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Hyped-up Alzheimer’s drugs fail in trials

Hopes of a breakthrough in treatment for Alzheimer’s disease have been dampened after two drugs hailed as potential game-changers proved ineffective in recent clinical trials.

A drug known as LMTX, or LMTM, received extensive media coverage last summer when it was heralded as the first drug that could stop brain deterioration, while another, Solanezumab, was claimed to slow the progress of Alzheimer’s, but both claims have now been proven to be false. Robert Howard, Professor of Old Age Psychiatry at UCL, says: “Even though we think we understand what the pathways are in the stages of these illnesses and what causes the illness, it’s quite clear that our understanding is a bit simplistic.”

Professor Howard, who has been involved in Alzheimer’s research for nearly 30 years, is currently conducting the MADE study to test whether the antibiotic Minocycline can decelerate progression of the disease. The media coverage claiming that LMTX halted the decline caused by the disease was based on a report released by the company of a secondary analysis that suggested participants who weren’t receiving any other dementia medication had shown improvements. “Fifteen per cent of the patients in the study appeared to show some sort of help, but those were all patients who weren’t also taking a cholesterol inhibitor,” Prof Howard explains. "The people who didn’t get one of the two drugs were all people who came from eastern European countries or places where those drugs aren’t commonly available. And we didn’t annealies about the way the trial was conducted.”

Solanezumab may trigger an immune response that forces plaques in the brain that can cause Alzheimer’s to disappear, but a trial showed that the removal of the plaques had no effect on the progression of Alzheimer’s. “We’ve had drugs based on this principle for at least 15 years, and they’ve all failed,” Prof Howard says. “Well, they’ve all succeeded in that they’ve all removed amyloids from the brain, but they’ve failed in that they haven’t made any difference to the course of human Alzheimer’s disease.”

The reality is that there is still no drug that can slow or stop Alzheimer’s, which is the most common form of dementia and affects 850,000 people in the UK.

Promoting the best in research
Acute awareness of mental health needs

A new research study is set to create the first national report on Acute Day Units and how they can best be used to improve treatment of mental health crises.

Severe mental health crises are becoming more common. One in four people today will experience a mental health problem in their lifetime, according to a report from the Mental Health Taskforce.

The problem is that the traditional hospital treatment for such crises is both expensive and unpopular with patients.

One current alternative to hospital admissions is Acute Day Units (ADUs), which provide intensive, short-term community responses to mental health crises.

Scant information is available on the ADUs as models of care – information that is essential to develop recommendations on how these services should support people in crisis.

The AD-CARE study (Acute Day Units as Crisis Alternatives to Residential Care) was designed to provide this evidence. “It’s a national study looking at these kinds of day units as an add-on to standard crisis care,” says the study’s chief investigator, Professor David Osborn.

“There haven’t been any comprehensive studies of them in the contemporary NHS. So we want to see what they do, how good they are at looking after people who are really unwell, and what impact they have.”

The treatment that is available at ADUs can vary greatly. They can include one-to-one access to medical professionals, group sessions, psychological treatments, physical health support, and peer support through learning from others with similar problems.

His study will begin in July with a mapping and typology exercise to survey crisis teams nationally and collect standardised data on service models. Five ADUs will then be studied in-depth, with users followed up over six months to assess their treatment.

A quantitative arm will compare people who receive ADU care with those who do not, based on their readmission to an acute pathway and satisfaction with services provided. Qualitative semi-structured interviews will further analyse the value and impact of ADUs.

Finally, the Mental Health Minimum Dataset will assess admission rates and establish whether they are lower in areas with crisis systems enhanced by ADUs.

These findings will generate a comprehensive report on the value of ADUs, and recommendations about service models.

“People can die from these conditions,” Professor Osborn says. “It’s key that we get interventions that the patients value, but that the interventions also work, that they really do get people better, and that they keep people well for longer.”

A new research study is set to create the first national report on Acute Day Units and how they can best be used to improve treatment of mental health crises.
Avatar powers could help lift depression

INTERVIEW: Professor Chris Brewin discusses his ground-breaking research into the potential mental health benefits of using virtual reality as self-compassion and depression therapy

With Deloitte international financial consultancy predicting that sales in 2016 will reach $1 billion, this has been dubbed “the year of virtual reality”. But the potential of the technology goes way beyond commercial benefits.

Chris Brewin, professor in clinical education and health psychology at UCL, is studying the use of virtual reality (VR) deep immersion for psychotherapy.

“Avatar powers could help lift depression. This is the first time VR has really been used in more relational contexts,” Professor Brewin says.

Adopting the perspective of a life-sized avatar and watching it move as you move produces the illusion that it is the participant’s own body – an effect known as “embodiment”. A few moments later, they “embodied” the child, and their soothing words and gestures were repeated back to them in their new body.

The scenario was repeated three times at weekly intervals, and patients were followed up a month later. The findings suggest that VR could reduce depressive symptoms, by reducing self-criticism and increasing self-compassion.

Professor Brewin developed his interest in the therapeutic power of VR after attending a talk by one of the world’s leading authorities on VR treatment, Professor Mal Slater, of the University of Barcelona and UCL, whose research has demonstrated how embodiment triggers automatic responses, depending on the situation the avatar embodied or the situation the avatar is in.

“I thought this would be a very powerful technique for psychotherapy,” Brewin says. “I asked Mal whether he thought we could use these sorts of techniques to help people feel more self-compassion.”

They then began to design tests to assess whether they could induce those sorts of feelings, following advice from Professor Paul Gilbert, an expert in compassion-focused therapy at University of Derby.

