Institute and Faculty of Actuaries

What if… artificial organs were sufficient enough to replace the need for donors?

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Impact on the Term Assurance and Critical Illness products

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Title

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Abstract

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Introduction

A "what if" question is an extremely useful question: it enables us to enter the realm of possibilities, identify the most likely scenarios and think through the potential consequences. Based on this analysis, we can highlight the areas that we need to look into now in order to better prepare ourselves for the future.

This article provides a history of organ transplantation followed by a detailed focus on the waiting list that exists in the UK. We explore the demand and supply side factors that explain why there is a shortage of organs and probe further into how these factors could change in the future. Finally, if artificial organs were sufficient to replace the need for donors, what would be the impact on our insurance industry?

Main text

1. A history of organ transplants

The first organ transplant carried out to treat organ failure took place in 1906 in Lyon, France. The procedure involved using a pig kidney and a goat kidney to treat two patients with renal failure. Survival times were poor with the first patient dying after 3 days and the second after 9 days[1]. The issue of organ rejection was a major obstacle then, as it remains to this day. Without dialysis machines available at that time, there were no real alternatives to having the operation.

The first successful transplant using a *human* kidney was in 1933 when a surgeon in Kiev[2] carried out an operation on a woman who attempted to commit suicide through ingesting mercury. It was successful because transplanted kidney functioned in excreting urine, however, the patient died after

48 hours. The post-mortem reported that death was probably due to the donor kidney not being preserved well enough, a mismatch in their donor-patient blood groups and lasting damage from mercury poisoning.

The 1950s saw a change in practice where organs from live donors were used, for example from relatives or those willing to donate. However, even with the use of these 'fresh' kidneys, organ rejection was still a challenge. This issue was bypassed in 1954 in Boston, USA when surgeons carried out the first successful kidney transplant, on identical twins[3]**.** The transplanted kidney lasted 8 years

Liver transplantation has been a comparatively more challenging procedure. Initial attempts at liver transplantation began in 1963 but attempts were unsuccessful due to multiple site infections. 1967 saw the first liver transplant where the patient survived for more than a year[4]. Further medical advancements over the next two decades, such as improvements in patient selection, perioperative management and postoperative immunosuppression were required before liver transplantation could be widely considered as a successful treatment for patients with liver failure[5].

The first successful human heart transplant was performed in Cape Town, South Africa in 1967 by Dr Christiaan Barnard. He is the brother of Dr Marius Barnard, who was instrumental in the introduction of 'dread disease' insurance in South Africa. Dread disease had the aim of providing financial support to people adversely affected by heart attack, stroke and cancer and has since evolved into today's Critical Illness product. Similar to liver transplants, initial outcomes of heart transplants were very poor. The classification of histological rejection and the use of ciclosporin, an immunosuppressant drug, in the early 1980s improved outcomes for patients.

2. Where are we now?

As at the end of September 2016, there were 6,599 patients on the NHS waiting list for an organ transplant. Whilst the number of patients on the waiting list has dropped in recent years (from around 8,000 in 2010), the numbers are still higher than they were in 2005.

Table 1 show that the one-year survival rates in the UK have increased over the last two decades. This is primarily due to technological advances. Both kidney and liver transplants have around a 95% one-year survival for transplants carried out in the 2011-14 periods, compared to 83% survival over the 1994-95 period. Heart transplant survival has increased from 77% to 84% over the same period.

	% one year transplant survival (No. at risk on day 0 in parenthesis)		**Increase in survival %**
	1994-1995	**2011-2014**	
Kidney	83% (2,579)	96% (3,261)	13%
Heart	77% (621)	84% (516)	7%
Liver	83% (905)	94% (1,785)	11%

Table 1: One year transplant survival rates. (Source: NHS Organ Donation and Transplantation Annual Activity Reports[6])

Table 2 show that the five-year survival has increased even more; from 69% for kidney transplants over 1994-95 period to 90% in the 2008-2010 period, an improvement of 21%. Comparably, heart and liver transplant survival has increased by 8% and 18% respectively.

