustained elevation of the systemic arterial pressure, hence ”high blood pressure”. It is a very common condition – it has been estimated that about a quarter of all adults in the world, most of whom live in developing countries, have hypertension, and the elderly more so than younger people [6]. It is an important harbinger of cardiovascular diseases, which account for about 30% of all deaths in the world [7]. The association between the blood pressure level and its consequences is continuous:

> ”The relationship between blood pressure and risk of cardiovascular disease events is continuous, consistent, and independent of other risk factors. The higher the blood pressure, the greater is the chance of heart attack, heart failure, stroke, and kidney diseases.” [8]

Hypertension is often defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood ≥90 mmHg, in subjects who are not taking antihypertensive medication. This dichotomisation of patients into the categories ”hypertensive” or ”normotensive” is by nature arbitrary, however, and the current view of hypertension management emphasises a holistic approach to cardiovascular risk: the blood pressure should be considered in the context of other risk factors (notably sex, age, smoking, blood lipids, heredity, obesity/physical inactivity, target organ damage and established cardiovascular disease) in the decision of whether, and how intensely, an individual patient should be treated [9].

Cardiovascular disease has been described as ”eminently preventable” [9], in that many of its risk factors may actually be changed by intervention. The benefits of treating high blood pressure are among the most well-documented in medicine[2] and doing so with drugs has been shown to reduce the risk of stroke by 40% and the risk of myocardial infarction by 15% [11].

The baseline treatment of hypertension consists in applying life-style measures where these are relevant, by reducing weight, excessive alcohol consumption and salt intake, by stopping smoking and by increasing physical activity [9]. Most patients with hypertension, however, end up getting prescribed drug therapy for their condition – in the Framingham study, the lifetime risk of receiving antihypertensive

2 There is, however, a line of thought which questions the usefulness of preventive medicine altogether [10]. But I will adopt the orthodox view here.

drugs for *all* members of the population was 60% [12].

Further, more than two-thirds of those with hypertension cannot be controlled on one drug and therefore need two or more antihypertensive agents [8]. In actual fact, even though so many people are prescribed drugs for their hypertension, few achieve control of their blood pressure. A previous analysis of the questionnaire material used in this thesis found that only 14% of medicating hypertensive patients had reached blood pressure levels ≤140/90 mmHg [13], and in a much larger sample of Europeans taking antihypertensives, only 8% attained the same goal [14]. The rate of control is higher among patients who have established cardiovascular disease (and are therefore at high risk of getting more of it), but, still at the European level, less than half of such high-risk patients actually reach ≤140/90 mmHg [15]. Most commonly, it is the systolic rather than the diastolic blood pressure which remains uncontrolled [8].

Uncertainty regarding blood pressure values

While hypertension, at a population level, is therefore a clear-cut case of a risk factor in need of better prevention, things are often a bit more complicated at the level of individuals. Although treatment is clearly beneficial at a group level, there is no guarantee that it will be of any use for a particular patient [16]. And, as regards the actual blood pressure values that decisions about treatment are based upon, there are many sources of uncertainty.

One is related to the arbitrariness of what ”controlled” actually means in a given situation. Just how serious is a reading of, say, 153/94 mmHg? In keeping with the holistic approach outlined above, answering this question is a matter of taking other risk factors into account, but many of these are also surrounded by uncertainty. In practice, having a ”normal” blood pressure may mean different things to different people, e.g. normal in relation to average values or in relation to some ideal value [17].

Errors in measurement is another source of uncertainty. This may be related to bad technique, hearing problems or digit preference on part of the measuring person (if it is done manually), or to faulty or ill-sized equipment and environmental noise [18, 19]. Further uncertainty stems from the fact that the blood pressure is subjected to physiological variation, both seasonal, circadian and situation-dependent. In order to obtain a representative value it may therefore be necessary to measure it repeatedly [8]. Getting several readings may not help, however, as

fluctuations tend to be systematically higher when people go to see their doctors (and perhaps nurses), a phenomenon known as the ”white coat effect”. “White-coat hypertension” is defined as having persistently elevated values in the clinic, in combination with otherwise normal daytime blood pressures. Patients often perceive stress as a major cause of chronic as well as temporarily high blood pressure levels [20, 21], and the white coat effect may be considered a special case of this phenomenon. It is unclear, however, what the significance is, in terms of risk, for people with white-coat hypertension. The general consensus seems to be that it is at least not a straightforward indication for treatment [22]. Possibly, however, people with white-coat hypertension are at higher risk of stroke [23].

The making of a decision about treating hypertension at the individual level may therefore be fraught by considerable uncertainty regarding the severity and representativity of the blood pressure readings that the decision is based upon. For this reason, it is hard to say exactly what the advantages of treatment will be. The advantages, in turn, have to be weighed against possible disadvantages [2, 24], among which side effects are of primary importance.

Side effects

Medication side effects may be thought of as any unwanted consequences of taking pharmaceuticals. In this wider sense, getting reminded about one’s hypercholesterolaemia by having to take a drug for it every day – and not liking to get reminded – would, for example, pass as a side effect. In medical contexts, however, the meaning of the term is usually limited to unwanted *symptoms* caused by pharmaceuticals. A pragmatic definition of a side effect is that it is any medication-caused symptom that is not desired in a given setting – and by this standard the terms “therapeutic effect” and “side effect” are interchangeable depending on the situation [25-27]. A more formal, and influential definition of a side effect, or ”adverse effect”, is that of Edwards & Aronson:

> “An appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product.” [28]

These authors use the term ”adverse effect” to point out that a judgement has been made about causality – that it has been decided that

the symptom was actually caused by the drug in question. This sets ”adverse effects” apart from ”adverse events”, which are whatever symptoms that may co-occur with the taking of medication without necessarily being caused by it [28]. It has been reported that, in trials comparing active substances against placebos in healthy volunteers, some 19% of these volunteers experienced side effects to the placebos [29]. According to the definition above, all these people therefore had ”adverse events” and none had ”adverse effects”[3].

The impact of side effects

For side effects in general, Pirmohamed and co-workers investigated almost 19 000 admissions to two English hospitals and estimated that 6.5% of these were directly caused by the patients' side effects (not counting deliberate or unintentional overdoses) [30]. Hospital bed occupancy related to side effects was estimated at 4%, and the authors concluded that side effects were a major burden to the health care system.

As concerns antihypertensive drugs, about a quarter of patients who take them report having side effects in response to an open question [31, 32]. Some patients have symptoms of their *high blood pressure* whereas others do not [31], and among the latter, the actual ingestion of drugs as well as their side effects may be the only tangible aspects of the condition. Some patients who have side effects find them useful (for example, the calming effect of β-receptor blockers may be appreciated [34]), but most dislike them and consider them a reason against taking the drugs [33, 35]. Physicians also cite side effects as a main factor behind changes in treatment [32].

Uncertainty in side effect assessment

But, given the weight people attribute to side effects, it is worrying that we, in practice, rarely know for sure if a symptom really is due to a drug or not. To make an assessment of a suspected side effect in an individual involves looking at the timing of symptoms in relation to administration of the drug, the dose-response relationship, the specificity of the symptom, and the consideration of other plausible explanations [28]. A formal assessment, as done at the department of Clinical Pharmacology where I work, results in a labelling of the side

3 Barring the possibility of some unknown active substance in the placebos.
4 In which case they would, in accordance with the ”pragmatic” definition above, not be considered as side effects; Benson & Britten called them ”palpable effects” [33].

effect as being either *certain, likely, possible* or *unlikely.* Alternatively, one can use either of the two cop-out categories *unclassified* and *unclassifiable* for pending or unassessable cases [28, 36]. Most side effects that are reported end up being considered ”possible” or ”likely” [36], but the agreement between different assessors is often poor. In the words of Karch et al:

> “The tolerance range for identifying adverse drugs reactions in clinical practice is so coarse that neither treating physicians nor clinical pharmacologists agree on most cases.” [37]

And, according to Koch-Weser et al:

> “The causative role of drug therapy in an adverse clinical occurrence is often largely a matter of opinion.” [38]

There are many reasons for it being difficult to assign a given symptom to a drug. Symptoms may be due to other things, and if the baseline prevalence of the symptom is high – such as, for example with headache – it will be difficult to prove that it was caused by the medicine. The figure of 19% having side effects to placebos mentioned above [29] indicates that there is a lot of ”noise” in the system. In the case of hypertension, although this is often regarded as an asymptomatic condition [39], many people actually report having symptoms of it [31], a matter that may clearly complicate the assessment of side effects.

To continue, many different medicines are often used at the same time, and this makes it hard to settle which one, if any, has caused a given symptom. Further, it is often very helpful to know if the symptom disappeared and re-occurred on stopping and re-starting the drug. If so, there was positive *dechallenge* and *rechallenge* [36]. But patients and prescribers are usually not very eager to experiment in this fashion, at least not by re-starting a drug that was stopped because of suspected side effects.

In practice, nevertheless, it has to be decided what to make of a suspected side effect. By doctoring the above definition by Edwards & Aronson a bit, we arrive at a briefer description of a ”true side effect” that may be useful in the following:

> “A reaction, resulting from the use of a medicine, which warrants alteration or withdrawal.”

The ”resulting” part reflects probability, which is the focus of causality assessment, and the ”warrants alteration or withdrawal” part implies that

the side effect must be *severe* enough to cause some action. I have already stressed that there are a lot of difficulties in assessing causality, and the same arguably holds true also for severity. For one, it depends on personal experience, which may be very difficult to communicate to another person. Therefore, a physician is not likely to have an accurate idea of just how severe a patient's symptom really is.

Also, the experience of severity (and probability) depends on the patient's attitude towards it. Benson & Britten found that patients used the tactics of ”seeing the side effect as minor” [33], or ”deciding that the side-effects didn't actually bother them too much” [35] for motivating themselves to continue taking their antihypertensive tablets:

> ”[some patients] balanced the continued need to make allowances for the unwelcome effect against pragmatic uncertainty that the medication was really to blame or the effect seeming only minor” [33]

So, returning to the problem of weighing advantages against disadvantages, it appears clear that both the ”pros” and the ”cons” are surrounded by uncertainty. One of the main tasks for patients and physicians, when they meet, is therefore to try to make sense of the facts that are relevant for decisions about drug therapy. The way this is done is an important aspect to consider in relation to the topic of medication adherence.

Medication adherence

This is a phenomenon with many names. Medication adherence (or, sometimes just ”adherence”) is the term I have used in the papers to describe the extent to which patients take medication according to the recommendations of health care staff [40]. The original (and still commonly used) word for this was *compliance*, which people interested in the subject later felt uneasy about because of its connotations to old-fashioned ideas about doctors ordering patients about [40, 41]. For this reason, many adopted the term *adherence* in its place, but later, for similar reasons as the first, students of the subject advocated a further change to the term *concordance*[5]. The definition of concordance differs from that of adherence:

> ”an agreement reached after negotiation between a patient and a healthcare professional that respects the beliefs and wishes of the patient in determining whether, when and how medicines are to be taken” [42] (quoted in [43])

5 If nothing else, this anxiety over words indicates that we are dealing with a sensitive subject. As far as I am aware, however, the Swedish term for this phenomenon, i.e. *följsamhet*, has not been subject to any controversies of this sort.

