MND Association response to the interim report of the Accelerated Access Review

Introduction

i. Few conditions are as devastating as motor neurone disease (MND). It is rapidly progressive in the majority of cases, and is always fatal. People with MND will, in varying sequences and combinations, lose the ability to speak, swallow and use their limbs; the most common cause of death is respiratory failure. Most commonly the individual will remain mentally alert as they become trapped within a failing body, although some experience dementia or cognitive change. There are about 5,000 people living with MND in the UK. A third of people with the disease die within a year of diagnosis, and more than half within two years. There is no cure.

ii. The MND Association is the only national organisation supporting people affected by MND in England, Wales and Northern Ireland, with approximately 90 volunteer led branches and 3,000 volunteers. The MND Association's vision is of a world free from MND. Until that time we will do everything we can to enable everyone with MND to receive the best care, achieve the highest quality of life possible and to die with dignity.

iii. Funding and supporting research into MND is one of the core elements of the MND Association's mission. We typically spend over £2.5 million on MND research each year and have a research portfolio of projects amounting to over £8 million. In addition, we are spending £5 million on additional projects as a result of donations received from the Ice Bucket Challenge phenomenon in 2014.

iv. This response addresses Propositions One, Two and Four of the interim report, and presents a case study showing how a rigorous clinical trial identified the harmful effects of an apparently promising treatment that might, under the review's proposals, have been rushed into widespread use.

1. MND Association position

i. We support the aim of getting effective and proven new treatments into the healthcare system more quickly. Improved methodologies for clinical trials and streamlining of some of the bureaucracy that can hinder research would, if achieved, be extremely welcome outcomes from the Accelerated Access Review.

ii. While treatments remain experimental and unproven, however, we do not support making them routinely available. Such treatments should be made available to patients only via rigorous methodologies that will improve our understanding of their effects, in order to make sure that they can be safely used in the wider patient population – if possible – at the earliest opportunity.

iii. We question the increasing tendency in the policy discourse to assert that there is a greater appetite for risk among patients with serious illnesses. This generalisation is made on page 11 of the interim report. While it may be true that some people living with MND are willing to take more risks with their wellbeing and quality of life than might be the case for a person in full health, others highly value their quality of life – however limited – and would not wish to gamble with it lightly. We strongly urge the review to avoid condescending and trite generalisations about the value that people with serious illnesses and disabilities might attach to their quality of life.

iv. Overall, we have some concerns about the direction of the review. Accelerating access is not the same as accelerating innovation. Genuine barriers to innovation should be removed, and we will always welcome this; but we do not support short-cuts that undermine or sidestep appropriate scientific rigour. Research is a worldwide enterprise and lowering our standards may only serve to cut the UK out of the global research effort in the long term. From the patient perspective, this would reduce opportunities to participate in research, which we know is greatly valued by people living with MND. The review should be mindful of these risks.

v. The review's focus on 'transformative treatments' also strikes us as limiting. Should it be taken to mean that work arising from the review will not encompass treatments for low prevalence diseases, however great their impact on those who develop them? If so, this appears to risk perpetuating a problem that is implicit within much of the interim report's discussion: historically, the voluntary sector has been left to make much of the running in respect of rare diseases, while the NHS and Government have been insufficiently proactive. We explore this in response to Proposition One. The solution can only be better leadership and more investment from the Government, although overall the review's aim appears to be to identify solutions that do not require further investment.

vi. We question whether the NHS can deliver the role envisaged for it in the interim report, in light of the funding settlement in the recent spending review. The cuts to social care and public health mean that the conditions outlined in the Five Year Forward View have not been met, and therefore the NHS's budget will not be sufficient for it to maintain current activity levels to 2020, let alone to meet substantial new demands.

vii. We would welcome clarity on whether charities, as both enablers of the patient voice and major funders of research, will be invited to sign the concordat proposed at the end of Proposition Five.

