Essay

Uncertainty

At the core of general practice

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Uncertainty is a core concept of medical activity, especially in general practice, where illness is evaluated at an early stage and available diagnostic tools are limited. In this paper, theoretical aspects of the concept of uncertainty are used to analyze the handling of uncertainty in two areas of the health care system: clinical encounters in primary care and at the public health level. Wynne's categorizations of risk, strict uncertainty, *and* ignorance *represent one approach that may be useful in acknowledging when a situation is not suitable for an evidence-based approach. Similarly, the concept of* post-normal science *is valuable in describing situations where uncertainty prevails together with high stakes, values in dispute, and an urgent need for decision making. Accepting that science cannot always reduce uncertainty but it can, rather, be a tool for analyzing an uncertain situation as a prerequisite for attending to uncertainty in a productive way—even when the end results are unfavorable. This paper provides examples of uncertainty in both clinical and public health situations.*

Introduction

This essay is based on a keynote lecture at the Nordic Conference of General Practice in Iceland 2017. My main aims are to explore uncertainty as a core concept of general practice and challenge the common understanding that uncertainty in medicine is a fault or a shortcoming. Also, I will discuss how we can communicate uncertainty to patients and the public without losing credibility.

It took me several years as a doctor to understand that uncertainty may be a source for better understanding of a field. In this essay, I will present examples of a theoretical framework of uncertainty, and I will apply this to cases from general practice and public health.

Uncertainty is a core aspect of all medical activity (Simpkin & Schwartzstein 2016). However, in general practice, uncertainty is especially pronounced; we see patients at an earlier stage than our fellow hospital doctors. We have less diagnostic tools to help us. We see the patient in the consulting room or at home but cannot follow them up continuously during the proceeding hours or days. GPs carry the uncertainty on their shoulders and take the blame when things go wrong. And things must go wrong sometimes!

Conscious and wise handling of uncertainty goes hand in hand with high quality of care. It is important to note that high quality is not the same as perfection. On the other hand, does pushing uncertainty away represent unsafe practice? The feeling of uncertainty is a constant source of uneasiness in medical practice. Why is that? What effects does professional uncertainty have on us?

- Uncertainty takes us out of our role as well-informed advisors. We expect ourselves to be able to give patients advice; that is why they come to us. We tend to believe that patients expect us to be certain of our views at all times. The role of a knowledgeable advisor is comfortable and places us neatly at the top of a hierarchy of knowledge and perceived wisdom. Who wants to come down from that position?

- Additionally, uncertainty can make us feel outright incompetent. Even though we may acknowledge intellectually that uncertainty is part and parcel of medicine, most of us do not welcome the feeling when it comes to us in the consulting room.

- Uncertainty makes us seek certainty. Looking for certainty in the form of evidence-based medicine is a good strategy to a point. Beyond this point, we need to explore the situation with a different mindset.

• Many professions have to deal with uncertainty, but it is specifically pertinent to our profession. Incorrect decisions may have devastating results for the patient. That is a heavy burden.

Frameworks and examples

A central question is this: how can doctors maintain professional credibility when we are uncertain? There are no quick fixes, and this paper will not provide ultimate solutions. However, I will present some approaches based on the research literature that shows handling of uncertainty may be found in empirical data, systematic analysis, and uncertainty theory.

A framework that has helped me make some sense of uncertainty was provided by the scientist Brian Wynne, who differentiates uncertainty into categories (Wynne 1992). Three of these categories are particularly useful for our purposes (Rortveit & Strand 2001):

1. The simplest form is *risk*. There are known outcomes to a situation, and they can be measured. We can test whether a new treatment is beneficial for a specific outcome as compared with a placebo. Medical research often works at this level.

2. However, many clinical situations are characterized by what Wynne calls *strict uncertainty*: you know the possible outcomes, but you cannot measure them. When a new influenza pandemic emerges, we know that it may prove to be either devastating or relatively mild in its effects. But we cannot predict the number of dead beforehand. A new pandemic will be characterized by strict uncertainty.