The term concordance is an interesting development, in that it involves a consensual agreement – it is not possible for a person to be ”non-concordant” on her own. Nevertheless, I will not go any further into this, but will stick to the more simplistic term used in the title of this thesis.

Extent, effects and causes of non-adherence

Medication non-adherence to long-term treatment is believed to be very common, perhaps in the order of 50% [4], but this depends on how it is measured and defined [40]. Although the reliability of such figures has been questioned [44], it seems reasonably clear that many patients do not take treatments as prescribed, and this is regarded as a major factor behind the poor control of people’s blood pressure levels [45].

Among causes that have been suggested for patients’ non-adherence to medical regimens we find side effects, poor memory, cognitive impairment, inability to pay for the drugs, complexity of treatments, poor instructions, lack of understanding of the illness, poor provider-patient relationship, and patients’ disagreement with the need for treatment [4, 40]. As noted in the preamble, however, interventions aimed at improving adherence have met with limited success (and the interventions have been rather complex and its effects not long-lasting) [4], so whatever is known about medication adherence has not been translated into much in the way of clinical benefits.

Physician adherence

Sticking to a treatment recommendation is of course only beneficial if the recommendation itself makes sense, i.e. if there is a proper indication for treatment (Figure 2)[6]. Conversely, if the indication exists and the prescriber does not prescribe accordingly, the patient misses out on the potential benefits of treatment.

6 And, although the advice may have been good at some point in time, it does not necessarily stay that way forever. Cornish et al., for example, described two cases of patients who, having been admitted to hospital for gastrointestinal bleeds, kept taking their own nonsteroidal anti-inflammatory drugs unbeknownst to the hospital staff [46]. In another study related to the same category of drugs, Wynne & Long found (albeit retrospectively) that high medication adherence was associated with suffering more gastric bleeds [47].

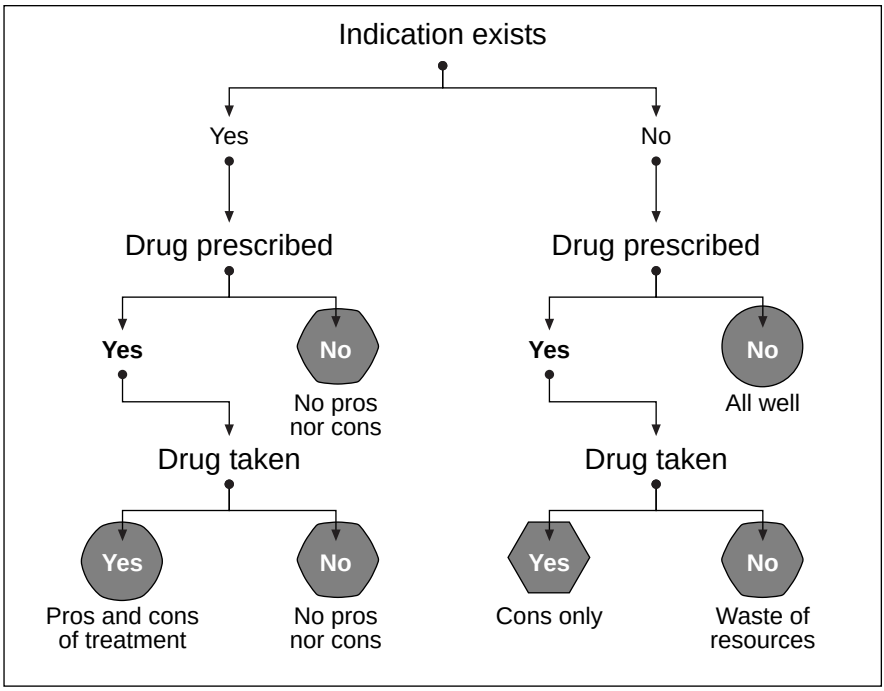

Figure 2: The “pros” and “cons” of treatment in different situations.

One may therefore, in analogy with patient adherence, speak of physician adherence to high standards of care [48]. The standards of care are often expressed in guidelines about diagnosis and treatment, of which there are plenty, especially in the cardiovascular field [3]. In further analogy with patient adherence, physician adherence to guideline recommendations is often described as being poor [3, 8, 15, 49].

Adherence and side effects

It was highlighted previously that patients and physicians alike regard side effects as an important reason for not sticking to the antihypertensive drugs. But is the relationship between side effects and medication adherence a simple case of ”the more of the former – the less of the latter”? At least three things may speak against the association being quite that plain:

First, as pointed out earlier, the severity and the causality of side effects are not assessed in isolation of reasons *for* being adherent [33, 35].

Second, patients may associate side effects of a drug with the drug's potency to cure [50-52]. In the words of Fallsberg:

> ”It is almost impossible to anticipate a cure or improvement without negative side effects. Rather, [patients'] conception [of medicines] expresses an acceptance of the view that the absence of side effects means that medicines cannot help” [52]

And as it seems reasonable to believe that patients are less eager to take medicines that cannot help, there may be an ”optimal dose” of side effects for adherence (a hypothesis related to this was investigated in paper 3).

Third, Morgan has suggested that

> ”the only medically acceptable reason for patients' non-compliance is the experience of side-effects” [53]

It is therefore conceivable that a patient who, for example, has a general dislike of medicines, may choose to express this aversion in terms of side effects.

Adherence and morality

Having, and behaving according to, a ”medically unacceptable” or ”unorthodox” opinion, amounts to challenging the view of the medical establishment [54]. Non-adherence may, in this way, be interpreted as a sign that people want to affirm their autonomy towards those who think they know better [55]. There is thus an element of disobedience to both patients' and physicians' non-adherence, and breaking the rules is in turn something that is associated with sin [41].

Another aspect of sinning that is relevant in this context, is that having hypertension may imply that the patient has not been able to resist the temptations of gluttony and sloth. Indeed, basically all the non-pharmaceutical measures that patients with hypertension are recommended to follow, are of a type one would generally associate with living an irreproachable life. In this vein, Lupton has proposed that having a health risk secondary to one's life-style is the modern equivalent of being a sinner [56]. So, if someone has brought a risk upon himself by not adhering to general principles of healthy living, then being non-adherent to recommendations about medication treatment is, in a way, just more of the same.

Adherence in follow-up appointments

A lot of hypertension care takes place in annual checkup meetings between patients and physicians. In view of what was stated above about medication non-adherence being a prime reason for poor blood pressure control (and hence of death and disability), trying to improve adherence is arguably one of the main functions of physicians in these appointments. Here, physicians are faced with the complex task of trying to make sense of blood pressure values, suspected side effects and other factors relevant to the treatment decision, while at the same time trying to inspire patients to follow their advice.

Physicians are, however, considered to be poor at recognizing non-adherence in the clinical situation [40]. This may be due to the fact that the complexity is overwhelming, and that things spoken about must necessarily be restricted to keep the consultation within its time frame of 15 minutes or so.

The way of speaking in these consultations is adapted accordingly. Physicians may, when taking a medical history, use two basic modes: one is ”diagnostic history taking”, which is directed at diagnosing a specific problem – it is ”problem-seeking” – and the other is ”comprehensive history taking”, which is more along the lines of a general survey. The comprehensive type tends to proceed in sequences of questions that are, in a way, designed not to bring up problems: they facilitate short ”No problem” responses. Going beyond these questions by supplying a more detailed and problematic response, for example concerning reservations about taking the treatment, therefore takes a lot more effort on part of the patient [57].

In summary, clinical practice deals with a complex reality, and a major task of those involved is to try to make sense of it [58]. In the following, I will describe how we attempted to investigate this sense-making in hypertension appointments.

Method

Overview

All data in this thesis concern patients who came for routine follow-up appointments for hypertension with their physicians. Three datasets were used:

1. questionnaires filled in by 1013 patients (paper 3)
2. audio recordings of 51 follow-up appointments (papers 1, 4 & 5), and
3. audio recordings of 33 semi-structured interviews performed after the appointments (paper 2).

The methods used for analysis differed depending on the type of data and when the analysis was done. Basically, the questionnaire material was analysed using descriptive and analytical (univariate and multivariate) statistical methods. The follow-up appointments were also analysed quantitatively (by counting words, etc), but the main mode of analysis applied here was qualitative: by exploration and categorisation of contents and identification of themes. The interviews were also mainly analysed qualitatively, although laboratory methods were used here as well.

Eligibility criteria

Patients who were eligible for the studies had to have hypertension as their main diagnosis at the consultation they came for. They also had to be under treatment with at least one antihypertensive drug (although in a few cases this criterion was not fulfilled). The physicians who participated were the ones patients had their appointments with, and the blood pressure values referred to in the studies were those measured in routine care by the physicians (or in some cases by nurses). For the questionnaire data, an additional criterion was that patients had to understand how the visual analogue scales were filled in. Patients were included in the order they appeared.

Ethical considerations

The studies based upon audio-recorded follow-up appointments and interviews were approved by the regional ethics committee for human research at the Faculty of Health Sciences, Linköping University, Sweden (study codes: 93237, 94080, 94140 and 94186).

The study based on questionnaires was of multi-centre design, and hence had to be approved by all the regional ethics committees for human research in Sweden (study codes: 95196 and 95306). The participant register used in this study was established with permission from the Data Inspection Board (study code: 7252/95). All studies were conducted in accordance with the Declaration of Helsinki[7] and all participants in the studies provided informed consent before enrolling.

Aims

As noted in the preamble, the overall aim of the project was

> ”To document and analyse prerequisites of patient adherence to antihypertensive medication in routine clinical practice” [1]

The *specific* aims of the papers in this thesis were:

Paper 1. To explore the structure and content of a follow-up appointment for hypertension and the decision-making that takes place in it.

Paper 2. To investigate hypertensive patients’ reasons for (not) adhering to medical advice about taking antihypertensive drugs.

Paper 3. To test the hypothesis that patients who report side effects believe they have a lower future risk of complications to hypertension, than do patients without side effects.

Paper 4. To describe how patients and physicians determine if a symptom is a side effect, and if it will affect treatment.

Paper 5. To describe how patients and physicians settle if the blood pressure is well controlled, or if it should lead to a change in therapy.

Study participants

Questionnaires

The objective here was to obtain a representative sample of all Swedish patients with high blood pressure who were in contact with health care because of their hypertension. The method was first tried out in a pilot study of 92 patients and their 29 physicians. As this led to modifications of the questionnaire, the data collected in the pilot study was not included

7 The version of the Declaration in use at the time of data collection was the one amended by the 41st World Medical Assembly, in 1989.