	% five year transplant survival (No. at risk on day 0 in parenthesis)		**Increase in survival %**
	1994-1995	**2008-2010**	
Kidney	69% (2,579)	90% (2,185)	21%
Heart	63% (621)	71% (270)	8%
Liver	64% (905)	82% (1,144)	18%

Table 2: Five year transplant survival rates (Source: NHS Organ Donation and Transplantation Annual Activity Reports)

However the existence of a waiting list is a worry

for many patients with end stage organ failure. In the 2015, 479 patients died whilst on the transplant list[7].

3. Why does the waiting list exist?

Simply put, the waiting list exists because the demand for organs outstrips the supply.

The demand for organs can come from lifestyle habits such as excessive alcohol intake and smoking, leading to organ damage and diseases such as cancer. The demand could also arise from accidents such as poisoning or physical trauma. Finally, senescence, the general deterioration of organs with ageing and wear and tear could give rise to a demand for organs in older lives.

The supply for organs could come from human donors, xenotransplantation (use of organs from animals), artificial organs and the stance we have on organ donation consent (opt-in or opt-out).

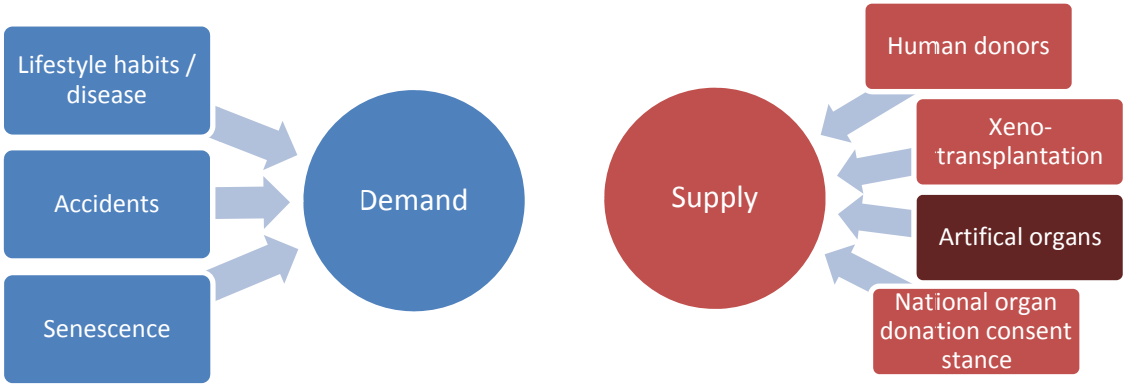
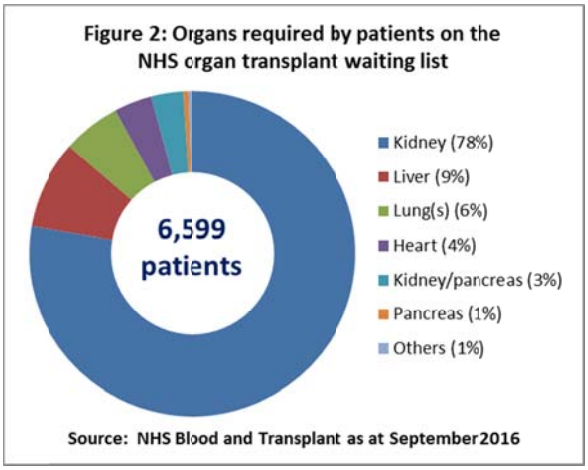


Figure 1: Demand and supply for organ transplants

The NHS with its patient database and operation theatres are where the demand and supply are matched. The overall capacity in the NHS could be a restrictive factor in matching demand and supply. Whilst the number of operating theatres has steadily increased from 2,200 in 1997 to around 3,200 as at the end of 2016[8], shortages in surgeons and nurses could restrict the speed at which organ transplants are carried out.

3.1. Which organs are in demand?

More than three quarters of patients (78%) on the waiting list require a kidney transplant. This could be as a result of diabetes, an infection or prolonged blood pressure leading to chronic kidney failure.



9% (roughly 580 patients) require a liver transplant; which could be as a result of some inherited liver disease, viral infection, autoimmune diseases, liver cancer or other toxins. These diseases cause the liver cells to die and scar tissue to form, resulting in loss of function.

