Social Values and Health Priority Setting Case Study

Title of Case Study	**Hematopoeitic Stem Cell Transplantation (HSCT) for Severe Thalassaemia in Thailand**
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Date of Submission	**18 July 2012**
Case Summary (approx. 350 words) Please include information here about why the case is of particular interest	This case is indicative of priority-setting problems which are particularly acute in low to middle income countries where life-saving or life-improving technologies are coming to market but where the infrastructure and financial resources are not yet available to make such interventions available on a large scale (even where cost-effectiveness is proven), thus raising great challenges around issues of equity. HSCT is a treatment for severe thalassaemia, a hereditary disease for which 40% of the Thai population carry traits and which 1% will develop in its severe form. HSCT is the only curative option for this disease. At assessment, HSCT for children of age 10 or younger was found to be cost-effective and within the Thai cost-effectiveness threshold. Nonetheless, limited capacity within the health system, along with the budget impact implications of increasing capacity, have proved barriers to decision making and to implementation. Further, there are also equity issues around access to the intervention which arise because of the extensive direct non-medical costs associated with this treatment.
1. Facts of the case Please include information on as many of the following as are relevant to the case: • 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-threatening, life-limiting etc. • How are the benefits of the	**Facts of the case** *Background* HSCT is a treatment for blood disorders, including severe forms of thalassaemia. Thalassaemia is caused by genetic mutations which compromise the body's ability to produce red blood cells. It causes chronic anaemia and if left untreated can cause organ damage, restricted growth, liver failure, heart disease and ultimately death. Thalassaemia is uncommon in the UK, but it is the most common gene-related hematological disease in Thailand. Approximately 40% of the Thai population (65 million) carry thalassaemia traits and about 1% have the disease. Incidence of the disease is estimated at 4,253 new cases per year. Usually infants with severe thalassaemia present with anaemia before the age of 1. Without treatment children with severe thalassaemia have a life expectancy of only a few years. Thalassaemia can be prevented by standard testing of couples intending to have children (although there are ethical issues around this in itself), however awareness of the disease is poor in Thailand, and guidance/incentives to medical professionals to test only exist in regard to pregnant women.

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?	HSCT is the only curative treatment for severe thalassaemia. The alternative (comparator) treatment is lifelong regular blood transfusion combined with iron-chelating therapy. Regular blood transfusions over a long period of time cause a build up of iron in major organs which can result in death, so iron-chelating therapy (ICT) is needed to remove this: patients must be on ICT administered via subcutaneous infusion for 8 - 12 hours per day, 5 - 7 days per week. Effective provision of ICT is often compromised by poor compliance due to the detrimental effect on quality of life, especially for young children. Further, blood transfusion in Thailand is hampered by a shortage of donated blood and by the high cost of blood screening. Life expectancy on the standard blood transfusion + ICT regime is around 30 years. *HSCT treatment* HSCT treatment involves extraction of stem cells from the bone marrow, peripheral blood or umbilical cord blood of an HLA matched donor (usually a sibling) and transplantation into the thalassaemic patient. During and for a period of months after the transplantation procedure, patients' immune systems are severely compromised: they receive anti GVHD (Graft Versus Host Disease) treatments as well as intensive antibiotics and must remain in a sterile environment for a minimum of 1-2 months, if there are no complications. If treatment is successful, they can return home but require ongoing, full-time care and a sanitised living environment often for around 1 year after receiving the stem cell replacement. Successful treatment provides a near-normal life expectancy and also restores near-normal functioning. Related HSCT is much preferred to unrelated HSCT as it offers a lower risk of rejection and other complications. Non-thalassaemic siblings are considered to be the ideal related donors. However, it is calculated that only 19% of severe thalassaemic patients will have an HLA match non-thalassaemic sibling (the average Thai family has 2 children; only 1 in 4 patients are likely to have an HLA-matched donor sibling; only 3 out of 4 of those potential sibling donors will be non-thalassaemic). For the other 81% of patients, unrelated donation is the only option, aside from the standard lifelong blood transfusion + ICT regime. The chances of finding an HLA match unrelated donor are statistically low, and in Thailand facilities for finding such donors are somewhat limited since supply relies partially on foreign donor registries. Unrelated HSCT is therefore more expensive than related HSCT due partly to administrative costs, partly to higher drug costs and also partly to higher incidence of post-transplantation complications. *Cost, cost-effectiveness and distribution of benefits across patient population* Compared to blood transfusion + ICT, the ICER of related HSCT was estimated at between 80,700 to 183,000 Thai Baht (THB) per QALY gained (£GBP 1,600 - 3,700). Unrelated HSCT was estimated at 209,000 to 953,000 THB per QALY (£GBP 4,200 - 19,300). In both cases, the cost per QALY increased with the age of the child, as the greatest benefit of HSCT is gained by younger children. Older patients who

had been on blood transfusion + ICT treatment for some years had poorer outcomes, higher rates of complications and a higher post-transplant mortality rate due to more progressive disease and the iron overload effects of prolonged transfusion.

