Dementia research: where have we been and where are we going?

There have been substantial changes in dementia research over the last 20 years. For example, we have gone from basic science to licensed treatments for Alzheimer's disease. But, more needs to be done if we are ever to get to the point of having a cure. Professor Clive Ballard, Director of Research at the Alzheimer's Society, talks to Dawn Powell about where we have been and where we need to go next.

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Dementia has a major impact on the UK, both as a healthcare burden and as an economic burden. About 750,000 people in the UK have dementia and this is expected to increase to 1·4 million by 2040. The cost of the condition to the UK, currently £20 billion a year, is also expected to rise over the next 30 years. Predictions are that it will increase to £50 billion a year.[1] However, despite it being a substantial problem in the UK, dementia has long been the poor relation of other conditions. In 2008, the Department of Health admitted that it invested eight times less money into dementia research than cancer research.[2] Professor Clive Ballard, Director of Research at the Alzheimer's Society, explains why it is vital for the development of the treatment of dementia that dementia research receives a more realistic portion of the Government's funding pie.

What does your role as Director of Research at the Alzheimer's Society involve?

I oversee the Society's research programme, particularly the strategy behind it. My role is also to represent research in the Society's management team. Another part of my job is to interact with any policy or media work that involves research.

Does the Society focus on a particular area of research or is its remit fairly broad?

The programme is very broad: it's "cure, cause and care". We cover everything from basic lab science to clinical trials of interventions in care homes. But we have put the emphasis on clinical trials, developing the evidence and translating that evidence into practice—either with drug treatments or with non-drug treatments. We have also invested in the very basic science.

The Society is unique because it has a high level of consumer involvement, which comprises of a network of 150 volunteers. These volunteers, who are people with dementia or people who care for them, help us to determine research priorities. One thing that they have highlighted as being a high priority is stem-cell biology, which the Society funds substantially. They also pointed out to us the importance of care provided to dementia patients in the general hospital setting. We now invest money into that area of research and we have also published a report on this topic as part of our campaign work. Therefore, the volunteer network influences our campaign priorities as well as our research work.

Overall, what has been the most significant research development in the last 20 years?

A significant development is that licensed drugs are now available.

It took 20 years from having the basic science in the late 1970s to having licensed treatment in the 1990s. Cholinesterase inhibitors and memantine are clearly significantly beneficial treatments, so we have stepped forward. But we still have some way to go before we are where we want to be in terms of treatment.

The second major development is in the field of genetics, which has been really important. We have now identified novel candidate genes and this has helped us to focus the basic biology on targeting specific areas for novel treatments.

Thirdly, and probably most frustratingly, is that we now have good evidence about care approaches that are particularly effective in care homes (eg. models of person-centred care and training). The frustrating aspect is that, despite the good evidence that these approaches work, they are not being implemented in practice. Therefore, the real issue is ensuring that they are used.

One of the criticisms of the available research is that the measures used to assess disease severity are unreliable. What are your thoughts on this issue?

There is a problem in how we evaluate drugs in clinical studies because the models we use are limited. In the UK, I think that this is a particular problem. If we look at the standardised effect sizes for cognitive improvement observed in the trials, it is something like 0·4–0·5, which equates to the drug having a moderate effect. If a drug with a moderate effect is considered to not be cost-effective, then that is concerning. Very few drugs are highly effective because for a drug to be highly effective, it would practically have to be an instant cure. Therefore, the bar is set very high and a treatment would need to be incredibly effective to meet that standard.

The Government[2] has admitted it spends far less money on dementia research than it does on other areas of research. What impact has this had and why has it spent less?

Public spending for dementia research is something between £25 million and £30 million a year, depending which figures you look at. But the investment for cancer research is somewhere in the region of £300 million. So there is an eight-fold difference in the funding level. It has had a huge impact.

At the moment, we are very good at the basic science but we have trouble translating the basic science into therapies. People in cancer research are very good at translating basic science into clinical therapies, and I think this is because they are able to do the number of trials required. If you have good candidate drugs, you need about 10 studies to produce one decent therapy. In dementia, we do not have the funding to do 10 trials. The net result is that it takes 20 years to produce each new drug.