6% (375 patients) require a lung transplant. Chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis, cystic fibrosis or pulmonary hypertension gives rise to the demand for a lung transplant.

Only 4% (245 patients) require a heart transplant. Diseases such as cardiomyopathy (where heart muscles are weakened or stiffened), myocarditis (inflammation of heart muscles) or coronary heart disease (blockages in blood vessels) could lead someone to require a heart transplant.

The demand for organs is likely to rise in the future. Whilst smoker rates are at an all-time low, urban air pollution along with more people working in cities is a concern for COPD rates. Obesity trends are also likely to lead to future demand in organs, in particular an increase in demand for kidney and heart transplants. It is estimated that obesity accounts for 80-85% of the risk of developing type 2 diabetes[9]. It is also estimated that 1 in 20 cancers in the UK are linked to being overweight or obese[10] (with stronger links to bowel, breast, kidney and oesophagus).

Demand for organs as a result of accidents is low but with an increasingly ageing population, senescence is likely to increase the future demand of organs. These changes in the underlying population may be different to the insured population, once we take into account socioeconomic class and lifestyle habits, for example, with higher smoker prevalence in lower socioeconomic class[11].

3.2. A closer look at the supply of organs

There were around 4,500 organ transplants carried out from April 2015 to March 2016 in the UK, arising from around 2,300 human donors. 78% of these organs came from deceased donors, whilst the remainder, in particular liver and kidney transplants came from living donors.

3.2.1. Human donors

With the main 'supply' being human donors the key challenge lies in matching the organs to the patient by tissue, blood type and other medical criteria, in order to decrease the chance of organ rejection. To manage organ rejection, where the patient's own immune system attacks the transplanted organ, the immune system is often repressed to decrease this risk. However a weakened immune system increases the risk of viral and bacterial infection, so a careful balance is required in terms of medication.

3.2.2. Xenotransplantation

In xenotransplantation, transplanting heart valves from pigs is a common procedure. Here, the pig cells are chemically stripped away before human cells grow around it, after implant. However, there are known issues with transplanting whole organs, namely the rejection of animal tissue, whether the organ itself could function in the human body and whether there is a danger of infection from animal viruses.

3.2.3. Artificial organs

Artificial organ technology is currently used as a stopgap before patients receive a biological organ. A company called SynCardia Systems[12] in the US provides patients with a fully functioning artificial heart. One patient was supported for nearly four years with the artificial heart before receiving a successful human heart transplant.

The University of California, San Francisco[13] has created an artificial kidney to tackle end stage renal disease with human trials scheduled for this year.

The liver has been much harder to replicate artificially. Liver cells carry out as many as 500 different functions and the liver is the only organ that can naturally regenerate lost tissue; even as little as 25% of a liver can re-grow to full size (unless the liver is cirrhotic)[14]. Portable artificial livers do not currently exist; we only have large dialysis machines. The Molecular Adsorbent Recirculating System (MARS) is an example of an artificial liver where the blood is taken out of the patient and passed through a blood, albumin and renal circuits to rid the blood of toxins and then reintroduced back to the body. You can also have a Bioartificial Liver (BAL) systems where hepatocytes (cells that make up 70-85% of liver mass) from either human or animal origin are used to clean the blood. Continual progress is being made to refine various systems however; the challenge of creating a device that grants patients with substantial survival benefit compared to intensive care still remains[15].

3D bioprinting technology is currently at the stage where tissue can be printed with capillaries, where these tiny channels allow vascularisation to take place so that cells can sustain themselves and survive[16]. In July 2011, surgeons carried out the first synthetic windpipe transplant by creating an exact replica of the patient's windpipe using 3D printing technology and soaking it in a solution containing stem cells taken from the patient's bone marrow[17]. After two days, the millions of holes in the porous windpipe had been seeded with the patient's own tissue.