The cost threshold in Thailand (based on societal willingness to pay) is between 100,000 and 300,000 Thai Baht (£GBP 2,000 - 6,000) which approximates to one to three times per capita GDP. The WHO suggests that technologies below the per capita GDP are very cost-effective, those between one and three times GDP are cost-effective, and above three times are not cost-effective (WHO, 2002).

At a cost-effectiveness threshold of 100,000 THB per QALY, the probabilities that related HSCT would be cost-effective were 81%, 59% 29% and 18% for patients aged 1, 10, 15 and 17 years respectively. At a threshold of 300,000 THB per QALY, the probabilities that related HSCT would be cost-effective were 96%, 88%, 70% and 60% for patients aged 1, 10, 15 and 17, respectively. For unrelated HSCT: at a threshold of 100,000 THB, unrelated HSCT is not cost-effective when compared with blood transfusion + ICT; at a threshold of 300,000 THB, the probabilities that HSCT would be cost effective were 68% and 54% for patients aged 1 and 10 years, respectively.

There are significant direct non-medical costs attached to HSCT treatment, especially in the Thai context. There are currently only 6 HSCT centres and 16 HSCT specialists in the country: many patients and their carers must therefore either travel or temporarily re-locate to cities where the HSCT centres are located. Additionally, the pre- and post-treatment care required means that, usually, at least one caregiver has to give up work to look after the patient. Direct non-medical costs to be borne wholly by families are estimated to be around 500,000 - 2,000,000 THB (£GBP 10,000 – 40,000) on average for the approximately time since pre-treatment until post-treatment periods (as an indication of affordability - the average teacher annual net income is 192,000 THB, dentist/GP is 375,000 THB, bus driver is 96,000 THB). Costs of loss of income for caregivers who give up work or take extended leaves of absence are additional to these costs.

Budget impact
Budget impact analysis was carried out on the basis of 200 new cases of treatment of related HSCT each year, out of 800 eligible cases. This was not based on the number of new cases of severe thalassaemia but rather took a practical perspective and was based on the current capacity of the health system and on related rather than unrelated HSCT for similar reasons - capacity is even more restricted in the case of unrelated HSCT due to limited donor pool etc. Naturally, if related HSCT were adopted and capacity for treatment increased, there would be improved economies of scale and therefore increased cost-effectiveness.

On the basis of 200 cases of treatment per year, the budget impact of HSCT was initially significantly higher compared to blood transfusion+ICT (98 million THB for HSCT compared to 7 million THB for blood transfusion + ICT). However, whilst the number of patients receiving lifelong blood transfusion + ICT will increase continuously over time, the number of patients receiving HSCT will *decrease* due to the curative nature of the

	intervention, with costs dropping off significantly after the first two years of treatment as the need for ongoing care diminishes. Hence, the difference in budget impact between the blood transfusion+ICT regime and related HSCT gradually decreases and over a longer time span the difference would eventually become negative - i.e. HSCT would become not only the more cost-effective but also the *cheaper* option in terms of budget impact.
2. Policy decision: process	**Policy decision: process**
Please include information on as many of the following as are relevant to this case: • 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? • 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?	The policy decision in the case of HSCT related to whether it should be included in the Universal Coverage (UC) scheme, upon which 80% of the Thai population rely for provision of healthcare. The National Health Security Office (NHSO) manages the Universal Coverage scheme and decides what it will include. HSCT (both related and unrelated) is already provided under the two 'superior' health insurance schemes in Thailand - for government employees and their dependents enrolled in the Civil Servant Medical Benefit Scheme (9% of the Thai population) and the Social Security Scheme (11% of the population). The NHSO requested an economic evaluation of HSCT as a result of the topic selection process carried out by the Health Intervention and Technology Assessment Process (HITAP), the institution responsible for assessing health technologies in Thailand. HITAP invites national public health agencies to submit the list of interventions they consider to be priorities for assessment, and selects the most commonly suggested of these proposals for assessment. HSCT was selected interventions for assessment in 2007. HITAP carried out a cost-utility and budget impact analysis of HSCT. HITAP's research methods, process and policy recommendations for each of the interventions it assesses are available from its website, and additionally it regularly publishes its research in peer-reviewed journals. HITAP presented its findings and recommendations twice to the NHSO Subcommittee for Development of the Health Benefit Package and Service Delivery. The Subcommittee meets in closed sessions, although representatives from HITAP and from the public health agencies involved in the topic selection process are invited and a record of the summary of the sessions is available on request from the NHSO, but this usually includes only the decision made, not the content of discussion. The public health agencies who propose the topic for consideration for inclusion in the UC package can appeal to the NHSO for them to re-consider a decision, but this did not occur on this occasion. As an assessment body, HITAP cannot appeal against a decision of the NHSO if it goes against its recommendations.
3. Policy decision: content	**Policy decision: content**
Please include information on as many of the following as are relevant to this case:	HITAP's study found that: • related HSCT was the most cost-effective treatment option for severe thalassaemia patients under 10 years of age (ie. it is more