3. *Ignorance* exists when we do not even know all possible outcomes. The introduction of a new drug will be characterized by elements of ignorance because all possible side effects are not known and cannot be foreseen.

This taxonomy can be used to classify many situations of uncertainty in the clinic. I will give some simple examples.

The first case is a 67-year-old male patient with hypertension who wants to try a beta blocker to reduce his risk of stroke. We can measure whether beta blockers reduce the risk of stroke in hypertensive patients as compared to placebo. From that, we can calculate our patient's *risk* of stroke. This means that we can give

advice based on evidence. However, we cannot predict whether this particular patient will actually avoid a stroke because of the medication.

The second case is a 36-year-old woman with chronic muscle pain who asks for a short sick leave certificate to get over a difficult period. Could giving her such a certificate mean the start of a disability pension career? Or may it prove to be exactly what she needs at this time—to get some relief and gain the strength needed to continue in her work? As a GP, you have a lot of information about her background, family history, and medical history, and this data leads you to think that she is different from the patients in clinical studies, so it is difficult to apply prediction models here. This is a concern for many GPs from time to time. If research and guidelines do not apply, the situation has elements of *strict uncertainty*.

The final example is a mother who requests the referral of her seven-year-old son with concentration problems for ADHD investigation. You know the boy's father has alcohol problems, and his mother is exhausted. If he gets an ADHD diagnosis, he may get helpful treatment. But it is also possible that a diagnosis may add to his problems in ways we cannot foresee. For example, diagnosing the boy and medicating him may conceal his domestic challenges and prevent him from getting the assistance that he needs from child protection services. This clinical situation has characteristics of *ignorance*.

By analyzing a situation using these categories, we may step back a little and ask ourselves what is actually needed. Have we enough and the right sort of information to make a decision together with the patient? The very asking of such questions implies a willingness to explore uncertainty.

I will now present hypothetical situations at two levels of our health care system. Both cases involve high degrees of uncertainty. The clinical case requires handling a patient in a situation where the evidence is insufficient. The public health case is about communication with the general public in circumstances when uncertainty prevails.

A clinical case

In the following situation, you must pretend that you are the GP, who must reach a conclusion at the end of the consultation.

Anne is a 74-year-old non-smoking Danish woman. She has hypertension but is otherwise healthy. She lives alone. She consults her GP on a Friday as she developed a cold with a fever four to five days ago. Since the symptoms began, she has

been coughing harshly, including during the night. Her coughing is mostly dry. She now feels short of breath but no longer has a fever. She feels a little weak but takes good care of herself. The GP examines her and finds no shortness of breath at rest. Her general condition seems okay. He finds wheezing at stethoscopy, predominantly at the lower part of both lungs. CRP is 52, which is relatively, but not very, high.

Should the GP prescribe antibiotics? This is a classic dilemma. They should not be prescribed unless necessary, but how can one know if they are necessary at this stage? GP research colleagues in the UK recently published a study in *BMJ* showing that antibiotics are not needed in most of these cases. Still, there is real uncertainty. Some patients do need antibiotics (Little et. al. 2017), but we do not know who they are.

Our decisions in each consultation matter. They have direct implications for the present patient and for future patients. On one hand, Anne may get sicker and sicker over the weekend, and she doesn't seem to have a trustworthy network who can take care of her. What if a prescription can prevent this negative progress? On the other hand, there is a public health aspect to this question. The doctor knows that, if all cases like Anne's are treated with antimicrobials, we will create a bigger resistance problem. The problem already exists; more than 200,000 newborns die from sepsis with resistant microbes annually (Holmes et. al. 2016). On top of this, in Norway, as in many other countries, the government has set goals to reduce the use of antimicrobials. In public debate, there is also a push to reduce the prescriptions.

The pressure on the clinician is high. There are good arguments for either way of handling the situation, but there is also a high risk of failure. The GP may turn to research to predict the likely future impact of the present decision.