The National Audit Office[3] reviewed this issue and said dementia is where cancer was in the 1950s, and I think that this is true to some extent. It is only in the last couple of years that public awareness about dementia has grown. Previously, the public perception of dementia was fairly nihilistic. As with cancer in the 1950s, dementia was ignored because it was seen as an inevitable sign of ageing or something that could not be treated. Now people are starting to recognise that it is a proper disease and that it is not just a part of ageing.

I think that the next challenge is showing people, now we have greater awareness, that we do have both drug and non-drug treatments. Also we need to show that research is not just pie in the sky and that it can actually deliver something that is tangible and beneficial.

Whoever* wins the general election will have to make substantial public spending cuts. Are you worried about how this will affect investment into dementia research?

Everyone, in whatever sector they are in, is concerned about spending cuts. The cuts will have an impact on all sorts of things, not just research but service delivery as well. But I think with dementia research, the biggest challenge is not the overall size of the pot potentially becoming smaller, but ensuring that the dementia share of the pot is realistic. At the moment, dementia's share is not proportional to the size of the problem. We also need to have a strategic plan in place so that we know which areas of dementia to investigate.

* Interview took place before the general election

On a wider scale, how has the global recession affected research?

Pharmaceutical companies across the board have been affected, and I do not think that dementia has been disproportionately affected. Certainly, companies have invested less money into research during the past year and are a lot more targeted in their activities. In the current economic climate, I do not think we will see a growth in funding from the pharmaceutical industry.

However, I think that there are ways around the decreased

investment. For example, the pharmaceutical industry could work with academia in research, which I think could be attractive to both parties. Traditionally, academia has had reservations about working with the pharmaceutical industry but actually the industry does bring a lot of investment into research. If we are going to harness the limited resources effectively, we need to find a way of making it work for all parties.

The use of antipsychotics in dementia has become extremely controversial. Why is there this controversy?

Of the 18 randomised controlled trials we have for the use of antipsychotics in dementia, only nine have been published and the bias has been towards publishing the positive studies. Antipsychotics are prescribed more than they should be, and the Department of Health found that probably 70–80% of the prescribing is unnecessary.[4]

But the biggest problem is the long-term use of antipsychotics. Risperidone is only licensed for severe aggression and only for six weeks, and other antipsychtoics are used off licence. NICE[5] states antipsychotics should not be prescribed for longer than 12 weeks, so we have very clear guidance about how we should use these drugs. The reality is, though, antipsychotics are used for one to two years. So, there is a huge disparity between the guidance and what is happening in clinical practice.

If we do not use antipsychotics, what are the alternatives?

One alternative is to use common sense and monitoring. Behavioural symptoms often present at a particular point and they often resolve fairly quickly, after support is provided to the patient during that period of time. Therefore, you do not always need to rush in with the antipsychotics.

There are also very simple non-drug measures that can be used that are very effective, such as short periods of social interaction. But, I think these types of approaches do require staff with some level of training and that is often the problem (ie. the relevant staff currently do not have this type of training).

Sometimes, doctors need to re-evaluate the options. Considering the level of harm associated with the use of antipsychotics, the benefit for an individual must be high. Therefore, if the patient has moderately distressing symptoms, they may be better off having that moderate distress than taking an antipsychotic. Antipsychotics should only really be used for people with an extremely high level of distress.

What about the pharmacological alternatives?

We have three compounds that are potential alternatives to antipsychotics: carbamazepine, citalopram and memantine. The evidence base for both carbamazepine and citalopram consists of small randomised controlled trials that show benefit for treating behavioural symptoms in dementia.[6]

The memantine data is very different because it was taken from a post-hoc analysis of a study that investigated cognitive improvement.[6] The post-hoc data suggest that behavioural symptoms do improve, and that memantine is a safe and effective treatment. But the caveat is that patients had moderate behavioural symptoms rather than severe.

All three of the drugs have advantages, but we do need more research. At the moment, physicians have a difficult choice—do they go for a treatment where there is an evidence base but quite high safety concerns? Or do they go for a treatment that has preliminary evidence but is probably safer?

It is always an imperfect choice when you are balancing those kind of issues.

Do you think that there will ever be a vaccine?

I think we probably will have a vaccine. I think we are moving forward and there are things in development. It comes back to being a numbers game. The more things you have in development, the more chance one will be successful.

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