

Social Values and Health Priority Setting Case Study

Title of Case Study	Novo Seven in haemophilia: clinical decision making and funding policies in Germany
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<p>Case Summary (approx. 350 words)</p> <p>Please include information here about why the case is of particular interest</p>	<p>This case is an example of how a set of very pressing social values challenges can arise out of one individual case at the clinical level. The intervention in question - Novoseven for the treatment of haemophilia - was, at the time the clinical case occurred, a new and highly expensive treatment, whose use and effectiveness in individual patients was relatively unknown. Further, due to the newness of the drug, no reimbursement decision had been made by the relevant agencies (the German Statutory Health Funds or ‘sickness funds’). The institution as well as the clinicians involved were therefore working in a context of financial and clinical uncertainty, respectively. The case demonstrates the challenges of social values that hyper-expensive interventions can present even in the context of very small patient populations, as well drawing attention to issues of organizational responsibility that can arise, especially in circumstances of uncertainty. The dominance of particular social values in this case - notably that of clinical need and the imperative to save life - serve to highlight the more general importance of these values throughout the German healthcare system.</p>
1. Facts of the case	Facts of the case
<p>Please include information on as many of the following as are relevant to the case:</p> <ul style="list-style-type: none"> • At what condition is the intervention, program or service aimed? • What are its effects? Eg. Is it curative, preventative, palliative, life-prolonging, rehabilitative? • Is there a relevant comparator? If so how does this intervention, service or program compare to the alternative? Include ICER estimates/QALY costs if relevant. • What are the significant features about the condition and/or about the patient population in this case? Eg. patient population is very young, very old, condition is rare, life- 	<p>Novo Seven is a drug for the treatment of haemophilia.</p> <p><i>Background</i></p> <p>Haemophilia belongs to a group of hereditary conditions that impair the body’s ability to control blood clotting/coagulation, which stops bleeding when a blood vessel All patients with haemophilia lack certain coagulant factors in their blood, leading to continued bleeding when any blood vessel is broken. Patients suffer from spontaneous bleeds (internal, including joints, brain etc) and prolonged bleeding times. Strong bleeds can be fatal if untreated.</p> <p>Patients with haemophilia A lack coagulation factor VIII: the incidence of this form of haemophilia is 1in 5-10,000 male births. Patients with haemophilia B lack coagulation factor IX: the incidence of this form is 1 in 20-35,000 male births.</p> <p>Since the 1970s, treatment has involved replacing the blood coagulant factors that patients are lacking. However, up to 20% of patients with haemophilia A and 5% of haemophilia B patients develop antibodies against</p>

<p>threatening, life-limiting etc.</p> <ul style="list-style-type: none"> • How are the benefits of the intervention distributed across the patient population and/or across time? • What is the cost or budget impact of the intervention/service/ programme? • What is the nature and strength of the evidence about the outcomes of the intervention, service or programme? Eg. randomized clinical trials, evidence on patient-related outcomes. • How did the issue about this case arise - for example, from clinical practice, from a policy setting, from a topic selection process? 	<p>the replacement clotting factors, making them ineffective. This is a rare condition, but requires that clotting agents from higher up the ‘cascade’ of factors are given: patients with antibodies against factor VIII, the most commonly used clotting agent, must therefore be treated with factor VII, bypassing the deficient clotting factor VIII. Novoseven is a recombinant factor VII clotting agent, and is therefore suitable for use in patients who have developed antibodies to factor VIII clotting agents.</p> <p>Novoseven is a potentially life saving treatment, and can be an option of last resort for patients for whom other factors have ceased to be effective. It is administered via injections, at between 2-6 hourly intervals, depending on the patient’s particular condition.</p> <p>The relevant comparator for Novoseven is an activated prothrombin complex FEIBA, or high doses of human factor VIII. However, some patients with antibodies can fail to respond to both of these interventions, leaving Novoseven as the only remaining option.</p> <p>In Germany, the patient population for whom the drug is relevant numbers between 1600-3000. They are predominantly male (haemophilia is a predominantly male condition) and of mixed ages.</p> <p>More than 80% of patients in the indicated group respond to the treatment. At the time when this particular case arose, it was intended for short term emergency treatment, but has come to be used since then for longer term treatment (weeks or months) and also for one-off, off label use for example in connection with cardiovascular surgery and neurosurgery.</p> <p><i>Cost and cost effectiveness</i></p> <p>This particular instance of the use of Novoseven arose several years ago when the drug was very new and with uncertain costs and cost-effectiveness, but it additionally occurred in a country where cost-effectiveness assessments are not undertaken.</p> <p>The cost of each injection of Novoseven was however known to be very high - around 6000Euros.</p>
<p>2. Policy decision: process</p> <p>Please include information on as many of the following as are relevant to this case:</p> <ul style="list-style-type: none"> • What stages/institutions were involved in the decision making process? • Is legal context important in this case? If so, in what way? • Who was involved? Eg. key stakeholders, the public, professionals, industry, patients, governmental or non-government policy actors. • How were they involved, and at what stages of the process? 	<p>Policy decision: process</p> <p>This case was one which arose in a clinical situation, and where no high level policy decision had been taken nor a policy process undergone. Novoseven had, however, been licensed for use for its indicated purposes in Germany and was available in some hospitals, at the discretion of pharmacists.</p> <p>It was unknown as to whether the social insurance providers (the statutory health or ‘sickness’ funds) who reimburse hospitals for treating patients covered by their schemes would reimburse in this instance - the lack of experience of use of Novoseven meant they had not had to make such a decision before, so had not established a decision protocol on the issue.</p> <p>Ultimately, the sickness fund did reimburse the hospital for the costs of treating this patient with Novoseven, and have continued to do so for other uses of the drug since. However, the reimbursement decision was not given until after more than 2 million euros had already been spent on treating this</p>