2. Case study: diaphragm pacing

i. The MND Association recently funded a randomised controlled trial (RCT) of diaphragm pacing, a promising technique that we hoped would prolong survival in MND. The results of the trial were deeply disappointing, and powerfully illustrate the dangers of pressing a treatment into service before its efficacy has been proved – if we had pushed for earlier access to the treatment for all patients, rather than conducting a trial, we can now say with confidence that we would have hastened the deaths of many people.

ii. When MND affects the muscles that control breathing, it results in respiratory insufficiency, and eventually in respiratory failure and death. Non-invasive ventilation (NIV) is already available, and approved for use by NICE, to relieve the symptoms of respiratory insufficiency and prolong survival. This arose directly from a clinical trial co-funded by the MND Association, and subsequent campaigning to secure a NICE guideline. We hoped to identify the benefits of diaphragm pacing and secure its use in the NHS in a similar manner and therefore funded, jointly with the National Institute for Health Research (NIHR), a trial of diaphragm pacing in ALS (another, more specific, term for MND) known as 'DiPALS'.

iii. Diaphragm pacing works in a similar way to a heart pacemaker, and was originally developed for use in the spinal injury population. As the name suggests, diaphragm pacing sends an electrical impulse to stimulate the diaphragm (the main muscle involved in breathing) to contract rather than the heart muscle.

iv. Small electrical wires are connected to the diaphragm muscle during an operation under general anaesthetic. These wires are also connected to an external device that can send a regular electrical impulse to the muscle, causing it to contract. By stimulating the diaphragm muscle through controlling impulse frequency and intensity, this technique aimed to improve respiratory function to complement NIV or as an alternative to NIV in MND.

v. An open label population-based study in America had found the procedure to insert the electrodes was safe, and suggested enhanced survival times; however, this did not have a control group, instead relying on historical data from different clinics. The Food and Drug Administration (FDA) approved diaphragm pacing for humanitarian use in the USA on the basis of this study, and the technique has seen increasing uptake in America and other countries.

vi. Lead researcher, Dr Christopher McDermott, based at the Sheffield Institute for Translational Neuroscience (SITraN) said: "We were aware of the work in the United States on diaphragm pacing in MND and we wanted to know if it would be beneficial for our patients. Therefore we decided to design a randomised controlled clinical trial of diaphragm pacing in MND. Funding bodies like the NHS and NICE need this evidence of benefit before a treatment can be made available in the UK. Also, because it is a treatment that requires a major operation, we wanted to make sure beyond reasonable doubt that diaphragm pacing is worthwhile for patients, adding sufficient benefit such as living longer and a better quality of life."

vii. A total of 74 people living with MND across the UK took part in the DiPALS study, with 37 being allocated NIV alone, and 37 being allocated NIV plus diaphragm pacing. The trial aimed to recruit 108 patients, but recruitment was halted in December 2013 because of concerns about survival in the group receiving diaphragm pacing. Existing participants continued to be monitored until June 2014, when pacing was discontinued in surviving participants on the instruction of the Data Monitoring and Ethics Committee. Median survival in the group who received diaphragm pacing was 11 months; in the control group it was 22.5 months. Therefore the treatment, which was widely expected to be found to extend life expectancy, appeared to halve it.

viii. Dr McDermott said: “The results from the DiPALS study are incredibly disappointing, because as a researcher and an MND doctor you start out with some hope that this is a treatment that can be truly beneficial for people living with MND.

ix. “Unfortunately, DiPALS did not show any benefits for diaphragm pacing in MND and, in fact, our study showed that it may actually be harmful. Although the results are disappointing, it was an important study to carry out as this evidence shows us that for most people there is no benefit in having diaphragm pacing and that the major surgery needed is something people living with MND should not go through.

x. “I am always humbled by the precious time and effort individuals give up to take part in our research studies. Those individuals who participated in DiPALS have contributed enormously to ensuring we understand the effects of diaphragm pacing in patients with MND and will ensure that we now put our focus and resources on developing other treatments that may help.”

xi. Speaking to Lancet Neurology, Dr McDermott added: "I would like to see some reflection on the increasing 'nothing to lose' philosophy that is occurring, and I think we have to ask ourselves 'is it right to lower the standard of evidence required for interventions for populations such as ALS?’ Our study suggests the correct approach is usually going to have to be an RCT of some description."[1]

xii. A second randomised controlled trial of diaphragm pacing in MND, this time in France, has recently (2015) been halted following similar safety concerns.

