

# Fair funding of extraordinarily expensive medication

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In 2010 the Swiss Supreme Court [9C\_334/2010] ruled that a health plan was not obligated to pay the costs of the drug Myozyme<sup>®</sup> for a 70-year-old-woman in the advanced stages of Pompe disease. The primary reason for the denial was directly related to the cost of the drug, which was estimated to be between 750 000 and 900 000 Swiss francs for a period of eighteen months. The court seemed not to have been persuaded that the drug was effective enough to warrant such costs. But the more legally compelling consideration in the eyes of the court was that considerations of legal equality would require Swiss health plans to cover an enormously large number of other health care interventions that had costs greater than 100 000 Swiss francs per Quality-Adjusted Life Year [QALY] saved and that are not now made available to patients with equally compelling health care needs. The court asserted that if such care were made available the annual aggregated costs would be about 90 billion Swiss francs, or 160% of the current cost of the Swiss health care system.

These certainly appear to be legally and morally compelling reasons for this court's judgment. However, in this commentary I will argue that the court's judgment may have been too broad, that there are moral considerations that would justify providing this drug to some range of Pompe patients, and that such a decision would not necessarily require as a matter of justice funding every other marginally beneficial and excessively costly intervention that medicine might conceivably offer to other patients potentially faced with a premature death.

We need to begin our response with a brief description of Pompe disease. It is an enzyme deficiency disorder. More specifically, it is a metabolic myopathy caused by a deficiency of acid-alpha glucosidase, a lysosomal enzyme. It is a result of a specific gene mutation, the consequence of which is loss of muscular function, including heart and lungs, with ultimate fatal consequences. It is a rare disorder with an estimated occurrence of one case per 40 000 births. There are two basic variants of the disorder: neonatal onset and adult onset, this latter having a much longer trajectory to death. Infants diagnosed with Pompe disease will almost always die before age one [1]. This outcome assumes that these infants are not diagnosed until several months beyond birth when clinical symptoms become evident and that these infants do not have access to the drug Myozyme (recombinant human alglucosidase alpha), which effectively replaces the missing enzyme.

The cost of this drug is directly related to the body mass of an individual. For an infant the cost might be 100 000 Swiss francs per year rising to 400 000 or more Swiss francs per year for a full-size adult. The latter costs were at stake in the Swiss court case. The reader should note that this is not a drug that is taken for a limited period of time. After diagnosis the drug must be taken for the rest of one's life. The drug was only approved for clinical use in 2006, which means we have limited clinical data with regard to the effects and effectiveness of very long use. Thus far, the drug seems to be very effective in that it halts the muscular deterioration that would otherwise prove fatal [2]. It does not seem to reverse the disease process; damage done cannot be undone. This would seem to be a morally and medically compelling reason for early diagnosis and early initiation of treatment [3].

Before addressing the Swiss case in particular, we need to comment on an issue related to early diagnosis. As noted, Pompe disease is a very rare disorder. When clinical symptoms appear, damage has already been done. Moreover, relatively few clinicians will be familiar with Pompe because of its rarity, which means that an accurate diagnosis will be delayed significantly most often. However, that problem can be avoided today by including Pompe disease in the newborn screening panel, thereby identifying genetically vulnerable individuals from the day they are born. What would seem to be a medically and morally desirable consequence of doing that is that we might be able to save the lives of infants for an indefinite period of time if they are started on enzyme replacement therapy at birth [4].

As noted, the primary reason now why these infants die before age one is the time lost in establishing the diagnosis of what in fact is the most severe form of Pompe disease. However, the morally awkward consequence of diagnosis at birth is that we might be successful in saving these infants for twenty years or longer. But the cost of saving those infants for twenty years could be somewhere in excess of five million Swiss francs per child. These are the sorts of costs that the Swiss Supreme Court found to be excessive, not legally mandated and violative of the equality rights of others with serious costly medical problems.

What generates the moral awkwardness is that this drug appears to be very effective. It «might» make possible twenty years of life or more of reasonable quality for these infants. We cannot say more than «might» because the drug has only been available for five years,

but nothing in the medical literature would suggest that the possibility of twenty-year survival represents excessive optimism.

In the United States some states include Pompe disease in their newborn screening panel. This does not seem to be true in Switzerland. By excluding Pompe disease from that panel nature will take its course and these infants will die for lack of timely diagnosis, thereby obviating the need to address explicitly the painful resource allocation question otherwise generated. But allowing nature to take its course in this way, pretending as if this is nothing more than an unfortunate outcome of a bad genetic deal (as opposed to an issue of justice requiring explicit justification) is at least morally disingenuous.

In the United States we currently save the lives of infants with necrotic small bowel syndrome by providing them with Total Parenteral Nutrition (TPN) at a cost of \$200,000 per child per year. We know when we initiate this therapy that TPN will usually destroy the liver of these children by age four, who will then die unless a liver transplant gives them two more years of life. We also spend hundreds of thousands of dollars to try to save the lives of premature infants born at twenty-three weeks gestation and 600 grams. Most will die in the NICU, and most who survive will survive with moderate to severe neurological damage.