An influential report from the UK, the so-called O'Neill report, came out in 2014 (O'Neill 2014). It was generated at the request of politicians, and it states that, by year 2050, 10 million people will die annually due to antimicrobial resistance. This is a huge number, and it received massive publicity. However, in 2016, a scientific paper by Dutch researchers refuted the basis for the numbers in the O'Neill report (De Kraker et. al. 2016). Among other weaknesses, the O'Neill report used hospital data to estimate the prevalence of severe infections, although this raises huge problems with generalizability. Whether 10 million people will die annually due to antimicrobial resistance by 2050 is a question for which the facts cannot be reliably established today. The O'Neill report reduced the question to a *risk* category,

where all we needed to do was find the right numbers and calculate. Instead, the situation is characterized by *ignorance*.

Predictions like this lead to discussions about methodology and accusations of inflated numbers. In my opinion, criticism of evidence-based medicine and guidelines is too often based on such a side-track discussion of accuracy of numbers. This leads to a distraction from the important work of finding answers.

The point is that we know we have to reduce the use of antimicrobials. How can we achieve that? This leads us back to the GP, who has to make a decision in the clinical encounter with Anne, which is characterized by uncertainty regarding Anne's health. We have to look to other research for guidance in this situation.

Reducing uncertainty in diagnosis and treatment is an important and justified part of our medical work. A lot of research, including evidence-based medicine, precision medicine, and computerized decision support help to reduce uncertainty, but these strategies need to be used wisely. Roger Jones, in a recent editorial in *British Journal of General Practice*, claims that it is time for a paradigm shift in general practice (Jones 2016). He says that we need to move away from guesswork and from our reluctance to investigate and to use evidence and risk assessment tools. There is truth to this, but he nonetheless seems to dismiss the necessity of dealing with uncertainty. Uncertainty is an inherent part of medicine, and rejecting that fact may be dangerous. Avoiding uncertainty at all costs is not part of our job. Still, this is a preferred strategy of many doctors, and many of us use it at least some of the time. Avoidance of uncertainty inevitably results in false positive test results, excess use of health care services, and, as an end result, overdiagnosis and overtreatment Macdonald 2017). This is a huge worry in Western societies today. In the long run, it may even lead to undertreatment as overconsumption may cause our health care system to collapse.

Taking real responsibility implies acknowledging uncertainty in clinical encounters (Simpkin & Schwartzstein 2016; Hatch 2017). We may admit uncertainty and still maintain credibility, but we need communication skills to do so wisely. Admitting uncertainty can even allow a larger degree of patient autonomy. In the case of Anne, it should be possible to discuss options openly with her. She may see solutions that the doctor does not. Shared decision-making may actually be facilitated in situations with uncertainty.

Additionally, we need to work with and not against the inherent uncertainty of medicine (Malterud et. al. 2017; Nowotny 2015). In fact, fewer errors are made by doctors who tolerate and work with uncertainty. Engebretsen et al. have written about the concrete use of uncertainty as a diagnostic tool, and they insist that

embracing uncertainty will keep the mind prepared for the possibility of "inverse insights" or surprises (Engebretsen et. al. 2016). This is not just about big surprises. In the clinic, all doctors experience small surprises multiple times a day. An open mind is necessary to learn from these surprises and use them actively. As the authors of a perspective article in the *New England Journal of Medicine* put it, the value of physicians may lie in the gray-scale space between certainty and uncertainty (Simpkin & Schwartzstein 2016).

In the example I presented earlier of the seven-year-old boy whose mother wanted him referred for investigation of ADHD, embracing the uncertainty rather than unsuccessfully working against it may prove beneficial. It may allow the doctor to gain all sorts of insights in conversation with the mother as well as the boy. On the contrary, reducing the uncertainty to a decision about whether to refer or not may result in lost opportunities to find long-term, useful solutions for the boy.

The public health case

Now we will move on to the field of public health, and I will use the issue of vaccination as my case study. The medical history of vaccination is a success story—and a powerful one.