<ul style="list-style-type: none"> • Was there disagreement between any of the parties involved in the decision process? • Do any rules or frameworks exist to guide decision making? If so, were they followed in this instance? • Do mechanisms exist for challenging the decision at any stage of the process? • How, if at all, is the decision process or the decision itself publicized? 	<p>individual patient.</p> <p>Almost all decision-making in this case occurred at a clinical level and involved solely clinical concerns, not those of cost. Hospital pharmacists were involved in sourcing extra supplies of Novoseven and in alerting clinicians to the cost of the drug, but were not in a position to make any decisions as to its use or availability. They themselves were in a position of uncertainty as to the effect of the drug and, in particular, how many doses would be needed and over what period of time.</p>
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3. Policy decision: content	Policy decision: content
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<p>Please include information on as many of the following as are relevant to this case:</p> <ul style="list-style-type: none"> • What decision was made about the intervention, service or program, if any? • What values were relevant in the case or in the decision itself? For example, values of cost-effectiveness, clinical effectiveness, justice/equity, solidarity or autonomy. How did they affect the decision itself? • Was the way in which these values were balanced affected by any specific features of the case? For example, end of life considerations, age of patients, impact on carers, disease severity, innovative nature of the intervention, social stigma or cultural sensitivity? • Did the case challenge established guidance or 'decision rules'? Eg. on cost-effectiveness, cost thresholds, age discrimination etc. If so, in what way? • Were any health system-wide considerations influential in the decision? For example, displacement of old technologies, professional practice issues, or infrastructure/feasibility considerations. 	<p>The clinical situation and 'decision' process (such as it was), were as follows:</p> <ul style="list-style-type: none"> - A haemophiliac patient had been transferred to a university hospital from a smaller regional hospital, where treatment with factor VIII to stop bleeding had been attempted. - This treatment had failed to stem the patient's bleeding and the regional hospital had exhausted all alternative treatments available to them (including human factor VIII and FEIBA, to which the patient had been non-responsive). - University hospitals in Germany have the most advanced treatments and technologies available in the country, hence the non-responsive patient was sent there for any treatment that the regional hospital was unable to provide. - The patient was assessed and found to have bleeding around the brain, and continued attempts to stabilize him using the conventional treatments failed. He continued to bleed and clinicians became aware that his life could be imminently in danger, given that bleeding around the brain had been found. - The attending consultant recommended treating with Novoseven. - The hospital in the pharmacy confirmed that it had only three doses of Novoseven in stock and could provide these to the clinical team. Clinicians had little idea of how many doses would be needed (recall that at the time, this was a very new intervention, and experience of use was highly limited - as such it was something of an 'unknown') and so requested more doses of Novoseven to be sourced from other university hospitals. - The pharmacist alerted the clinicians as to how expensive Novoseven was and that it was uncertain whether the statutory health funds would reimburse the hospital for using it. - When contacted, the statutory health funds were unable to give a reimbursement decision in a short time frame. - Clinicians continued to treat the patient in the absence of any knowledge about a reimbursement decision. - More doses of Novoseven were sourced and the patient continued to be treated with 2 hourly injections for several weeks. He stabilized but remained in a coma. - After approximately 2 months of Novoseven treatment, the patient regained consciousness, although suffered significant brain damage and was unable to wash or feed himself and could only speak a few words. - The total cost of treatment for this patient was estimated at over 2million Euros. At the point at which treatment was stopped, the hospital did not know whether or not they would receive reimbursement for these costs.
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- However, ultimately, the statutory health funds did reimburse the hospital.