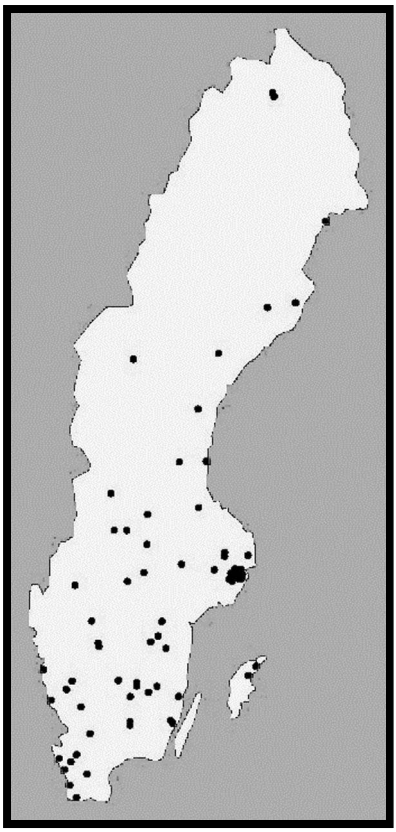

Figure 3: The distribution of sites participating in the questionnaire study.

in the final material.

In order to get a geographically representative sample, it was decided that 20% of the clinics should be in the north of the country (Norrland), 40% in the central area (Svealand) and 40% in the south (Götaland). First, 203 primary health care centres and 47 clinics of internal medicine were picked by randomisation from the register of Swedish physicians (Läkarmatrikeln). The randomisation was performed by the company Clinical Data Care, based in Lund, Sweden. Letters were sent off to the 250 clinics, and after three written reminders and telephone calls, 55 primary health care centres and 11 internal medicine clinics agreed to participate (Figure 3). The staff at the 184 centres that did not participate cited lack of time or high work load as a cause of this.

In all, 1013 patients taking antihypertensive drugs were included. In addition, data was collected from 135 patients who did *not* take antihypertensives, and from the 212 physicians who saw the 1013+135 patients. No data from the latter two categories was used in this thesis, however. More details about recruitment of participants have been published previously [1].

Follow-up appointments

For the collection of the appointment material, clinics known to have hypertensive patients were approached – they were chosen in order to get a mix of primary (urban/rural) and tertiary (urban only) care. In all, 11 clinics were asked to participate, by way of sending letters, and five agreed to do so. The staff at the six clinics that did not participate said the reason for this was excessive work load and lack of time. In the five participating centres, suitable patients (as per the eligibility criteria) were

identified from the calling lists. These patients were sent letters describing the study, asking if they agreed to take part in it. For those who did, the consultations were recorded on standard audio cassettes. The tape-recorder was operated by the physicians, so no researcher was present during the consultations.

The aim was to obtain 50 recorded consultations. After enough material was deemed to have been obtained at one place, collection continued at the next place. In all, 67 patients were approached and 51 decent tape-recordings were obtained. Thus, data from 16 patients were lost underway: of these, 4 did not turn up for the appointment, 6 did not want to be tape-recorded, 3 did not want to participate for unknown reasons and 3 agreed to participate but the tape-recordings failed. Among these 16 patients, 7 were male and 9 female; their mean age was 61 years (range 40-91). Actually, of those 51 recordings that were included, a further 8 were incomplete to some degree: in 3 of these, only the history-taking phase had been recorded, in 4 the last part of the discussion phase was missing (participants went to another room to finish the consultations and did not bring the tape-recorder) and in 1 the opening and closing phrases were missing. The mean length of these eight incomplete consultations was 10 minutes (range 6-15), as compared with 14 minutes (range 4-50) for the entire material.

The clinics that participated were: two primary health care centres in a city, where the methodology was first tried out (number of patients=5); a rural primary health care centre (n=16), an urban private practice (n=15) and a hypertension unit in a university hospital (n=15). All these centres were located in the South of Sweden and provided care for the general population.

Interviews

The patient interviews were performed directly after the follow-up appointments, by KIK, who presented herself as a nurse doing research. The interviews were also audio-recorded on standard cassettes. The aim was to obtain 30 interviews. Forty-four patients were asked to participate and 33 agreed to do so; reasons for not wanting to take part overlapped with those mentioned above. Sixteen of the 33 patients were recruited from the rural primary health care centre and 17 from the university hospital's hypertension unit[8].

8 The reason we got 17 interviews but only 15 appointments from this site was that the tape-recordings failed in two appointments.

Questionnaire content

The questionnaire we used was based on a five-page instrument developed by Os et al. to investigate symptoms and side effects among patients treated with different antihypertensive drugs [59]. This questionnaire was modified by adapting some of its questions about side effects and symptoms, and the resulting version was validated prior to use [1, 31].

Three sections of the questionnaire were used for paper 3: demographics/medical background data, an open question about side effects and in all 12 questions about estimated risks of future complications. Data on demographics and treatment were filled in by nursing staff at the clinics, by referring to the case notes and asking the patients. Data on risk factors were completed by the patients' physicians. Patients were asked the following question about side effects: ”Does your present medication for high blood pressure cause you any inconvenience? (Yes/No)”, followed by a request to specify the inconvenience in case of a positive reply.

Information about estimated risk was collected using visual analogue scales (Figure 4). The wording[9] shown in the figure was for the question concerning risk *with* antihypertensive medication: the ”risk *without* medication” question was identical, save the substitution of the word ”without” for the word ”with”. The score on each scale was obtained by measuring the distance (in mm, scales were 100 mm long) from the left end of the scale to the patient's mark. This was done at entry of the data into a database, using a digitiser.

9 Two questions in the Swedish original contained clarifications not shown in Figure 4: ”Further increase *(worsening)* in blood pressure”, and ”Stroke *(bleeding in the brain, clot in the brain)*”.

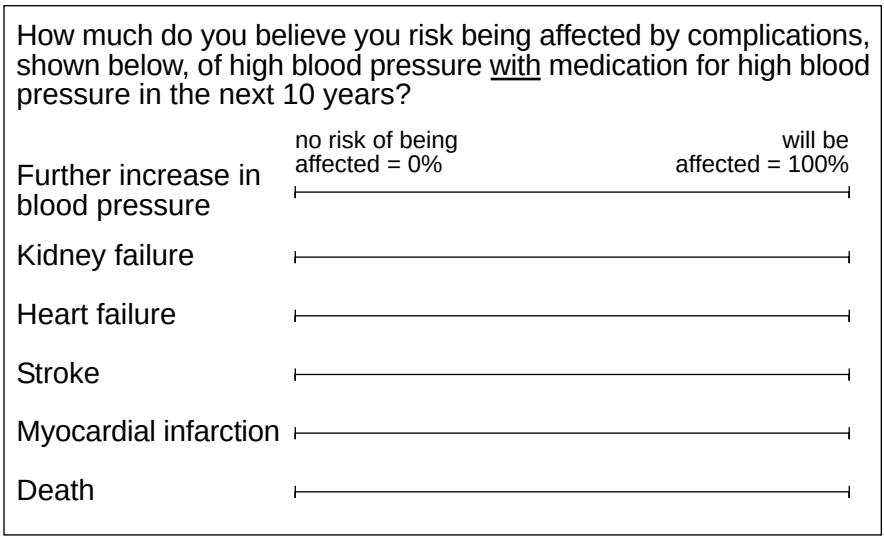

Figure 4: Questions about estimated 10-year risk, to be filled in by patients.

In order to make sure that patients understood the use of visual analogue scales, the clinic nurses demonstrated how to answer a sample question that was not related to the study topic, and observed the patients doing so. We have no data on how many patients were excluded because of inability to follow these instructions, but the general impression, elicited by a question in plenum at a study meeting with about 50 study nurses present, was that nearly all patients understood the use of visual analogue scales.

Interview content

An interview guide was used – it contained the following topics to be covered:

Knowledge about or opinion of the follow-up appointment (7 questions); of high blood pressure (21 questions); of the antihypertensive drug (15 questions); of experience of treatment (6 questions). Questions were also asked about patients' education about cardiovascular disease and medication (8 questions) and background data (6 questions).

All questions were asked in an open-ended form, to allow the patients to express their opinions. The first drug-related questions were: ”What sort of medicine are you on?”, ”Why was your medication started?” and

”What do you know about the effects of your medicine: how does it affect the blood pressure and the symptoms?”. The interviews were semi-structured: on the basis of patients’ answers, more detailed follow-up questions were asked to clarify their meaning, and the order of questions was allowed to vary in response to the natural progression of the conversation. The questions aimed at medication adherence were: ”Have you thought about changing your medication yourself?” and ”Have you sometimes thought about not taking the tablets?”, but information relevant to this topic also turned up in response to other questions.

Transcription

The tape-recordings of interviews and consultations were the source material of papers 1, 2, 4 and 5. The analyses were based both on these tapes and on transcripts (word-to-word printouts) of them. The tapes were first listened to, and then the bulk of analysis was made using the transcripts. Some tapes were then returned to, in order to check if impressions gained from transcripts were reasonable.

Two different kinds of transcripts existed: one ”basic” that encompassed the entire dataset of appointments and interviews, and another that concerned only a few chosen stretches (”excerpts”) from the appointments. The first kind was typed by ESC, a professional secretary. The second kind, done by myself, was of the type shown in Excerpt 1 (page 37), which differs from the first in that it contains more details about pauses, overlapping talk and hesitations, i.e. things that are not usually written in text. This additional information was displayed according to the transcription conventions suggested by Linell [60] (Figure 5).

The basis for using this more complicated style of transcription was the assumption that things like pauses do not occur at random; that they may, on the contrary, convey important information [61]. Re-transcribing involved listening carefully to the same parts over and over again, and in this process, in addition to overlaps and such, some words were detected that had not been included in the basic transcripts[10].

10 In one case the credit for having said something also changed from a patient to a physician. It was obvious that there was a wealth of information that had got lost in the transit from audiotape to text. Re-transcribing *all* consultations in this manner was not an option, however, as it was very time-consuming (especially when people mumbled or spoke at the same time). The problem with loss of information is, in any case, something one has to live with – for example, the choice to work with *audio*tapes instead of *video*tapes reduced the available information by magnitudes. Also,

UPPERCASE	word spoken louder and/or with emphatic stress
she said [that	overlapping talk starting at [
[right	
(xxx)	undecipherable talk
=well but	no pause between turns
...	pause (less than a second)
(.)	micropause (less than a ¼ second)
(2.0)	timed pause (here: 2.0 seconds)
ye:s	lengthening of a sound
tra-	speaker interrupts herself in word
in case--	speaker leaves utterance incomplete
°now°	speech in low volume (”sotto voce”)
here	laughter in speaker’s voice
((phone rings))	comments

Figure 5: Transcription conventions, after Linell.
See footnote 11 (page 27) for definition of a “turn”.

The translation of selected parts of the appointments and interviews into English was done in a way that was fairly faithful to the original wording. For example, the Swedish *man* was often translated as ”one”.

Laboratory analyses

Patients in paper 3 (based on the interviews) who took atenolol, amlodipine or ACE-inhibitors (captopril, enalapril or lisinopril) were asked for blood samples to measure drug concentrations. Samples were obtained from 23 patients: 8 took atenolol, 9 amlodipine, 5 ACE-inhibitors, and 1 atenolol as well as an ACE-inhibitor. The analyses were made using methods that were standard at the time, at the departments of clinical pharmacology and clinical chemistry at Linköping university hospital, Sweden.