I am not going to comment on the question of whether such costly interventions are obligations of health care justice. Instead, I contend that the question that needs to be asked is how high a priority funding enzyme replacement therapy for infants born with Pompe disease ought to have relative to these two other treatments listed above, especially if enzyme replacement therapy proved to be as effective as seems possible. This is the kind of question that I believe the Swiss Supreme Court should have raised, even if this were not the sort of question that could be properly adjudicated in that court. Put another way, the appeal to legal equality (or moral equality) is not sufficiently nuanced to yield just allocation judgments in what are complex medical and moral circumstances.

I now turn to the case that came before the Swiss Supreme Court. This was a case of adult-onset Pompe disease. The adult version is «less severe» in that the degenerative course of the disease may stretch out more than ten years. But the eventual outcome will be fatal. Again, early diagnosis and early initiation of enzyme replacement therapy is highly desirable in order to protect functionality and maximize life expectancy with reasonable quality. But the earlier therapy is initiated the greater will be the aggregated costs of that therapy. If twenty-year survival is a medical possibility for individuals diagnosed in mid-life, then lifetime costs for that therapy could be as great as ten million Swiss francs per person. These are the costs that got the court's attention and elicited the judgment that no one has a legal (or moral) right to such expensive care.

What I am certain of is that the court is correct in believing that no society can afford to provide every form of life-prolonging care, no matter how expensive that care might be, and no matter how marginal the benefits gained might be. I, and the vast majority of health policy analysts today, would affirm that the need for health care rationing is inescapable, including the rationing of many forms of marginally beneficial life-prolonging care [5]. However, it is not at all obvious for now that enzyme replacement therapy yields only marginal benefits. It appears to be very effective in sustaining a reasonable quality of life for an indefinitely prolonged period of time, though achieving that outcome is extraordinarily expensive. But what would seem to be morally relevant in the context of a wealthy society is that the total number of patients who would be potential candidates for this therapy would be very tiny.

I agree with the court that protecting legal equality is of fundamental social importance. But health care needs are not distributed equally. Health care needs, quantitatively speaking, will vary enormously from one individual to another over the course of a lifetime. And health care needs will be extraordinarily heterogeneous across individuals. Further, as Callahan has observed, what we identify as health care «needs» is typically related to current medical technology [6]. We would not be discussing this issue of providing enzyme replacement therapy for Pompe patients if this therapy had not been invented. The point I am making here is that the concept of protecting legal equality in the context of health care needs is enormously complex and not readily resolvable by either simple legal rules or moral principles.

What I have argued for in my own work is the need for a sustained process of rational democratic deliberation to identify rationing protocols and health care priorities that we collectively would be willing to live with as being «just enough» for our future possible selves with presently unknown health care needs [7]. The sort of issue that needs to be addressed (and that courts might be poorly placed for addressing) pertains to health care priority setting. We presently have at least thirty cancer drugs that cost about \$100,000 for a course of treatment that will gain no more than a few extra weeks to a few extra months of life for patients with advanced cancers [8]. Relative to these drugs, how high a priority ought enzyme replacement therapy have for Pompe patients if these drugs are effective for twenty years? Relative to the \$100,000 per year we spend for long term care for end-stage Alzheimer patients, how high a priority ought enzyme replacement therapy have for Pompe patients? These are the sorts of questions we need to ask ourselves through a rational democratic deliberative process. Properly conducted, such deliberative processes will yield more than just rationing protocols that are likely to emerge from courts.

Finally, to return to the court decision itself, the court contended that this patient was confined to a wheel

chair as a result of her Pompe disease. The court noted that many other patients must live their lives in a wheel chair without having to be given a drug that might cost 500 000 Swiss francs per year. But this is a *non sequitur*. Patients who are paraplegics will be medically stable for many years in a wheel chair. They have no medical need for additional costly life-sustaining interventions. But this Pompe patient will deteriorate without enzyme replacement therapy and die prematurely. This is a morally relevant factor to which this court seems to have given no weight. Again (without knowing all the medical details for this patient), if this patient were doomed to die within the next year or two and enzyme replacement therapy would not alter that outcome more than marginally, then a good case could be made for saying she had no just claim to this therapy. But this would be irrelevant to other patients with adult-onset Pompe disease diagnosed sooner with much better life-prolonging prospects if they have access to enzyme replacement therapy. Regrettably, the court failed to call attention to this distinction.

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## A wise and just decision

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The Swiss Supreme Court revealed an expensive bill in its reasons for the judgment. The annual drug cost for treating a patient with constrained breathing ability (Pompe's disease) is half a million Swiss Francs. 2.8 percent of the Swiss adult population is estimated to suffer from a similar restraint due to chronic obstructive pulmonary disease (COPD). If each of these patients received half a million francs worth of medical treatment, the total bill would amount to 90 billion francs and the current average monthly social health insurance premium would have to increase by 1100 francs to cover it.