- 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.

cost-effective than the conventional blood transfusion + ICT regime in QALY terms)

- Initial budget impact of related HSCT for severe thalassaemia patients under 10 years of age was significant, related to blood transfusion + ICT (91 million THB). However, due to the curative nature of HSCT and relatively short treatment time compared to the continuously increasing costs of lifelong blood transfusion + ICT, HSCT would have the lesser budget impact over time.

HITAP recommended to the NHSO that related HSCT be approved for inclusion in the Universal Coverage scheme for use in severe thalassaemia patients under the age of 10. HITAP presented the results of its study twice to the NHSO subcommittee in 2007, but the subcommittee failed to reach a consensus and made no decision on whether to include HSCT on the UC list at that time. It was thought that the reasons for this were the large initial budget impact of the intervention compared to the existing regime, along with the limited capacity for delivering HSCT treatment within the existing infrastructure.

The subcommittee has since reconsidered the issue and approved HITAP's recommendations in principle on the basis of equity and disease severity considerations, but postponed implementation until after the results of a feasibility study on how to increase capacity for providing both related and unrelated HSCT.

Relevant social values

Issues of social values arise around the equity of access to treatment, because of the limited availability which results from problems of budget impact and limited capacity for providing the treatment as follows:

- If only 200 patients could be treated, as per the analysis in HITAP's study, there remained the problem that HSCT treatment would not be available even to the remaining 600 patients who could take advantage of an HLA matched donor sibling. The issue of equity which arises here is how to determine which 200 patients should be selected from the possible 800 who have HLA matched donor siblings.
- Clearly, this problem of rationing would be resolved, or at least lessened, if wider access to the treatment could be provided. However, although the subcommittee recognized that related HSCT treatment was cost-effective and that the long term budgetary implications showed HSCT to be the cheaper option, nonetheless the initial budget impact of providing treatment to 200 patients is high, compared to the existing transfusion + ICT regime.
- Importantly, there is very limited capacity in the health system for providing this treatment - only 6 centres across the country and only 16 trained specialists (it can take up to 5 years in Thailand for a clinician to train in HSCT techniques). This means that, notwithstanding the budget impact implications, it would be a challenge to treat more than 200 cases per year *anyway*, given the intensity of the care and specialist attention required. Of course increasing capacity would involve budget impact in itself, but it also involves time - especially in the establishment of centres and the training of specialists.