The point of measuring these blood levels was to get a more objective idea about the extent to which the participants actually took their drugs. There were, however, no established levels that indicated ”adherence”, so we considered all those who had detectable concentrations of amlodipine or atenolol as being ”adherent”. For the ACE-inhibitors, what

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...the focus on the consultations themselves implied a heavy restriction on what got measured: presumably a lot of highly relevant information was to be found in the small-talk that took place in the staff room after the consultations, or at dinner the same evening in patients’ homes. In a way, the research process as I have experienced it has meant taking an already heavily restricted material and cutting down the complexity of it to almost zero by, short-sightedly, gazing exclusively at one or a few aspects of it at a time.

was measured was not actually the drug concentration, but rather the activity of the angiotensin-converting enzyme. This gets inhibited when patients take the drugs, and we had knowledge of average concentrations and variability among people *not* taking ACE-inhibitors [62]. We decided to consider all those who had ACE activity of less than one standard deviation below the untreated population mean as being ”adherent”. We did not have any proof of this being a practically valid cutoff, however.

Statistical considerations

Appointments and interviews

We used the program SPSS, versions 9.0 to 11.5 (SPSS, Chicago, IL, USA) for statistical analyses. The methods employed in the analyses of follow-up appointments and interviews were quite basic. For comparisons of how much patients and physicians spoke, non-parametric univariate tests were used (the Mann-Whitney test and Wilcoxon’s matched-pair signed rank test). The variables here were the number of words spoken, the number of words per turn[11] and the number of new topics introduced. Word counts were done manually, as automatic counts would have included row numbers and other non-words[12].

There was, however, one intricate issue in the analysis of the appointments that was related to statistics. One of the basic assumptions here was that what was said emerged in dialogue, i.e. that people’s utterances could not be considered in isolation of their context. The basic unit of analysis was therefore patient-physician *pairs*, rather than patients and physicians taken on their own. Consequently, in displaying the results, it would be inappropriate to present things spoken by ”patients” or ”physicians” as groups. We did not stick to this principle when showing lists of categories, however, as we could not think of a good way of incorporating duality in such lists.

Questionnaires

The statistics used for the questionnaire material were a bit more complex. We knew from a previous analysis [31] that 26% of patients reported side effects and that this was associated with a number of other factors. The objective of the present analysis was to investigate a

11 A ”turn” is a continuous period when one speaker holds the floor [60].
12 Counting words – a very menial task – was one of my jobs when I first got involved in this project.

hypothesis about there being a link between having side effects and believing one's drug was powerful. The measure we used for "powerful drug" was patients' risk estimates, and in order to see if these were *independently* associated with having side effects, a multivariate method – a regression model – had to be used [63]. We used logistic regression, as this is suited for a binary dependent variable such as a "No" or "Yes" reply to the side effect question [64]. The 10-year risk measures were also entered as binaries – above (1) or below (0) the median for the entire population, but as independent variables. This procedure was chosen because the visual analogue scales yield ordinal data – for this reason it would not have made sense to enter the actual distances in mm [65].

Power

Whenever statistical tests are used, it is important to calculate the power, which reflects the likelihood that a true difference between two (or more) groups is detected as being statistically significant [66]. A power calculation had been made for the questionnaire data, but this was based on another hypothesis and another main outcome variable than that in paper 3, and was therefore not relevant for it [31]. Thus, the power was not known[13].

The question of "power" for the qualitative analyses was another issue. The point of doing the qualitative studies was not to obtain statistically significant differences [67], but rather to generate descriptions that could lead to insights into what was going on in the consultations, and to be able to say something relevant about patient's views of their condition and its treatment. Nevertheless, it had to be decided what number of appointments would be recorded, and how many interviews were to be performed. This was, in practice, more a matter of deciding on a number that seemed reasonable, a matter that was in turn informed by what other researchers in the field had done. It was thus defined on beforehand that about 50 appointments and 30 interviews would suffice, and during the course of collection of the data, the first impressions gained of the material indicated that this would be enough.

13 But, as the result of our analysis turned out to be statistically significant, worries about "clinically important but non-significant" findings were not so relevant.

Analysis of things spoken

Coding and categorising

The main approach for analysing the data from interviews (paper 2) and appointments (papers 1, 4 & 5) was qualitative. In the interviews we looked mostly at what patients said in response to the questions, whereas in the appointments, in addition to the face value of what the participants said, we also focussed on the interplay that took place between them.

The basic methodology was one of searching for ”patterns”, ”themes” or ”tendencies” in the data, which could be helpful for illuminating the topic of medication adherence. But with something as complex as human interaction there are infinite patterns to look for, and a large part of the process therefore consisted in trying out different ways of viewing the data and deciding on which of these ways seemed most useful. In the course of this, many provisional ”aims” of the studies were dropped[14]. At least for papers 4 and 5, therefore, the ”specific aims” listed earlier were arrived at while working on the analysis[15].

Discourse analysis

In papers 4 and 5, it was stated that the method used was ”broadly discourse analytical”. The vagueness of this statement has to do with the fact that I do not know enough of the method of discourse analysis to proclaim myself a follower of it. It is concerned, however, with the processes of interpretation by which people negotiate meaning [69], or ”the production of versions of the world through discourse” [70]. It therefore deals with ”talk in social practice” – the way people perform tasks, such as defining what is going on and what the ”facts” at hand mean, through speaking with each other [70]. Since the meaning of what is said is defined by its context [71], the context itself is of fundamental concern in discourse analysis.

An example of the process

The above description probably does not go very far in way of an explanation of what actually took place. So, here is an attempt to describe the process of analysis as it was, roughly, in papers 4 and 5.

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14 One early ”aim” was, for example, to look at the four gender dyads (female physician/female patient, etc) to see if there were any differences in how the people in them communicated. But what I came up with seemed like a bad sequel to ”Men are from Mars, women are from Venus” [68], so I left it.

15 Similarly, in paper 3, the hypothesis was post-hoc.

To begin with, I had some, more or less vague, idea about what to write about, for example ”speaking about risk”. After reading up on this and writing an introduction, I read through the 51 transcripts, marking up passages which seemed relevant and making notes of them. Marking up essentially meant labelling stretches of text with a heading (called a ”node”), for example ”risk talk”. This was done using the computer programme NVivo[16] version 1.2.

Very often, while working like this, new observations were made and new ideas emerged. For example, the observation that physicians, when talking about risk, often expressed themselves in terms of uncertainty and used diminutives such as ”this is *a bit* outside my field” instead of just ”this is outside my field”. This observation could then spin off two new nodes, called ”diminutives” and ”use of uncertainty”. Further, provisional nodes that seemed pointless or too vague were killed or re-defined, as situations came up that prompted this. By way of example, finding a patient who spoke about an upcoming rectal prolapse operation would bring up the issue of what kinds of ”risk” were to be investigated, and this could prompt the splitting of the ”risk talk” node into the nodes ”cardiovascular risk talk” and ”other risk talk”.

Also, in the process of coding the material, it often became obvious that I knew too little about certain subjects. I then had to go back and look for literature to cover up on these gaps. On returning, I usually had to start coding anew, both because I then looked at the material in a different way, and also because I had forgotten the exact way of coding in the meantime. A similar phenomenon was sometimes evident when I got to the last appointment and had a look at the one I started with – often the coding had got more inclusive or mutated towards the end. In order to fix this, re-coding until things were felt to be standardised was necessary, and the co-author(s) also had to go through the material and judge if they felt my findings were reasonable.

Eventually, this way of working yielded a number of categories and themes felt to be relevant. It was then a matter of describing these and choosing excerpts of the consultations that could be used to illustrate the themes to readers[17].

16 Although I eventually stopped using it because it was so slow and unstable. The nodes themselves were not all that useful anyway: it was rather the process of assembling them that mattered.

17 Doing this was not without its problems. Candidate excerpts had been collected in an electronic paste-book, but picking out which ones to show was difficult. Long-winded excerpts were not possible due to space limitations, and for the same reason, it was desirable that the same excerpt could be used for showing multiple things of interest. And,

...even though context was very important, it should preferably be possible to read them without too much background information. Further, although qualitative research is not about achieving an ”on average” view of populations [67], it was preferable that the excerpts were reasonably varied as to demographics – including only excerpts with women and specialists in geriatrics would, for example, have looked odd. Further, I did not want to pick out the ”worst” examples I could find – worst, that is, in the sense of how people appeared to behave, as I felt this would be unfair to the participants and perhaps fuel readers’ prejudice about doctors or patients (depending on what prejudice they had in the first place). Everybody says silly things from time to time, and it is very easy to make someone seem stupid or disagreeable when a few lines of speech are cut out, typed down with all kinds of details and put under scrutiny. To go on, after some excerpts had been chosen while trying to keep the above in mind, another problem emerged: they started having a life of their own. Inevitably, when re-transcribing an excerpt, writing about it and generally looking hard at it in order to remember why it was chosen, it tended to become more and more the archetype of what it was supposed to exemplify. This was especially evident after returning to do analysis after absences for regular work. On doing so, it was particularly difficult not to look at the excerpts as definitions of the patterns they were meant to illustrate. One way of avoiding this trap was by going back to the candidate excerpts that were *not* chosen.

Results

Baseline characteristics

The baseline characteristics of patients were similar between the questionnaires, the appointments and the interviews (Table).

	Questionnaires	Appointments	Interviews
Number of participants	1 013	51	33
Age (years)	62 (19-87)	58 (34-83)	58 (35-83)
Male:female ratio	448:565 (44:56)	26:25 (51:49)	18:15 (55:45)
Years since hypertension diagnosis	12 (0-61)	10 (1-34)	10 (1-30)
Number of anti-hypertensive drugs*	1.6 (1-4)	1.5 (0-4)	1.6 (0-4)
Systolic blood pressure (mmHg)†	155 (104-235)	155 (110-210)	153 (120-200)
Diastolic blood pressure (mmHg)‡	88 (50-140)	91 (70-110)	90 (70-111)

Table: Characteristics of patients in the three datasets.
Values are mean (range) except male:female ratio, which is n (%).
* By definition, the participants in the questionnaire population were prescribed at least one antihypertensive drug.
† Valid n=978 (97%) for questionnaire data.
‡ Valid n=980 (97%) for questionnaire data.

Questionnaires

As noted previously, 26% of all patients answered ”Yes” to the question about having side effects of antihypertensives. Nine patients did not answer ”Yes” nor ”No” to this question, and were excluded from further analysis. The systolic blood pressure values were similar between the ”Yes” and ”No” groups: 155 (SD 21.3) vs. 155 (SD 19.4) mmHg, but the diastolic blood pressures were somewhat lower in the ”Yes” group: 87 (SD 9.5) vs. 90 (SD 9.3) mmHg.

As regards the visual analogue scales, 182 patients did not respond to all 12 questions about future risk with and without antihypertensive medication. The ”Death with medication” question was the one most often skipped: this happened in 93 (9.3%) cases.