Are Swiss citizens really willing to ensure that patients with Pompe's disease and similar sicknesses are treated with the latest medical technologies, and also willing to accept the corollary of paying five times more for health insurance? This decision requires a valuation of the utility of medical outcomes. And, since the potential outcomes are improvements in the quantity and quality

of life, one has to follow the Supreme Court and value life itself. More precisely, not the specific life of Mrs A and Mr B is at issue, but a statistical life – a computed number that combines changes in mortality risk and quality of life and that can be tagged with a price.

A generic measure for health outcomes, often used in health economics and medical studies, is the QALY (quality-adjusted life year), which considers quantity and quality of life in a multiplicative way. Quality of life is measured on a cardinal scale ranging from 0 for the worst possible outcome (usually death) to 1 for the best outcome (perfect health). A well-founded procedure to measure the quality of life is the so-called standard gamble for decisions under uncertainty, which was axiomatized by von Neumann and Morgenstern [1]. In this approach a respondent is faced with an illness that leaves him in a defined suboptimal health state and a treatment which would cure him with probability *p* and lead to immediate death with probability 1-*p*. The suc-

cess probability  $p$  is then varied until the respondent is indifferent between the certain health state without treatment and the gamble implied by the treatment. The resulting indifference success probability marks the weight that is attached to the given health state in the QALY calculation [2].

Evidenced-based literature on the treatment of Pompe's disease with the drug Myozyme® is thin. The LOTS study [3] showed a significant effect on patient performance in the six-minute walk test and in forced vital capacity (FVC) of the lung. Patients in the treatment group were able to walk 28.1 meters further on average than the control group over the 78 week observation period. With respect to FVC, the difference between the treatment group and the placebo group was 3.4 percentage points (56.7% and 53.0%, respectively). No effect on mortality has been reported, and no QALY calculation is available to date. Kaplan [4] offers a quality of life weight for the effect of surgical treatment for COPD equal to 0.03 on the 0–1 scale. If we use this figure as a proxy, the Pompe's disease patient would have to be treated for about 33 years to produce a benefit equivalent to one year of life at full health. According to the QALY ruling by the Supreme Court, the drug treatment cost of 500 000 francs per year implies that a patient's life year had to be valued at 16.5 million francs to justify the investment.

Empirical studies on the value of a statistical life are based on questionnaires or data from markets where risks are traded – e.g. the labour market or markets for airbags and other safety features. Viscusi and Aldy's [5] survey of the pertinent literature offers a range of 5.5–7.5 million US\$ for a statistical life. From this figure, the value of a life year can be calculated as follows. The average residual life expectancy of an adult Swiss person is around 50 years. Dividing a value of life of 5 million francs by 50 years gives a value of a life-year of 100 000 francs, which corresponds to the figure quoted by the Supreme Court. Whether or not 100 000 francs is the appropriate threshold for one year in perfect health is of course a political matter. The high standard of living in Switzerland might well imply that an average Swiss citizen's willingness to pay for a QALY exceeds this threshold. On the other hand, it is certainly doubtful that the average citizen would accept the 16.5 million francs per QALY in the Myozyme case.

The valuation of life, by the way, is really a decision we make all the time. In a hurry, we sometimes cross a dangerous street even though we may end up dead in the worst case. Many of us also voluntarily engage in additional risks such as rock climbing, skiing off-piste or riding motor bikes; risk for fun is the trade-off in these cases, and it always involves a valuation of life. If individuals do it, the government acting on their behalf should to do it as well in order to allocate resources among health and safety purposes in a more rational way. It is noteworthy that a government allocates rations when defining the public health basket. It does

not deprive citizens of services since they can, on principle, access medical care through private markets. The public coffers would be overstrained in no time if they were required to cover all medical services that are available today and that will be in the future. Recent studies indicate that the share of health care costs in the gross domestic product of the USA could rise as high as 40 percent by 2050 [6]. It is unimaginable that the government or a social health insurance collect 40 percent of the citizens' income and reallocate it to their medical needs. The expected efficiency loss of such an endeavour would be huge. Confining the social health basket represents a major challenge for governments in the Western world. Nobody knows how societies will deal with it, but quite obviously there is no way around this decision.

The Supreme Court ruling on Myozyme concerned an identified life rather than a statistical life. Does the above reasoning still apply? Two further points are of relevance here. First, the success of treating the Pompe's disease patient is doubtful. Even if the patient's health did improve, it is difficult to relate this causally to the drug treatment. The Supreme Court convincingly argues that, if outcomes are uncertain, it is the expected value that is relevant not the individual outcome. Second, the drug treatment cannot stop the progression of the illness, which will finally lead to an early death. Hence, this case is not about the successful treatment of a life-threatening illness, which might allow for a rule of rescue. The concept of the value of a statistical life thus fits this specific case quite well, making the Supreme Court's ruling a wise decision.

Why is the ruling also just? If money is spent for one purpose, it will not be available for other uses. It must therefore be allocated to those uses that provide the highest value to society. To the extent that the citizens of Switzerland are all equal before the law, the good is also the just.

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