The Wake Forest Baptist Medical Centre in North Carolina, USA has grown kidney cells, placed them on an artificial renal device and implanted it in animals. These cells were able to form kidney structures and produce urine-like fluid (LINK). After this success, they were able to design a 3D printer that could print a kidney prototype. The device is still experimental and requires further testing. The same company has also been able to use human liver cells to successfully engineer miniature livers that function in a laboratory setting. The next challenge would be to test this in animals and then grow billions of liver cells in one go to produce a large enough liver for human transplant.

The artificial organ market is expected to grow at 9.1% compound per annum from 2017 to 2022 from $26.8 billion in 2016 to $45.2 billion by 2022[18]. Given the lower risk of organ rejection and the ability to mass produce organs in order to meet the demand, it is a very promising industry that could solve the current organ supply shortage.

3.2.4. National organ donation consent stance

The national organ donation stance can have an influence on the availability of organs. A panel study of 48 countries over a 13-year period (2000 to 2012) that had an opt-in/opt-out consent showed that opt-out consent is "associated with an increase in the total number of livers and kidneys transplanted"[19]. However, it also noted that in France and Brazil, adopting an opt-out stance had a detrimental effect on donation; partially attributed to mistrust in the medical profession.

Figure 3 England, Scotland and Northern Ireland currently have an opt-in stance, where people need to sign up to the organ donation register in order to donate their organs on their death. In December 2015, Wales introduced a soft 'opt-out' system for consent, so people can either register to opt-in or opt-out but if they do nothing, they are regarded as having no objection to donating their organ (i.e. deemed consent).

In a 2008 review of UK's consent stance, the Organ Donation Taskforce concluded that an opt-out system "should not be introduced in the UK at the present time"[20]. They noted that the investment required may not generate additional donors and that alternative method of improving public awareness and investing in the organ donation infrastructure could increase donor rates.

4. Considerations for the insurance industry

Major organ transplant is a listed condition under a typical Critical Illness product. In 2014, the Association of British Insurer's (ABI) amended the major organ transplant definition under its Statement of Best Practice (SoBP) to include the qualification 'from another person'.

2014 ABI definition

Major organ transplant – *from another person*

The undergoing as a recipient of a transplant *from another person*, of bone marrow or of a complete heart, kidney, liver, lung, or pancreas, or inclusion on an official UK waiting list for such a procedure.

For the above definition, the following is not covered:

Transplant of any other organs, parts of organs, tissues or cells.

4.1. Short term impact: the next 5 years

In the short term, we anticipate a limited impact on the Critical illness product. If someone required an organ transplant, they would go on the waiting list and this in itself would be a trigger for a CI claim under the existing definition. Thus, it does not matter whether a transplant comes from a human donor, from an animal or an artificial source, or indeed if the operation happens at all.

For mortality products, by carrying out an artificial organ transplant, we're effectively delaying the death of a policyholder from organ failure. The SynCardia artificial heart transplant patient who survived for nearly four years before a human heart transplant is a good example of this. However, the extent of such improvements on mortality would be small as it is restricted to the minority of policyholders who require an organ transplant in the first place.

4.2. Medium term impact: 5 to 25 years

As the organ transplant technology develops, artificial organs are likely, in my view, to play an increasingly important role in organ transplant procedures. The timeframe for this will depend on the organ in question, with artificial heart transplants already being carried out and artificial kidney development looking promising. These two organs alone would reduce the current waiting list by more than 80%.

The key benefits of artificial organs are that they open up the possibility of mass production and patients are less likely to suffer from organ rejection. Subject to continued technological progress and capacity in the NHS, transplant waiting lists could significantly reduce or even disappear altogether.

Currently, being placed on the waiting list for an organ transplant by itself triggers a Critical Illness claim payment. Should the availability of artificial organs mean that the waiting list disappears, it will start to matter much more whether the policyholder receives an organ from a human donor or from an artificial source. There may be a period of uncertainty here, where the industry questions whether artificial organ transplants warrant a partial or full sum assured payment. However, given that the risks are much lower, the conclusion may be that artificial transplants are not as life threatening as human donor transplants.

Another potential grey area for a valid payment is if the transplanted organ was a bioartificial organ or if it was grown in a laboratory using human cells. Would the payment still be declined because it the organ did not originate from a human donor?