All six measures of estimated 10-year risk *with* medication were highly intercorrelated – that is to say: they showed similar patterns of

distribution. The values were highly skewed: overall, patients put their marks a lot nearer the ”no risk” side of the scales – the medians were 10-16 mm from this extreme (Figure 6: empty bars).

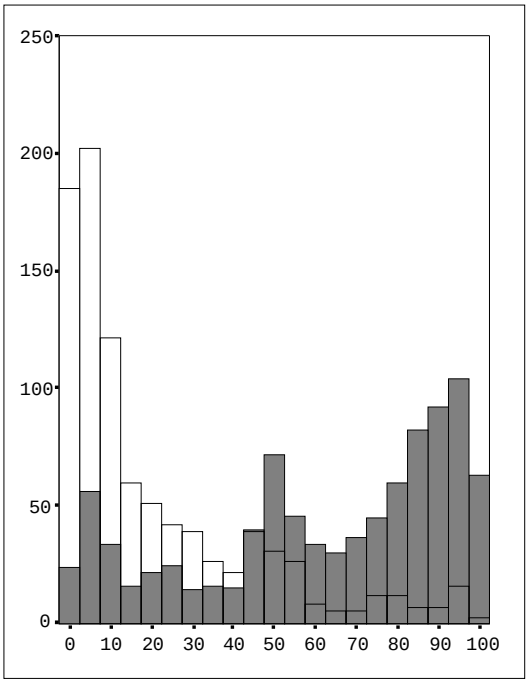

Figure 6: Patients’ estimates of 10-year risk of death *with* medication (empty bars) and *without* medication (grey bars). X-axis: distance from left end of visual analogue scale (mm). This end was marked “no risk of being affected = 0%”. Y-axis: number of cases.

As for the six estimates of 10-year risk *without* medication, they were somewhat like mirror images of the ”with medication” scores – only less skewed, and this time towards the ”will be affected” side of the scales (Figure 6: grey bars). These estimates were also very much alike each other, with the exception of ”kidney failure” – the medians were 68-78 mm away from the ”no risk” end for the five other measures, but for the kidney risk this distance was 53 mm.

The hypothesis

Patients who reported side effects differed by a few mm in their risk estimates from those who did not. This was only seen for the estimates

of risk *with* medication, however. Also, it differed in the opposite direction of what we had hypothesised: i.e. those who reported side effects also scored *higher* on estimated risk. The differences were not dramatic but enough to yield statistical significance in univariate tests.

When we entered all the ”risk with medication” estimates into the logistic regression model, we got a similar result: one of the risks – the one for stroke – came out as statistically significant, in addition to the factors already known. The odds ratio was 1.76 (95% CI; 1.26-2.45).

We had entered the risk scores in a binary format where marking above the median was = 1 and below the median was = 0, so the standard interpretation of this odds ratio was that ”A patient who scored above the median had a 1.76 times higher risk of also reporting a side effect”. As pointed out in the methods section, however, we were not looking for a cause-and-effect relationship so this odds ratio was taken merely as a sign of an association. No similar association was found when the scores for risks without medication were tried out in a separate logistic regression.

Implications

What would be the implication of this finding? Why did those who reported side effects also give higher estimates of risks with medication? Well, perhaps it was an indication that patients weighed the perceived benefits of treatment against its disadvantages, so that those who thought they had a higher risk were prepared to put up with more side effects, as suggested by Benson & Britten [34]. We suggested a few other explanations in the discussion section of paper 3, but it was very hard to say anything about it without knowing more about the contexts in which the patients placed our questions. I will therefore not hypothesise further about this here; suffice it to say that the differences in risk estimates between those with and those without side effects were, in any case, not very dramatic.

Follow-up appointments

Papers 1, 4 and 5 were based on the tape-recorded follow-up appointments, and the results of these three papers are here presented in a collated format.

Words, turns and topics

Physicians spoke more than patients (1176 vs. 903 words on average) and initiated more new topics (9 vs. 3). In order to qualify as ”new”, a

topic had to be about something that was not a continuation of that spoken about previously. Many of the topics brought up by patients were unrelated to hypertension – common ”other” topics were those of joint pains and drugs other than antihypertensives. These topics did not, however, lead to much deliberation. Similarly, when physicians asked about risk factors other than hypertension, this tended not to generate a lot of discussion.

When asking about the antihypertensive drugs, effects and side effects were the issues most commonly brought up by patients. Side effects were mostly spoken about in terms of ”inconveniences” or by referring to the specific symptoms, rather than by using the expression ”side effects”. This expression, or rather its equivalent in Swedish, i.e. the word stem *biverk**, was uttered altogether 20 times, in 15 (29%) of the 51 appointments.

Decision-making – preliminary findings

We had touched upon the topic of decision-making in a previous study [72], where we attempted to describe ”communicative strategies used by physicians to motivate the patient to take the antihypertensive drugs”. Here, we highlighted that physicians would, as a first step, simply claim that the drug was good and useful. When the need arose, such as when patients came over as reluctant to accept advice, this baseline method could be elaborated by referring to physiological or pharmacological explanatory models. Another method used by physicians was to de-emphasise side effects. These findings were intriguing, but the topic was clearly not exhausted. In paper 1, the general impression about decision-making was that it was in the hands of the physicians, and that the two major determinants for decisions about therapy were the blood pressure and any side effects. The subject was then looked into more closely in papers 4 and 5, with emphasis on these two factors.

Structure and content of the follow-up appointment

The consultations followed a pattern that was roughly similar both between different patients and different physicians. Apart from the close similarities in the overall division of consultations into phases of opening, history-taking, physical examination, discussion and closure, there were also obvious parallels in how these individual phases were enacted. Physicians’ opening questions were similar, as were their ways of asking about symptoms, medication adherence, and side effects. Seemingly, physicians used ”mental checklists” of things that had to be covered. In

general, physicians' questions were more open-ended at the beginning of the consultations, and became progressively more closed towards the end.

An excerpt (Excerpt 1, a longer version of that used in paper 5) will be used to illustrate some aspects. This excerpt was taken from a follow-up appointment between a 43-year old male patient (”P”) who had hypertension since three years and who took atenolol and amlodipine, and a 42-year old male GP (”D”). The patient's blood pressure was 130/85 mmHg. The excerpt is from the beginning of the tape-recording. The consultation it occurred in was in all eight minutes long, excluding a break when the physician left to print out prescription sheets.

In this excerpt, the physician made some preliminary remarks (lines 01, 04) and then asked an open-ended question about the medications (line 06). The patient then took the opportunity to develop this into a topic, by remarking that he had doubts about taking two drugs (lines 07-14). Although patients generally spoke more in the beginning of the consultations and less towards the end, many also gave very brief responses to physicians' initial questions, particularly when these were of the ”ticking things off a list” type (the ”comprehensive history-taking” mentioned earlier [57]). In Excerpt 1, however, the patient was obviously very eager to bring up his point and the physician did not really get the opportunity to go on with any mental checklist he might have had.

01 D: okay (.) you're here for your blood pressure checkup
02 ((flipping through papers))
03 P: mmh
04 D: and you're on (1.5) two medications
05 P: yeh
06 D: and how do you get on with that?
07 P: (1.2) we::ll (.) it works alright it's ju- (.) the que-
08 question is just if I need them both (.) that's the
09 thing
10 D: ye:s
11 P: you keep thinking you're an that perhaps you're ...
12 that it's better than (.) that you're healthier than it
13 really is ... or healthy if you can speak about that
14 in this context
15 ((1 minute later))
16 P: e:h (.) but these ones have been alright (.) the on-
17 the only thing I think really is that I'm so BLOODY
18 tired in the evenings
19 D: ye:s
20 P: but perhaps that's part of it, I don't know
21 D: depends a bit on what you do in the daytime as
22 well [((laughs))
23 P: [he- ye:s
24 P: of course (.) but e (.) okay but I don't have a
25 physically demanding job I have a work managing
26 job yeah so-
27 D: =yes
28 P: it's ... it's a matter of the office and the car
29 D: okay
30 P: it's there I've got myself the hypertension as well
31 D: =ye:s
32 P: so:eh ... no but I think since I started with the drugs
33 I'm MORE tired in the evenings than I was before,
34 if I express myself in that way
35 D: you experience
36 P: =yes
37 D: a deterioration so to say
38 P: =yeah (.) absolutely
39 D: yeh
40 P: I believe I do, NOW it goes perhaps a bit with the
41 season we've ha- h (.) had you're usually a bit more
42 tired in the evenings in the spring and so on
43 D: mm
44 P: bu:t ... nah (.) I-one ... I think I feel a bit (.) more
45 tired maybe than- (.) and at that I'm AWFULLY
46 bad at doing (.) physical activities you see
47 D: mm

Excerpt 1, from a follow-up appointment. D: physician. P: patient.

Making sense of suspected side effects

After the patient had announced his misgivings about using two drugs (lines 07-14), they spoke for a minute (not shown) about a medicine that the patient had used previously and that had been discontinued due to side effects. The patient's statement in line 16 occurred after this and was therefore to the effect that the new drugs were better than the old one. He then added, however, with emphasis, that he was very tired in the evenings (line 16-18), thereby launching this symptom as a suspected side effect. This was followed by a statement of uncertainty (line 20), spoken in an irritable and dejected tone (as heard on the tape) that differed from his otherwise very pleasant way of speaking.

This display of discontent was taken by the physician as a call for an assessment on his part. His response was to the effect that an alternative explanation to the symptom may exist, although he did not suggest anything specific (lines 21-22). In response, the patient supplied more arguments favouring a link between the drugs and his symptom (lines 24-28) and went on to stating bluntly that there was a temporal association between the drugs and his tiredness (lines 32-34), confirmed in lines 35-38. He then, however, shifted his ground by spontaneously introducing first one alternative explanation (it being springtime: lines 40-42) and then another (lack of physical activity: lines 44-46). In the 2½ minutes that followed (not shown), they talked mostly about the patient's difficulties getting started with different kinds of physical exercise, with the physician expressing sympathy about this. Consensus thereby seemed to have developed for the "lack of exercise" explanation. This part of the appointment, in turn, ended with the physician suggesting that they measure the blood pressure. This was another typical feature of the appointments – the physicians largely controlled the transitions between different phases of the consultations.

A notable feature of the interaction in Excerpt 1 was that most of the deliberation was carried out by the patient, with the physician keeping a seemingly low profile. This was a bit unusual, as physicians tended to speak more. On the other hand, the physician's statement in lines 21-22 was crucial insofar as it clearly showed that he was not prepared to accept the patient's side effect account unquestioningly. As the physician's argument was very vague, it was open to interpretation by the patient, whose way of making sense of it was that the physician suggested that his daytime activities were too physically demanding. In all, the patient used three strategies to argue his case: stressing that the symptom was

severe, maintaining his suspicion in spite of the physician's opposition and pointing out a temporal relationship.

He also, however, spontaneously introduced alternative explanations to his tiredness, thereby arguing against his own hypothesis. Lines 44-46 marked a change in his reasoning: here, he seemed to hestitate about what he had previously said and decide to go for the "lack of exercise" explanation to his symptoms.