Vaccination is a public health task in which GPs often play a prominent role, either as providers of the vaccine or as advisors. In the medical profession, we often talk negatively about "vaccine sceptics." They threaten modern society, we believe, because they do not trust the truth-seeking scientists and the medical do-gooders. I want to challenge this narrative a little. To do that, I will use two examples.

First, we will consider the case of the measles. In the middle of the twentieth century, this extremely contagious disease affected almost all children and resulted in enormous six million deaths annually due to complications (Elliman & Bedford 2007; Goodson & Seward 2015). In 1963, a vaccine was made available, and later, the combined MMR vaccine was quickly taken up by parents. They knew what was at stake. The results have been amazing as can be seen from the convincing number of measles-related deaths in 2015, estimated at 135,000. However, though the vaccine is undoubtedly effective, that doesn't automatically mean it is safe. In 1998, Wakefield and coworkers published a pilot study of 12 children, linking the MMR vaccine to a new-found syndrome that included autism. This caused inevitable concern among parents. In the years after this publication, no

studies were able to replicate the findings, and in the end, Wakefield's work was proven fraudulent. He lost his research and clinical credentials. The paper in which the results were published was retracted by the journal *Lancet*; this is why I have not included it in the reference list, although it is available. In the UK, MMR vaccine coverage fell from 92% in 1995 to 80% in 2003, inciting a major threat to herd immunity. Measles was declared endemic in Britain in 2008 for the first time in 14 years, and there is no doubt that Wakefield's false study is the reason. The vaccine uptake is now increasing. However, the fake story lives on.

The effects of this study have been increased by other currents in modern society. Today's parents have never seen the effects of the diseases that we vaccinate against, such as polio or measles, unfold before their eyes. The threat does not feel real. At the same time, the opinions of experts are being questioned to a larger extent by the public and the media. The media often gives equal coverage to opposing views, even when scientific facts can be established. Vaccines seem to be a perfect field for conspiracy theories. These unjustified and dangerous attacks on medical progress are challenging for us as professionals.

In the MMR case, we have facts; there is no uncertainty. We know it works, and we know it does not cause autism. However, real uncertainty existed in the few years before Wakefield's fraud was proven. After 35 years of success with the MMR vaccine, parents all over the world became genuinely uncertain about the safety of the vaccine, and they still are. It is difficult to explain that a paper published in one of the medical field's most prestigious journals was based on fraud.

Parents who are uncertain about whether to vaccinate their children do not need our contempt. They need support and valid information. Valid information includes openness about the fact that not all vaccines are equally safe or equally effective. We tend to overlook that point. As doctors, our first duty is to do no harm. In the prevention of diseases, this is incredibly important, and the safety of vaccines can take a long time to establish.

The next case is a situation in which all of the facts could not be established before decisions had to be made. In the summer of 2009, we realized that an influenza pandemic was on the way. Three questions were crucial: how dangerous would the pandemic be? Was the vaccine effective? Was the vaccine safe?

The uncertainty related to these three questions was fundamental. Still, action had to be taken by health authorities all over the world. How could one know how to make the right decisions?

Public health authorities chose different strategies; these differences are exemplified by Norway and Denmark (Gil Cuesta et. al. 2016). In Norway, vaccination

was recommended for the whole population, and 41% were vaccinated. In Denmark, vaccination was only recommended for risk groups, and 6% were vaccinated.

In hindsight, the following has been documented: the pandemic flu was generally relatively mild. However, the risk of fetal death was almost doubled among pregnant women who had influenza (Haberg et. al. 2016). This is no small complication. Furthermore, vaccination seemed to reduce the risk of fetal death. Vaccination in 2009 reduced mortality and admission rates in the influenza season 2010/11. Denmark came out less favorably than the other Nordic countries, where vaccination rates were much higher (Gil Cuesta et. al. 2016). There was an increased risk of narcolepsy after influenza, but this risk seemed to be more strongly associated with the pandemic vaccine (Trogstad et. al. 2017).