4. Discussion	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. • Anything else you think significant or interesting about the decision.	The social values issues most prominent in this case centre around challenges of equity in a situation where limited capacity and budget impact restrict access to the intervention in question. Some of these equity issues are as follows: • *How to determine access to related HSCT for only 200 patients amongst the 800 potential candidates (ie. those with an HLA match non-thalassaemic sibling) - which 200 patients get access and on what basis?* One option would be to determine access on the basis of which patients gain most benefit from the intervention. This would also be advantageous from a cost-effectiveness perspective since it would improve the cost per QALY gained. Since the younger the patient, the better the outcome from HSCT treatment, the rule for determining access would thus be that, say, patients under 2 are prioritized. However, it is possible that there may be more than 200 patients under 2 who present for treatment: the principle for access then by default turns into 'first come first served'. Can this be justified to the parents of the 201st 2 year old thalassaemic patient? Another option would be to determine access on the basis of severity of disease. This would likely lead to prioritization of older children since their disease would be more advanced. Thus it would point in the opposite direction from the previous option where younger children were prioritized and where best outcome was part of the criteria: in cases where the disease is more advanced and where there may be problems of iron build up in organs resulting from blood transfusions, complications are more likely and health outcomes therefore not as good as those with less advanced disease. Priority might also be given to younger children not on the basis of health gain but rather on the basis of 'fair innings', albeit in a much shorter time frame than that to which the concept usually refers. That is, younger children could be prioritized on the basis that a 2 year old child has simply had fewer life years than a 10 year old. However, whilst HSCT is the only *curative* treatment available, it is not the *only* treatment available, hence it is not that the 2 year old's life is being *saved* but rather that it is being *improved.* On this basis, it is possible to argue in the opposite direction that in fact it is the 10 year old who should be prioritized given that they have already suffered with the disease - and a treatment regime which is detrimental to quality of life - for 10 years whereas the 2 year old has suffered for only 2 years. This also raises the wider issue, outside of HITAP's recommendations, of limiting the treatment to children under 10, since those over 10 will clearly have suffered with the disease for an even longer period of time. There are numerous other options for determining access - for example, a simple 'first come first served' principle or a lottery approach. Are these strictly impartial and 'patient-blind' approaches any more or less equitable than those which take account of specific (relevant) features of individual patients?

- *Related versus unrelated HSCT*

  Whilst there are numerous equity issues relating to allocation of resources to potential *related* HSCT patients, there is also the fact that the vast majority of severe thalassaemia patients do not have the option of related HSCT since they are either single children or have no HLA matched non-thalassaemic sibling.

  Unrelated HSCT was shown in HITAP's analysis to be cost-effective at the higher threshold of 300,000 THB at a probability of 68% for patients aged 1, reducing to 54% for patients aged 10. Not only cost-effectiveness was considered as the main issue in HITAP determining whether unrelated HSCT would be recommended, but also the fact of limited system capacity and the feasibility of obtaining HLA matched material from donors.

- *Non-medical access issues: direct non-medical costs and disease/treatment awareness*

  The direct non-medical costs related to HSCT treatment are significant, in terms of costs of travel, food, accommodation and so on, and in costs of loss of earnings for caregivers. Some HSCT specialists have established bursary funds to help families with non-medical costs, but these are very limited. These considerations played no apparent role in the subcommittee's decision but in practice they may have a significant effect in terms of equity.

  It is possible that those relevant costs could in effect condition access to related HSCT treatment, even in cases where the child was one of the 200 prioritized for treatment. If the families were unable to afford these costs, and no financial help were available to them, it is possible that they would have to allow their child to remain on the blood transfusion + ICT regime.

  Awareness of thalassaemia and of treatment options is low amongst the poorer sections of society in Thailand, despite efforts over the last 20 years to improve it. Awareness of treatment options are much higher in the most educated and economically advantaged groups, with these parents becoming increasingly well informed with regard to HSCT and pushing for access.

  Lack of awareness amongst poorer patients and their families means that they do not ask about the possibility of HSCT treatment, and medical professionals often do not offer it as a possibility to them, aware of the current lack of UC coverage, but also the system capacity issues and the associated direct non-medical costs.

  So there is the possibility of 1) rationing by ignorance whereby only the more educated in the population even get to know about the treatment in order to consider accessing it; and 2) rationing by virtue of non-medical costs, whereby only wealthier families could afford to travel to HSCT centres in the cities (although this could change with increased system capacity and more HSCT centres).

	More generally, however, this case is indicative of priority-setting problems which are particularly acute in low to middle income countries where life-saving or life-improving technologies are coming to market but where the infrastructure and financial resources are not yet available to make such interventions available on a large scale, thus raising great challenges around issues of equity. In this case, it is evident that infrastructure and financial limitations, along with the equity problems they raise, proved to be a major barrier to policy formulation and implementation, even in a case where cost-effectiveness had been proven, thus demonstrating how economic analyses alone are insufficient in guiding practical policy decisions where equity issues are so pressing. Given the significance of system capacity issues in this case, the question also arises of how to deal with 'hard facts' in terms of justifying restrictions on access to treatment. Whilst 'limited capacity' alone may be insufficient justification for denying access to treatment - whilst there is *any* capacity, decisions about who gets access to those limited resources must be justified in terms of equitable prioritizing - does it carry no weight in justifying restricted access to treatments? It is surely a *reason*, even though perhaps not a *justification*.
5. References/Links to relevant documents	
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