What made the patient change his line of reasoning like this? Did it mark a genuine shift in his beliefs or was it something he did for the sake of keeping on good terms with the physician? This we cannot know, but it was clear that he contributed actively to the re-interpretation of his problem in a way that shifted the "blame" for it from the drug he was taking to his own life-style, i.e. to himself[18].

Making sense of blood pressure values

The consultations could thus be looked upon as places for a struggle between different ways of looking at things – in this case between evening tiredness as an effect of a drug, or alternatively, as an effect of the season or of a sedentary life-style. In paper 5 we argued that the same was true for interpretations of the measured blood pressure values, in that participants used different ways of contextualising "high" (or, more rarely, "low") readings. There were both similarities and differences between side effects and blood pressures in this regard. Patients and physicians were generally more in agreement about the blood pressure – overall, both tended to look upon blood pressure values a bit above the reference values of 140/90 mmHg as not being a cause of concern. For side effects, the situation was more commonly one of having different standpoints, with the patient defending the side effect and the physician arguing against it – at least, this was the case when it was the patient who had first suggested a side effect, which happened in 14 consultations. The blood pressure was therefore more of a "common enemy" than were side effects.

Further, in the case of the blood pressure levels, they could easily be compared with *other* values – something that was not always possible with side effects. We found that the main mode of comparison was between the patients' actual (or most recent) measurements and their own, previous values, rather than the reference values. The notion of

18 This impression was supported by the patient speaking of himself, in the talk that followed (not shown), as being "lazy".

”normality” used here was therefore mostly a relative one, not an absolute [17]. At the same time, it was apparent that blood pressures that diverged from the reference values triggered more deliberation. We also found that the systolic blood pressures were higher in those consultations where physicians did not openly state their treatment preferences before the prescription took place.

Upgrading and downgrading

We found that the concepts ”upgrading” and ”downgrading” were useful for describing the sense-making that went on in the consultations. In paper 4, we used the related terms ”foregrounding” and ”backgrounding”. By this, we meant discursively ”moving” a given observation, such as a blood pressure value or an account of a suspected side effect, in and out of different contexts in order to make it seem more or less a reason for changing the therapy. In the case of blood pressure values, participants could put emphasis on, or de-emphasise, the degree of similarity between the measured value and the patient’s (hypothetical) ”usual” value – the up- and downgrading of representativity. The main way of contextualising a value to achieve this was in terms of ”stress” or ”lack of rest before measurement”. Another way of discursively treating the blood pressure, was by arguing that the blood pressure was, or was not, serious enough to be a cause for alarm. This we called up- and downgrading of severity (Figure 7).

For side effects, there was no ”value” to treat discursively. Rather, the tactic here was to emphasise or downplay the probability that the symptom was caused by the drug, or to do the same with the severity of the symptom: up- and downgrading of causality and severity (Figure 8). Here, it was notable that severity was mostly the domain of the patients, whereas physicians tended to focus more on causality.

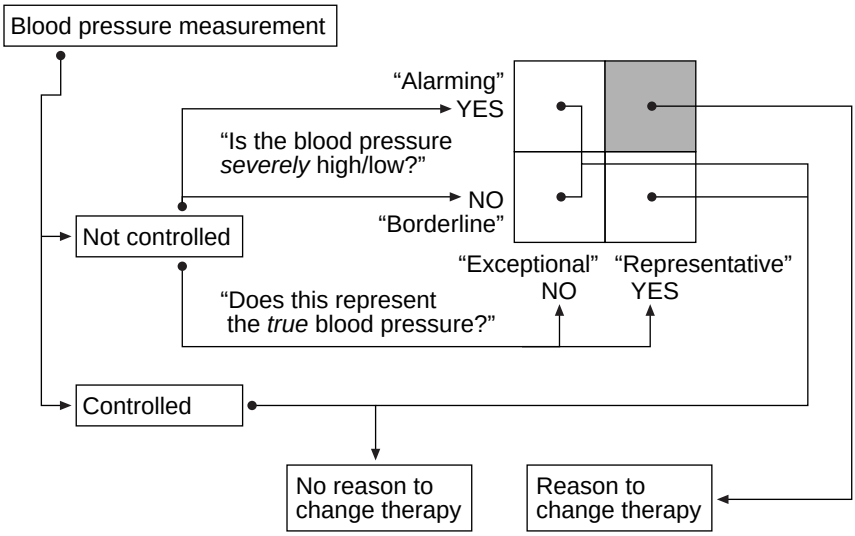

Figure 7: Suggested scheme for the assessment of a measured blood pressure value. When the blood pressure, taken at face value, seems to be "Not controlled", it is subjected to further interpretation in terms of *severity* and *representativity*. Here, discursive up- and downgrading may take place, shifting the judgement in the direction of "more/less severe" and "more/less representative". The end result of this process is the qualification of the blood pressure as being a cause for changing the drug treatment (Yes/Yes: grey square) or not (any No: white squares).

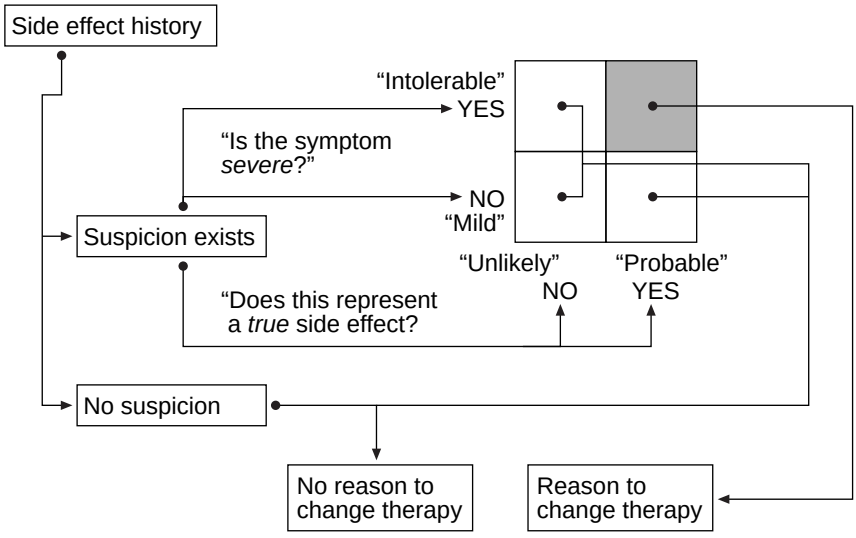

Figure 8: A suggested scheme for the assessment of a suspected side effect, in analogy with Figure 7.

One thing that became evident, finally, was that the blood pressure and side effects were not evaluated in isolation of each other. Rather, these determinants of treatment choices were considered in parallel. For example, an assessment of the blood pressure that favoured maintaining the treatment unchanged[19] could be invoked as a reason not to let a suspected side effect influence the treatment.

Interviews

While the aim of paper 2 was to investigate hypertensive patients' reasons for (not) adhering to medical advice about taking antihypertensive drugs, we did not actually ask the patients "What are your reasons for taking or not taking the tablets?". Rather, this was inferred from patients' responses to questions related to this. On the other hand, we did not attempt to "read beyond" what patients said in the interviews. Excerpt 2 illustrates this. The patient ("P") was a 54-year-old man who had hypertension since five years, he was taking atenolol and had a clinic blood pressure of 150/90 mmHg. "I" is for the interviewer. The translation was made directly from the basic transcript.

01	I:	Have you ever felt that you should change the
02		medication on your own, in any way?
03	P:	No! (No.)
04	I:	Have you sometimes thought about not taking the
05		tablets?
06	P:	No! Absolutely never. I haven't ever done that,
07		actually.
08	I:	And do you usually remember to take them?
09	P:	Yes.
10		((one question later))
11	I:	What do you think would happen if you did not
12		take these tablets?
13	P:	Well, I suppose eventually one would get a stroke
14		or a heart infarction (Hmm.).
15	I:	You think so?
16	P:	Yes. It's that – that which is ... I suppose that that's
17		the (Hmm.) main risk, or if there could be any other
18		diseases but I'm not aware of that. (No.)

Excerpt 2, from an interview. I: interviewer. P: patient.

19 This was the outcome in 33 (65%) consultations.

Reasons for adherence and non-adherence

As seen, this patient did not admit to having any thoughts about modifying the drug regimen he had been prescribed. In all, 19 (58%) patients were, like this patient, labelled ”adherent”. Eleven (58%) of these 19 patients cited ”trust in the physician” as a reason for sticking to the advice of the same physicians. But although it was a fair guess that the patient in Excerpt 2 trusted his physician to make all the decisions about drug treatment, he did not explicitly mention ”trust in physician” as a reason for staying on the drugs at any stage in the interview. Therefore, his reason for being adherent was marked as ”wanting to avoid myocardial infarction and stroke”. Twelve accounts of the ”avoiding complications” reason were given, and 9 (47%) patients expressed a desire to ”control the blood pressure”. Finally, some patients took their drugs to avoid having symptoms of hypertension.

Among the 33 patients, 14 (42%) patients reported *not* following recommendations. The definition of being ”non-adherent” that we used was very inclusive: if the patients described any significant current or previous behaviour of this sort, they were considered non-adherent. The figure of 19 (58%) adherent and 14 (42%) non-adherent patients did, therefore, not refer to the present state of affairs. Also, as has been pointed out by other researchers, patients commonly express both reservations *against* and reasons *for* taking antihypertensives [34]. Our dichotomisation of patients into categories having reasons either ”for” or ”against” was therefore, in hindsight, oversimplified.

In looking at patients’ reasons, anyway, we found that those who reported non-adherence had more elaborate underpinnings to their decisions than did the adherent patients, who appeared more vague about why they behaved as they did. The most commonly stated reason for non-adherence was the presence of side effects (7 of 14 (50%)). The negative of this reason, i.e. ”not having any inconveniences” was, also, referred to by 4 of the 19 adherent patients as a reason for sticking to the advice. As for the non-adherent patients, their second most common explanation (4 (29%)) was a general feeling about there being something unnatural or unsavory about (Western) drugs[20].

20 This finding had also been made in other settings, although, as pointed out by Pound et al., we had not read those publications when paper 2 was written [73].

Laboratory analyses

The idea of doing the laboratory analyses was, initially, to compare the results of these with what the patients had said. It turned out, however, that almost all (20 out of 23) of those who had blood samples taken were classified as ”adherent”. Also, as the definition of ”adherent by self-report” did not necessarily concern the here and now, the comparison ended up being less relevant.

Interview data in relation to appointment data

In the studies in this thesis, we did not make use of the possibility of looking at individual patients using *both* the interviews and the consultations. An attempt to do so had been made earlier, however [72]. Here is perhaps a good place for another try. Thus, returning to the patient from Excerpt 1, he had the following exchange with the interviewer (Excerpt 3).

I: Was there anything new that you had to decide about in today's consultation?
P: No, there wasn't, because it's no more than a couple of months since I was last here, really. (No.) And the medication I'm on now has been the same for more than a year, so nothing has been changed. We decided today, I asked: Do I really have to take two drugs (Hmm.) but the doctor thought I should go on – at least for another year with two drugs, as it works fine. (Hmm.) Today, the values are really good. (Hmhm.)