We know this now, a few years after the pandemic. However, when the decisions regarding vaccination strategy had to be made, these outcomes were not known. The situation was characterized by *ignorance* in Wynne's taxonomy (Wynne 1992).

How can such situations be handled in a trustworthy way? We all love situations in which facts are clearly established by science. Within the current scientific paradigm, the general understanding is that scientific knowledge reduces uncertainty. The invention of the MMR vaccine is a success story of normal science. However, when the public becomes uncertain in spite of reliable scientific facts, scientific success does not help us much. We cannot reach herd immunity against measles when people do not trust the vaccine.

Post-normal science is a concept in which uncertainty is a key feature that cannot be erased (Funtowicz & Ravetz 1993; Ravetz 2004). As discussed in the clinical case, we sometimes need to embrace uncertainty because there is no other way. This is also the case in public health and policy matters. How can we work *with* uncertainty instead of denying it?

Post-normal science provides a tool with which to analyze complex problems in the interface between science and policy (figure 1). In complex situations of this kind, facts are uncertain. The *stakes are high*, meaning that the outcomes may be successful or devastating depending on the decisions made. On top of these two factors, *values are in dispute*. These may be political values, moral values, or economical values, indicating that two people may view the situation differently independent of the facts that may be established. Finally, *decisions are urgent*, meaning that we cannot wait for the normal process of science to establish the facts.

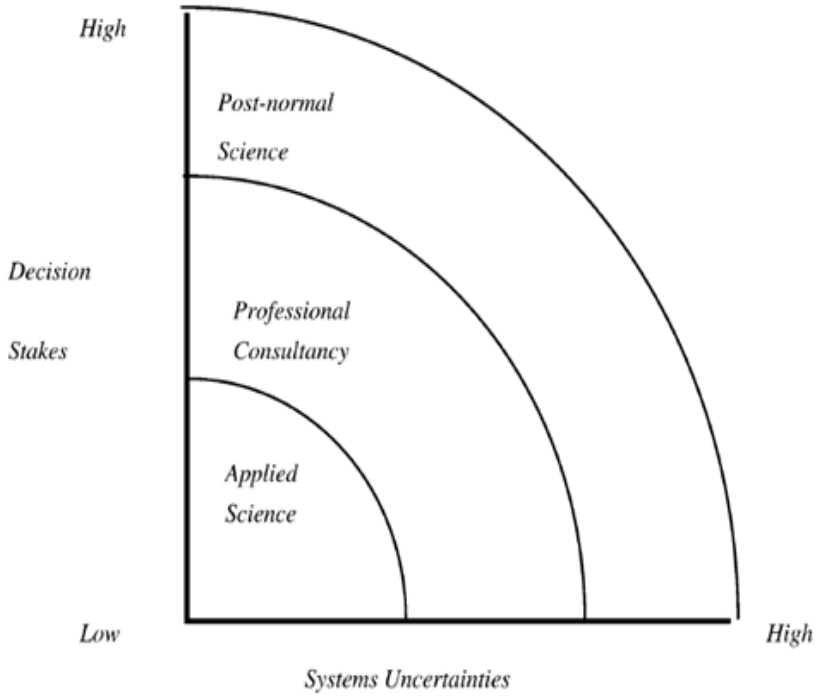

Figure 1. Evaluation of uncertainty and decision stakes according to the framework of Ravetz (Ravetz, 2004).

Normal science operates in circumstances where uncertainty is low, and the stakes are often also low. Professionals, like GPs, work in the zone where uncertainty and stakes are higher. With a post-normal problem, uncertainty is very high as are the stakes, and the situation is unstable. Normal science — Including evidence-based medicine — cannot guide us in this situation (Greenhalgh & Malterud 2017).

Analyzing these factors may be the first step to acknowledging how difficult the situation is and, in the end, reaching a trustworthy decision. A "trustworthy decision", in this case, is different from "the right decision", which can only be judged in hindsight.

To bring perspectives from post-normal science into reality means that we need to communicate uncertainty to the public, and we need to do it well. Research investigating uncertainty communication may guide us.