It should be noted that if 'liver failure' or 'emphysema' (lung failure) are covered as separate conditions in a CI product, a payment could be made under these definitions, irrespective of whether we meet the claims trigger for organ transplant.

If we assume that we only use artificial organs for major organ transplants, the current CI definition would lead us to have zero incidence rates (assuming we stick firmly to this definition). Realistically, even with zero incidence rates for a typical CI product, the overall price would only reduce by about 1% (assuming the demand for organs remain fairly stable); since the magnitude of these rates are small.

On a typical term assurance product, the direct impact is also fairly small. Those lives on the waiting list that would have died would now get an artificial organ, meaning that their deaths would be delayed (until they die of some other cause). The mortality improvements would increase if artificial organ transplants become a routine procedure. It is the long-term impact of using artificial organs that is likely, in my view, to have the most significant impact on the insurance industry. Forecasting the changes in the supply and demand of organs, as well as changes to the underlying demographics and other medical advances is extremely uncertain.

4.3. Long term impact: 25 years+

In the long term, there are significant benefits to using artificial organs. We could eventually get to a stage where currently complex organ transplant procedures become routine with little risk of organ rejection. Say you're a smoker and you find that your lungs are working at a sub optimal capacity; well you can get yourself a new set of lungs. Furthermore, you can do this whilst you are still relatively healthy.

By using artificial organs, the incidence rates of the other conditions on a Critical Illness product could start to come down. A person diagnosed with a localised cancer where the severity is not high enough for a claim payment could have the affected organ replaced. Therefore, insurers would not need to pay out on this cancer progressing in the future. Similarly, those at risk of heart attacks as a result of the organ itself could get an artificial heart. This argument above still holds if xenotransplantation becomes the solution for the organ shortage, although concrete evidence of overcoming its disadvantages remains to be seen.

A society where artificial organ transplants are a common procedure may not exist if the costs of carrying out these procedures are prohibitively high, especially in the current age of austerity and cutbacks in NHS budget. However, as artificial organ transplant technology matures, the marginal cost of reduces and it starts to make financial sense to replace a diseased organ, rather than treat the symptoms.

On a term assurance product, we can start to see further mortality improvements; not only from those with organ failure but from other diseases too. For example, those that would have died from localised cancers or cardiovascular diseases could have their organs replaced and deaths delayed. The overall impact will depend on the speed at which the technology gets incorporated into mainstream medicine.

Conclusions

There have been substantial advancements in organ transplant technology resulting in improved survival times; 5-year survival times for a kidney transplant is 90% as at 2008-10, compared to 69% from 1994-95. However, the current reliance on human donors not only makes organ rejection a key hurdle to overcome, it also restricts the overall supply and leads to a waiting list.

The use of artificial organs could overcome both issues; there is significantly reduced incidence of organ rejection and the organs themselves could potentially be mass produced. However, whilst artificial organ transplants have been carried out worldwide, these operations are currently used as a stop-gap before patients receive a non-artificial organ.

The use of artificial organs is unlikely to have any impact on the CI product in the short term and a very small improvement on term assurance policies.

In the medium term, as the technology matures, costs decrease and artificial organ transplants become routine; the increased supply of organs is likely to reduce and potentially eliminate the waiting list. Without the waiting list, the current CI definition for organ transplant means the policy will pay-out if the policyholder receives a human organ but not if it is an artificial organ. Given this wording, we could start to reduce the incidence of the major organ transplant condition. On the term business, you are likely to see small improvements in mortality.

In the long run, if artificial organ transplants could become a cost effective way of treating multiple diseases; anyone with a cardiovascular disease or localised cancers could have the affected organ replaced, thereby potentially reduce the incidence of heart attack and cancers on our CI business. The impact on term assurance policies could be significant; if we can delay the deaths of several lives by five to ten years we could see a wave of mortality improvements.

Validating and quantifying these scenarios would require a lot of assumptions about the future and could take considerable time. You would have to look at other medical advances and their respective costs, for example immunotherapy could be more cost effective at treating or preventing diseases than organ transplant. On the demand side, you could argue that the need for artificial organs is as high as ever, considering the rising obesity levels and the ageing population.

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