3. Proposition One: Putting the patient centre stage

i. We agree that patients should be well informed about potential treatments in the pipeline and given access to trials and pilots. People with MND often take an active interest in research developments, and the MND Association provides extensive information about latest developments and opportunities to be involved.[2] This is an important role for the voluntary sector, but from an MND perspective we do not believe there is a gap in practice that needs filling.

ii. We also agree that patients should have a say in prioritisation, particularly given that so much research is funded by patient organisations. It is through this route that both NIV and diaphragm pacing came to be the subject of trials. In terms of evaluation and implementation, again patient organisations already make much of the running, for instance via the MND Association’s campaign for NICE guidelines on NIV and latterly MND care as a whole – none of this would have happened without a strong patient voice. The question is not why patients are not able to demand these things, but rather why the Government and NHS are not more proactive – without the patient voice, few if any of the advances in MND care over the last decade or more would have happened.

4. Proposition Two: Getting ahead of the curve

i. It is in this section particularly that we are concerned about the emphasis on the ‘truly transformative’ apparently to the exclusion of treatments for rarer diseases. If

[1] http://www.thelancet.com/pb/assets/raw/Lancet/stories/audio/laneur/2015/laneur_300715.mp3
[2] http://www.mndassociation.org/research/publications/information-sheets/ and http://www.mndassociation.org/research/mnd-research-and-you/get-involved-in-research/

this is the intended meaning, patient organisations will have to continue making the running as they do now.

ii. As currently proposed, we do not feel able to support the idea of commercial access agreements to introduce experimental treatments to wider use at an earlier stage. Treatments that are still in development should be deployed in an experimental context, although we would support effective measures to reduce costs and delays associated with this process. The importance of this is shown by the results of the diaphragm pacing trial. If such a scheme had been operational in the early 2010s, it seems possible or even likely that diaphragm pacing would have been given the proposed 'conditional yes' status, with what we now know would have been disastrous consequences. In practice, cost considerations might have prevented this, as diaphragm pacing is relatively expensive, but the point holds true: such a new mechanism would introduce very considerable risk to patients.

iii. We see more cause for optimism about the proposed new designation of a treatment or innovation as 'showing promise', which we agree might succeed in leveraging further investment. Any accelerated NICE appraisal pathway as part of this must, of course, maintain the rigour of NICE's current assessments.

iv. This section contains further proposals that have potential to be positive, depending on how they are developed: improved timescales for access to patient trials; evaluation through commissioning; new trial methodologies to accelerate evidence generation and reduce cost. If these can be developed to be as rigorous and reliable as existing methodologies, we will support them; if they are less rigorous and reliable, however, they will represent no more than short-cuts, and ultimately undermine the UK's position in scientific research globally. While we acknowledge that RCTs are not without problems, we do not share the apparently growing scepticism, reflected in the interim report, about their usefulness for even rare and rapidly progressive diseases: as we have seen, they have been used to good effect in MND.

v. We await more detail on these points from the review with interest, and some caution.

5. Proposition Four: Galvanising the NHS

i. Although the vanguards for new care models being developed under the Five Year Forward View hold some promise for embedding new ways of working in the NHS, ultimately we find it hard to be optimistic about the likelihood of the NHS being 'galvanised' successfully.

ii. Although the settlement in the recent spending review will ease the NHS's immediate cash crisis, the cuts to social care and public health spending will place additional demand on the NHS that will ultimately outweigh the new funding. The imposition of demands for seven-day working on the NHS also represent a burden that the funding calculations in the Five Year Forward View assumed would not apply.

iii. By 2020 the NHS is likely to be a highly reactive service, responding primarily to crises in patient care and unable to prioritise research and innovation. The ageing

population will bring a major growth in demand for specialists in neurological and neurodegenerative conditions, but the NHS is not recruiting the necessary additional clinicians, nor does the Government's new mandate to NHS England recognise this problem. The growing demands on the time of the neurologists we do have will make research into MND and other conditions ever harder to undertake. Any fund to redesign systems to promote innovation would therefore have to be of a substantial size and made up of new funds – not repurposed NHS funds – in order to be effective.

For further information contact:

John Kell
Policy Manager
MND Association
David Niven House
10-15 Notre Dame Mews
Northampton
NN1 2BG

020 72508450
john.kell@mndassociation.org

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