Scientific experts and professionals tend to believe that providing information to the general public about scientific uncertainty would have a series of negative consequences (Frewer et. al. 2003). The experts in one study believed that such

information would result in distrust in science and might cause panic and confusion. They were further concerned that the public is unable to conceptualize uncertainty; this is a real problem that the public shares with professionals, such as doctors. Lastly, the experts viewed the public as a whole as irrational. Clearly, experts do not seem to trust the public.

What, then, about the public—what do they expect from the scientific community when it comes to uncertainty? The experts are right in that the public is not easy to deal with (Albertson & Gadarian 2015). People as a whole are, indeed, ambivalent (De Boer et, al. 2005). Generally, they seem to want to avoid uncertainty. Doctors are the same—we are human, and this is our reflex. However, when uncertainty exists, the public want transparency. Furthermore, they trust sources that communicate that uncertainty exists to a greater extent than they trust other sources. Artificial threats, such as chemicals in food, are less tolerated than natural threats, such as salmonella in food. Education plays a role as always. Uncertainty concepts are difficult to understand, especially for the less educated. Finally, attitudes about government and authorities play a role in how uncertainty information is perceived. The more trust a community has in general, the more it will tolerate uncertainty communication. This latter point is an advantage in Nordic societies, where trust in society, government, and authorities is generally high.

Whatever the risk perception, the public expect information about uncertainty to be both complete and well communicated. The expectations are high, and the scientific community needs to live up to them if we want to maintain our credibility.

The science adviser to the prime minister of New Zealand, Peter Gluckman, has gained useful experience in uncertainty communication. He has presented a useful framework to navigate in situations that have the hallmarks of post-normal science (Gluckman 2014). Such situations are numerous. Examples are food security issues, climate change, terrorism, and public health issues. The above example of the pandemic influenza vaccine is typical.

Gluckman's advice is sober and worth listening to. Here are a few points that he has made:

- While one cannot expect to reach all of the general public, it is a priority to maintain the trust of many. Open scholarly debate may not be advisable during a time of crisis, but balanced information about uncertainty is still needed.

- Protecting the independence of advice is important but proves to be difficult, particularly in times of crisis.

• For us, as researchers and clinicians, it is important to understand that, while we should *inform* policy, we do not *make* policy. This seems to be particularly hard for members of the medical profession to understand. Remember that values are at stake, and that is the domain of politics.

• The facts are truly uncertain; we must recognize the limits of science. We cannot claim, in situations of uncertainty, to possess the right answer.

• Still, science often can give valid information about aspects of a situation and must be given privilege as an input to policy. Politicians' values are *as* important as the values of the medical profession, but politicians do not get to decide whether scientific results are valid. However, as professionals, we need to use our privileged position responsibly. We do not always do so.

• Denying or avoiding uncertainty in medicine is dangerous. We must fight the idea that more science reduces the need to handle uncertainty: among ourselves, among our patients, and among the public.

This is the only way to maintain trust, both in the consulting room and in public debates. In the aftermath of the new presidency of the USA, we have seen a pro-science movement to serve as a counterweight to the fake news coming from the president and his regime. I support this movement. However, I am worried by the tendency within that movement to claim that science is clean, trustworthy, and always correct in its conclusions. Science is a strategy that has moved our world forward at high speed. However, true science comes with doubt, with scientific debate, and yes, with uncertainty. Therefore, good science requires humble scientists, and effective health care services require humble medical professionals.

Even when scientific findings are inarguable, we need to proceed with the understanding that people may view the world differently than we do. That is not the same as giving alternative views equal weight. Future research must grapple with uncertainty more, not less, than it has in the past. The medical sciences are increasingly embracing existing bodies of work on uncertainty within the social sciences (Wynne 1992; Nowotny 2015; Albertson & Gadarian 2015). Multidisciplinary efforts are truly needed in this challenging area. The long-term struggle will be to work with uncertainty, not against it, and to maintain credibility through openness about uncertainty.

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