((one question later))

I: Are you happy about the decision to continue with both your drugs?
P: I'll have to accept it. (Hm.) I have to trust my doctor. (Hmhm.)
I: Do you think you'll be able to follow that decision, then?
P: Yes. I think so. I do.

((29 questions later))

I: Have you ever thought about changing your medications all by yourself?
P: Well, I don't know if I'd want to say that. But on the other hand, I suppose now perhaps I question, as I do think that – now the pressure is fine, so shall I really go on taking this much – taking two kinds, is that necessary? And – but that's what the doctor here felt I should do, at least for another year or so. Before we do the next examination. (Hm hm.)

((three questions later))

I: And why were you supposed to go on [with the medication]?
P: Well – I didn't really get any motivation, he kept
I: that to himself, I suppose but – I have to trust him.
P: (Hmhm.)

((12 questions later))

I: And why would you like to stop the medication?
P: (laughing) Well, well, well you know, all kinds of drug intake is – well, I'm sort of a bit sceptical about it, I mean at the end of the day it's nothing the body really needs, you know (No.) so the less medicines you take I think you basically feel better you see (Hm.) that's what I think.

Excerpt 3, from an interview with the same patient as in excerpt 1.
I: interviewer. P: patient/interviewee.

Here, the patient summarised the events in the consultation and highlighted what seemed to be his basic dilemma: he did not like to take drugs, he had a cause for thinking that he took one pill too many, but the recommendation of the physician was to go on taking two tablets. It appeared that the reason this patient had for being (self-reportedly) adherent rested almost exclusively on his trust in the physician. As regards the suspected side effect of being tired in the evenings, the patient was ambivalent about it: at one stage in the interview he asserted that there was no problem at all with the drugs, while in another part he mentioned that he brought this symptom up as a suspected side effect in the consultation (data not shown). At any rate, he did not elaborate on it in the interview, so it seemed that the consultation had the effect of bringing the topic to the background. In the last part of Excerpt 3 (lines 38-44), the patient described, laughingly, his general dislike of medications. The laughter this provoked suggested a ”guilty secret” on part of the patient, or perhaps what he found amusing was the irony of being sceptical towards pharmaceuticals and still taking them every day.

Discussion

In the introduction, I portrayed medication adherence as being a very complex subject, and I described blood pressure values and suspected side effects as phenomena that are sometimes difficult to assess in the clinical situation, due to the uncertainty that surrounds them. In the results, the follow-up appointments were described as places where the participants tried out different ways of interpreting the ”facts” at hand, and where physicians had the last say in the decision-making (papers 1, 4 & 5). Further, we tested a hypothesis that was essentially about the interpretation of side effects (paper 3), and described patients as stating reasons such as ”trust in physicians” and ”experiencing side effects” for and against being adherent to treatment recommendations (paper 2).

What is to come out of all this? Well, to begin with, although physicians had the privilege of getting the last word in the interpretation of blood pressures and side effects in the consultations, the patients undoubtedly got the last word in their day-to-day life, where medication (non-) adherence actually takes place. It would therefore have been of great interest to know the degree to which interpretations made in the consultations affected patients' privately held views and their behaviour. To measure this, one would have had to somehow allocate different interpretations to different groups and then observe the groups' behaviour. We, of course, did nothing of the sort. A general objection to research such as ours is indeed that ”it makes little difference what people say: what counts is what they do”. A counter-objection is that there is quite obviously a link between saying things and doing things. As stressed by Linell,

> ”the process of verbalization involves the simultaneous shaping of expression and content” [60]

That is to say, people have often not thought about a topic until they speak about it, or at least, what they have previously thought about in a vague fashion is elaborated into something more concrete by speaking about it. In line with this argument, patients' reasons for keeping to prescribed drugs may (or may not) have been strengthened through the interaction with their physicians.

In this context, it is notable that the reasons ”trust in physicians”, ”fear of complications” and ”wanting to keep the blood pressure under control” were clearly related. Wanting to avoid complications and control the blood pressure implies having taken on board Medical Science's

statement that ”hypertension causes death and disability”. We found few, if any, indications of people radically doubting these underpinnings[21], although there were, as seen in Excerpt 3, signs of people not liking drugs in general (thus expressing ”drug resistance” [73]).

Yet, what went on in the consultations could be described as a negotiation, or a struggle between the interpretations of physicians and patients. Patients and physicians therefore appeared to have, at least partly, different agendas. This seems a bit odd, in that it was really all about two adult citizens meeting, voluntarily, with the aim of ensuring a long and healthy life for one of them. What rational basis could there be for having guilty secrets, lying, imposing one’s will upon someone else, and pretending to go along with decisions while not intending to, in a setting like that?

Adherence revisited

Well, perhaps rationality is overrated as a way of explaining people’s behaviour. At least if ”rationality” implies that we all act according to a desire for longevity [74]. This may be so for several reasons. To begin with, such a concept may not be applicable on an individual level. Evans et al. have made the remark that, from an evolutionary perspective, it may actually be counter-productive to behave in line with accurate ideas about risks and benefits. For people living in primitive circumstances, they say;

> ”No doubt pregnancy is very risky indeed under such conditions, and so it might be adaptive under those conditions to be *overconfident* about one’s chances of safely producing healthy offspring.” [75], italics as in the original

Also, the society one lives in may entertain values that make it seem, for example, unmanly to worry about one’s future death:

> ”Cowards die many times before their deaths;
> The valiant never taste of death but once.” [76]

Yet other reasons for not ”behaving rationally” may be a general resistance towards the ”medical way” as a threat to one’s autonomy:

> ”Non-compliance – irrational from a medical standpoint – may express [...] deliberate strategies by patients to affirm their autonomy, to negotiate with physicians, or to reject an attributed incapacity.” [55]

21 But follow-up appointments for hypertension would probably have been an unlikely place to find patients expressing these views, in that the act of turning up at the appointment itself signals a degree of respect for medical science.

Likewise:

> ”The ‘problem’ of ‘non-compliance’ is the failure of medicalization to extend beyond the consulting room into the spheres of everyday life where people take their medicines. Hence, the challenge to medical dominance may occur not in the public but in the private realm, in the guise of non-adherence to prescribed medication.” [54]

As seen, this critique blends into a more general denunciation of the medical establishment’s way of employing pharmaceuticals[22].

But let us, for a moment, ignore these possible explanations and look at a hypothetical case of a patient with asymptomatic hypertension who has been prescribed an antihypertensive medication which she has no trouble remembering to take, which causes her no side effects and towards which she has no practical barriers (like high cost or swallowing problems). She has been told that the medication protects her against future disability and death and she has no reason to believe that the expert who told her this and prescribed the drug would lie to her. She has no general qualms about medical science being oppressive and is not concerned about being unmanly. Let us say, to continue, that she still does not take it.

In this case, the one rational explanation of her non-adherence which springs to mind, is that she has not *really* understood what she has been told, in which case the logical thing to do is to provide her with more education. This logic has been followed by a number of researchers, but, in the words of Schroeder et al. who investigated interventions aimed at increasing adherence to antihypertensive drugs:

> ”Patient education alone seemed largely unsuccessful.” [45]

Possibly these patients, who were genuine and not hypothetical, had barriers against being adherent that were not overcome by their increased knowledge (or the education was poor), but if ”not knowing it” would be a credible explanation of non-adherence, at least some effect could have been expected. This highlights a basic paradox: how can people do things they know are bad for them? On this subject, Aristotle remarked that:

22 Of which the use of psychopharmaceuticals tends to bear the brunt; this has been described as a ”morally misguided enterprise” [77].

> ”it is a strange thing, as Socrates thought, that while knowledge is present in his mind something else should master him and drag him about like a slave. Socrates in fact contended generally against the theory, maintaining there is no such state as that of imperfect self-control, for that no one acts contrary to what is best conceiving it to be best but by reason of ignorance of what is best. With all due respect to Socrates, his account of the matter is at variance with plain facts” [78]

It is indeed, and there are many examples of this in the literature. Here is one taken from a book about the rock band Mötley Crüe. On Valentine’s day, 1986, band member Nikki Sixx almost died from an overdose of heroin. When he was about to get thrown into a garbage container and left to die by his frightened drug dealer, he was saved by the fact that he woke up momentarily to vomit on the dealer’s shoes, thus giving evidence that he was not yet dead. This near-fatality did not keep him from further behaviour of the same kind, however:

> ”Of course, I didn’t learn my lesson. No one in the band ever seemed to learn his lesson, no matter how many warnings God gave. Two nights later, I was at it again.” [79]

While the 1986 version of Nikki Sixx may have been an extreme example of someone who did not act rationally, it cannot be claimed that he was unaware of the dangers of illicit drug use. But his behaviour was immature in that he did not think about the consequences of what he did. So, not thinking about one’s future is something fundamentally childish, and trying to improve medication adherence is therefore, in a general sense, the science (or art) of training people to think about the future[23]. That is, to protect future beings from those who exist in the present.

Another area where future people have to be protected is that concerning abortion. Clearly, a bundle of cells that may develop into a human being cannot claim its own rights, and so needs someone to defend them for him/her/it[24]. But how can it be that it is at all possible to make a simile between medication adherence among adults and the issue of abortions? Why should future versions of ourselves have to be protected in the same way as a totally different person needs protection?

In response to this question, the philosopher Hazlitt[25] has proposed

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23 This highlights an interesting link between the fields of patient education and the upbringing of children.

24 Depending on creed, the time for seriously starting to consider that a bundle of cells have rights to defend may be 40 days after the conception (in Islam and Judaism), or directly after the conception (in some varieties of Christianity) [80].

25 I found out about Hazlitt in a text written by John Barresi [81]. This I found, in turn, by googling for the phrase ”empathy with future self”.

that our ”future self” is in essence no different from ”other people”, as in both cases we cannot have any immediate experience of what it is like to be them. In the words of Hazlitt:

> ”It is plain we are not interested in our general, remote welfare in the same manner, or by the same necessity that we are affected by the actual sense of pleasure, or pain.” [82]

And

> ”That which is future [and] which does not yet exist can excite no interest in itself, nor act upon the mind in any way but by means of the imagination.” [82]

Hazlitt thus argues that whereas we have real experience of the past and the present, we have no experience of what we will become in the future. In contrast with the past and present self, the future self is unknown and must therefore be the result of an act of imagination; consequently, the notion of our self extending into the future is just a convention. In this way, doing one’s future self a favour (say, by taking a prophylactic treatment) is in principle no different from doing a stranger a favour: they are both acts of altruism.

I think this goes some way towards understanding the problem of non-adherence. If the future person for whom an antihypertensive drug is taken is fundamentally just someone else, say, one of the people in the painting by Stas Shuripa on the cover of this thesis, the problem of not attending to this person’s rights is understandable in terms of her not being there to defend her rights. As is a common experience in work meetings where someone who should be there is in fact absent, those present tend to take advantage of him (for example by assigning him to tedious work). With this outlook, the reason for there having been more consensus about the blood pressure in the consultations we studied – both tended to regard it as ”not as bad as it seems” – than about side effects – where patients tended to defend their symptoms against physicians’ doubts – was quite simply that the person who had a stake in the blood pressure was not there.