Whilst there was no policy decision as such in this case, there are a number of factors which are explicitly mentioned in the German legal framework for statutory health insurance, and which may have been brought to bear, had an explicit decision process been undertaken. These are as follows:

- Solidarity and personal responsibility
- Effectiveness and quality of care
- Protecting against life-threatening diseases and principle of last best hope/last resort
- Religious needs
- Medical necessity
- Sufficiency
- 'Economy' or non-wastefulness of resources (but *not* cost-effectiveness)
- Appropriate treatment for purpose
- More recently, for new interventions and especially for innovative biological components - additional/marginal benefit, fixed pricing, number of potential patients who could benefit, overall cost impact on the statutory health fund, cost-benefit analysis.

Cost-effectiveness analysis is not currently permitted in Germany.

4. Discussion

Please use this space to reflect on, for example:

- The reasons or values explicitly used in making the decision. Do these reflect any institutional decision rules or statements of value, for example commitments to equality, non-discrimination or fairness? Do they reflect wider social, moral, cultural, religious values, and if so how?
- Considerations not explicitly taken into account in the decision, but which may nonetheless have been important 'background' factors. These might include, for example, public opinion, political sensitivity, moral sensitivity, and international reputation, as well as cultural, social, moral, religious or institutional norms.
- The impact of the decision making process on the decision itself, if any.
- Any issues relating to implementation. For example, whether access may be restricted by capacity issues, even if the intervention, service or programme is provided on a 'universal' basis.

Discussion

There are a number of issues of social values that are highlighted by this case, both in terms of content and process values:

- Decision uncertainty and organizational responsibility
The clinicians were the only people making decisions in this case: whilst at the clinical level this is appropriate, they were nonetheless operating in a decision vacuum so far as the cost and reimbursement of Novoseven was concerned. The enormous cost of treating this individual patient could have had serious consequences for the hospital budget and ongoing resource allocations if the sickness fund had not ultimately decided to reimburse. Whilst clinicians were aware of the cost of the drug, it was not their concern or responsibility to limit its use on grounds of cost: their concern was with clinical need only (and this is particularly significant in the German context, as discussed below).

There is arguably an important element of organizational responsibility at stake here, and whilst this relates to the cost of the treatment being provided, it also relates to a situation of moral hazard in which clinicians might have found themselves, had things turned out differently.

In relation to costs, it is possible that this case (and others like it) could have had very serious financial consequences for the hospital in question, had reimbursement not been approved. This could go so far as to put in doubt the ongoing financial viability of an institution, but it most certainly raises serious questions about the opportunity costs to numerous other patients of devoting such large amounts of resources to

- Anything else you think significant or interesting about the decision.

one individual. However, it is interesting that in Germany opportunity costs are not taken into consideration, given a strong and fundamental commitment to the value of each life being equal (see discussion below). It is therefore impossible to 'trade' one life against another as some might suggest is the case with the concept of opportunity costs.

On issues of organizational responsibility and moral hazard: whilst the hospital pharmacy had three doses of Novoseven in stock, it was not certain that more doses could have been sourced from elsewhere, or that the amount they could obtain was sufficient for the patient's requirements, thus potentially leaving clinicians in a position of having begun treatment, stabilized the patient, but then having to stop treatment due to lack of availability of the drug. A similar situation could also have arisen if the sickness fund in question had made a decision earlier in the course of treatment that it would not reimburse the hospital for use of Novoseven, and hospital managers decided that treatment should not be continued. In either of these situations, clinicians would have been in the position of having to explain the non-clinical grounds for the sudden cessation of a treatment that appeared to be working to stabilize the patient. This kind of organizational uncertainty arguably leaves clinicians in a very difficult position, both clinically and ethically.

- Priority of values of clinical need and equality

The case highlights what is notable of the more general approach in Germany, that clinical need is the uppermost value outweighing all others - and most notably values around cost and cost-effectiveness. The concern of clinicians in this case was simply to continue doing everything that could be done for the patient in question, no matter what the cost. Underlying this in the German context is a fundamental commitment to the notion that all lives are equal and that therefore no one patient is any less worthy of treatment than any other, regardless of cost. In this context, to carry out cost-effectiveness assessments or take into account opportunity costs is considered to be putting a 'price' on life. The legacy of 20th Century German history still plays a powerful part in maintaining such commitments to the absolute equality of each person's worth and the moral inadmissibility of 'pricing' one person's life as worth more than another's.

Nonetheless, questions remain as to how sustainable this approach is, given the increasing number of highly expensive, highly technologically advanced treatments such as the biological components involved in Novoseven, which are likely to come to market in the near future. Whilst the patient population for Novoseven is very small, this may not be the case if similar components become available to treat more common diseases such as cancer. Germany may then be forced to face the question of how it prioritizes such interventions without 'pricing' life.

5. References/Links to relevant documents	
	<p>This case is drawn from the experience of a clinician working in this hospital at the time when this case occurred. For more information, please contact the case study author.</p>