But of course, it cannot be quite that easy. We could easily postulate a whole range of ”third parties” being absent or present in a patient-physician consultation. To begin with, the patient most likely feels accountable not only to her present self and (albeit less so) her future self, but also to those in her immediate surroundings – for example a husband. The physician-as-a-person-now is, in turn, also accountable to the future version of himself (which may be scorned for having undertreated

the patient, for example), and also to those who make up his professional context – the staff at his workplace, colleagues he speaks with, whoever may read the case notes he writes and, in a more overarching sense, medical science itself[26].

Validity

Validity is another word for ”truth”. The validity of a study is high if the researchers have used methods that enable them to give an accurate description of the phenomenon they have studied [70]. What were the threats to validity in our studies? On the quantitative side of things, the multiple statistical challenges to the data that took place in the questionnaire material may have yielded spurious associations [63]. Another threat to the truthfulness of our results is that the participants in the studies were fully aware of being observed, and it is well known that the knowledge of being observed may affects people’s behaviour [74]. So, for example, if the behaviour of patients and physicians in the follow-up appointments was altered by the presence of a tape-recorder, whatever we found may not have any bearing on what goes on in “real” clinical practice, which is not tape-recorded. Also, those who volunteered for the studies may not have been representative of the full population of patients and physicians. To continue, those who replied to questions in the questionnaires and interviews may have responded in a way that they thought was socially desirable, in line with a ”medical” way of viewing things [54].

While all this is possible, however, it is hard to imagine that those who ended up in the studies would have differed radically from other patients and physicians involved in hypertension care. As such a patient or physician, it is arguably very difficult to interact in a manner that is alien to one’s normal behaviour. Further, the consultations were, superficially, unremarkable in that they did not seem to differ very much from those I have experienced in my own life as a doctor. So, although there may have been discrepancies between study participants and ”usual people”, they were probably quantitative rather than qualitative.

Yet another potential source of trouble is that, for the papers in this thesis, most results were heavily dependent on the interpretation of human interaction that was made by its authors. In fact, the results *were*, to a large degree, the interpretations [67]. And, as pointed out in the methods

26 The latter categories may be seen to represent the ”institutional” side of the physician, in contrast with his ”personal” side [60].

section, the ways of approaching this kind of data are basically infinite. So, what is there to say that I did not come up with interpretations that were spurious, misleading or the result of my imagination being fuelled by drinking too much coffee? In short, that I saw things that did not exist, just like a mock turtle (Figure 9)? Well, although that is certainly (also) a possibility, there are some things that speak against this as well. Firstly, the co-authors, whose judgement would have had to become deranged too, in that case. Secondly, that we did not build interpretations on rare or single findings, but rather on recurrent patterns, in order to avoid anecdotalism [70]. Third, that I frequently had misgivings of the mock-turtle type myself, especially after returning to work with the tapes and transcripts after absences for other work or parental leave (and such absences were many and long); on these occasions I would often feel very doubtful of things I had written previously. But, in the end, the reader must judge the validity of these findings for himself or herself: if they seem unreasonable and at variance with the reader's own impressions and experiences, there is not much we can say to change it.

Figure 9: A mock turtle, by Lewis Carroll. By permission of the British Library, shelfmark Add. 46700

To go on, the subject of validity may also be applied to side effects, by posing the question "what do we truly know about them?".

Side effects revisited

Returning to the description of follow-up appointments as arenas for trying out different ways of interpreting observations, I would like to make some remarks about this in relation to pharmacovigilance, i.e. the countrywide system for reporting and evaluating suspected side effects [36]. I am, on and off, co-responsible for assessing the side effect reports that arrive at our department of Clinical Pharmacology. This task is essentially about making a judgement of causality and severity of the side effects that are reported to us by prescribers, and relaying these assessments to the Swedish Medical Product Agency. One of the recent cases was, omitting the details about drug, condition and symptom, as follows:

”Woman aged 67 years started treatment with [drug] because of [condition]. After approximately 10 days she was affected by [symptom]. The treatment was stopped and the [symptom] disappeared”.

This was all the information available in this report, which I labelled ”likely”, i.e. the level between ”certain” and ”possible” [28]. Taking away specifics about the drug and symptom, what remained was a case of a symptom appearing and disappearing after the drug was started and stopped. Evidently, what one thinks of this is very dependent on one’s preconceptions about the symptom and the drug’s propensity to cause it. For example, replacing [drug] with ”inhaled salbutamol” and [symptom] with ”tremor” yields a clear-cut case of an expected side effect. If, instead, ”oral nystatin” and ”feeling of resignation” were inserted, as an assessor I would not be inclined to label it ”likely”, due to my idea of this drug as one that does not usually cause mental side-effects (which would be confirmed by looking it up in a pharmacopoeia)[27].

So, previous knowledge and expectations exert a heavy influence on how I make my assessments[28]. But, when taking into account what I know on beforehand, various kinds of biases may sneak in, such as for example a tendency to regard emotional side-effects reported by elderly women as less ”real” than other kinds of side effects. Also, a comparably small part of what I ”know” about side effects is based on immediate experience with the drugs: most will inevitably be derived from public sources of information. But, if such ”textbook” data on side effects do not adequately represent the truth, those side effects that have not yet become ”official” will stand a smaller chance of ever becoming so[29].

The impression of the consultations we studied was that the same phenomenon applied there, in that physicians were more prone to consider established side effects as being ”true”. Also, aspects not directly related to the side effects themselves entered into the picture: as pointed out, suspected side effects were not assessed in isolation of the blood pressure values (Figure 10). The application of conceptual ”filters” to side effects is not limited to physicians; as demonstrated by Benson & Britten, patients may downgrade their notions of causality and severity of side effects in order to motivate themselves to keep taking their

27 In the original, the drug was simvastatin and the symptom genital pruritus.
28 The reasoning employed here is therefore Bayesian, in that I do not pretend *not* to know anything prior to each assessment, as is the case in classical statistical inference [83].
29 Conversely, side effects that are actually awarded official recognition will enjoy a self-sustaining feedback loop, a ”bandwagon effect”.

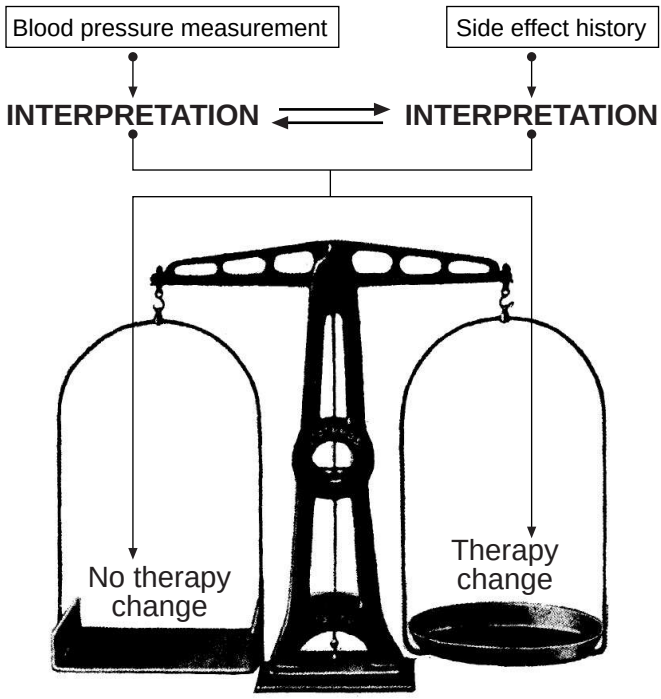

Figure 10: Blood pressure values and suspected side effects were interpreted in relation to each other, the overall assessment resulting in a treatment decision. For the sake of simplicity, other factors that may influence this decision are not shown.

antihypertensive drugs [33, 35].

While such considerations on part of physicians and patients may be pragmatic, they also imply that there must be a whole series of filters that are applied to reality: of those ”true” side effects that appear in people, only a fraction will be relayed to health care staff [84], and of these in turn, very few will ever be reported to the authorities [85]. Once at the level of the authorities, side effects will stand a decent chance of ending up in some kind of database [86], but in the process of getting there, they may also be categorised into oblivion if they do not fit the predefined labels of pharmacovigilance systems [87]. A further hurdle at this level is that the same agency will often be responsible for approving drugs for marketing as well as assessing the aftermath of their own decisions, and may therefore tend not to look into potential problems as closely as they should [87].

More generally speaking, side effects make health professionals uncomfortable. It is against the basic credo of medicine to cause them. In the second section of the Hippocratic oath[30], the physician pledges to:

> ”Prescribe regimen for the good of my patients according to my ability and my judgement and never do harm to anyone.” [88]

So, causing a side effect could easily be interpreted in terms of the physician having poor ability, poor judgement or even being malevolent. As pointed out by Illich, iatrogenicity (physician-caused disease) indirectly casts blame on the physician [89].

To summarise, due to all these filters, the “truth” about side effects is, by definition, something agreed upon. Side effects are therefore ”social constructions” [25, 90]. One approach to arriving at a more truthful idea about side effects is to bypass the filter present at the level of health professionals, by allowing patients to report side effects directly to the authorities. Fortunately, such an extension of the present systems of pharmacovigilance, most of which have so far only allowed reports from prescribers, seems to be underway in many countries [91].

30 This oath has lost a great deal of relevance in the 2500 years since its creation, but this part of it still makes a lot of sense.

The future

I will finish by some remarks about what could be done in future research. The reader may have noted that I have, so far, avoided the topic of home and ambulatory (24 hour) blood pressure measurements. These methods of obtaining blood pressure values have developed over the last 40 years [92] and have been hailed as superior to usual, clinic measurements in that they yield values from patients' daily life, are immune to the "white-coat effect" and allow the recording of many more values than do conventional methods [93]. However, a recent investigation by Sega et al. concluded that:

> "The long follow-up of the PAMELA sample provides evidence that office, home, and ambulatory blood pressures are similarly predictive of the risk of cardiovascular and all-cause death" [94]

And, of course, the same problem of interpretation in relation to what is "typical" and what is not applies to measurements obtained by these methods:

> "An ambulatory record ideally should be obtained as the subject carries out a typical day without excessive mental or physical stress." [92]

Nevertheless, it would be very interesting to investigate what patients and physicians make of ambulatory and home blood pressure measurements in consultations.

To go on, in order to learn something useful about reasons for adherence, it would make sense to focus on patients who resist taking medicines altogether. Few researchers have done so, however [73]. But it would presumably be very hard to involve these people in research, especially if the person who tried to do so was a physician such as myself [54]. Therefore I might be better off heading in some other direction.

But, generally, in order to get anywhere with the dilemma of medication non-adherence, I think it will be necessary to apply as many different ways of looking at the problem as possible. This implies having many different kinds of scientists involved. In short, medication adherence is a phenomenon that is much too important to be left only in the hands of health care professionals.

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Note: all internet content was accessed in December 2005.

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