The eight-minute scenario they developed was conducted on 15 depression patients aged 23-61 from Camden & Islington IAPT. The scenario was repeated three times at weekly intervals, and patients were followed up a month later. The findings suggest that VR could reduce depressive symptoms, by reducing self-criticism and increasing self-compassion.

“Although some clinical psychologists are using VR, particularly for fear-based disorders, this is the first time it’s really been used in more relational contexts,” Professor Brewin says.

The results show that even virtual beings can induce compassion. Three repetitions of the scenario resulted in significant reductions in depression severity and self-criticism, and a significant increase in self-compassion. Four patients showed clinically significant improvement.

“I think you need to get the person to sort of consciously imagine being in a different situation or create imaginary scenarios in their heads,” Professor Brewin says. “So it all depends on their ability to do that – to go into it.

“Lots of patients find that difficult because they may not feel that they deserve compassion, or because it makes them very uncomfortable doing it. They’re not consciously trying to do that. They’re not trying deliberately to feel self-compassion; it’s more like they’re experiencing it by being in the situation.

“We’re not telling them what to feel, we’re just allowing them to experience what it’s like to have another avatar representing themselves expressing compassionate feelings towards them.”

Professor Brewin is now applying for further funding to develop a full randomised controlled trial of a more intense treatment, based on the methods used in the initial proof of concept study, to assess the clinical possibilities of interventions using immersive VR.

He wants to use more and different scenarios in the future study, and also encourage people to use the techniques in their everyday lives between sessions. Another area he wants to test is the visuals in the simulation, as the illusion of presence remained powerful despite the crude graphics used in the pilot.

“We’re interested in whether it helps if the avatar looks more like the patient themselves,” he says. “We want to experiment a bit – like giving lip-synching to the adult avatar and seeing how the compassionate words, maybe giving them a compassionate facial expression, or changing their body shape so it’s more like the individual.

Professor Brewin believes that changing body ownership has potential benefits for a wide range of treatments.

Embodying an avatar that’s very different to their own body could help people who don’t like their body shape, or don’t want to think about their body ownership for fear that it would be like to have a different kind of body through using these techniques. People are being done that are normally very difficult and painful, seems to help a lot in reducing the distress of the procedures,” he says.

He expects a response to the funding application in February 2017. If successful, he hopes to start the three-and-a-half year study in April, involving depression sufferers recruited from Camden and Islington IAPT.

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The thing that most patients say thank you for is just being willing to carry on engaging with them.

One person came into a hospice I worked in a while ago for end-of-life care. Although he was in the last couple of weeks of life, he brought with him 24 bottles of champagne and 24 cigars, because he intended to have one every remaining day. He didn’t run out of champagne and cigars, but he did get to enjoy some before he died.

People really share their lives with you when you’re involved in palliative care, and that’s very much a privilege. We can’t control everything, so we’re looking for different measures of success when we’re not able to provide a cure.

So what does success look like in that context? It involves going back to basic definitions of palliative care around providing for their physical needs, but taking fully into account their social, psychological and spiritual needs. In terms of specific goals, it needs to be tailored to the individual.

I first got involved in palliative care when I was a medical student. My first experience of research was looking at how patients were given bad news, particularly those in respiratory clinics being diagnosed with chronic illnesses. I did some research with the palliative care team looking at their experiences and supporting them in those interactions.

After completing a PhD in medical education looking at the initial clinical experiences of medical students, I worked as an academic clinical lecturer.

In March 2014, I applied for my current consultant post at Central and North West London (CNWL) NHS Foundation Trust, and I’ve been acting as the research lead for the service since May.

Many of my interests are around qualitative research methods to understand experiences, how practice works, and how people learn through practice. My education interests are in developing teaching and trying to improve how palliative care is offered.

What I enjoyed most in my work with patients was spending time with people, looking at their illness with them in a holistic way, and having an ongoing relationship with them to ensure they have quality of life.

From a research point of view, it was a practical approach that very much viewed patients as partners – not so much studying them as working with them to understand their experiences and how that could inform improvements.

We want to develop rigorous research, but we want it to have practical applications to the patient group we’re serving. We’d like to be more engaged in being a participating site − not so much studying patients as working with them to understand their experiences and how that could inform improvements.

The team is now working to establish why some doctors’ predictions are more accurate than others, and whether prognostic accuracy is a skill that can be taught.

Doctors are often inaccurate when predicting how long people with terminal illnesses have left to live, according to new research.

The results showed a wide variation in errors, ranging from an underestimate of 86 days to an overestimate of 93 days.

Researchers from the Marie Curie Palliative Care Research Department at UCL reviewed 4,642 records of clinicians’ predictions for palliative patients nearing the end of their lives.

No sub-group of clinicians was consistently shown to be more accurate than any other, despite suggestions that older and more experienced doctors would make more accurate assessments.

The study was led by Paddy Stone, a professor of palliative and end-of-life care at CNWL. “Delivering the most appropriate care and treatments for those with terminal illnesses is often dependent on doctors making an accurate prognosis,” Professor Stone says. “Knowing how much time is left can also better equip patients and their families to manage the situation and decide how they spend the final days.

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**A word to the wise on statins**

Q&A with debate over the pros and cons of statins featuring regularly in the media recently, Professor Liam Smeeth, chief investigator of the StatinWISE study, sheds some light on the issue.

**Q. Why has there been so much recent controversy about the use of statins?**

There was a lot of media coverage in 2013 and early 2014 suggesting that muscle pain is a very common side-effect of statins. So we did some research – and it showed that a lot more people were giving up statins in the immediate period after this media coverage.

I think there are two different communities of sceptics. One is the hardcore group, who I think have misrepresented the evidence. They say statins are not effective – but we know they are effective. They also say that hundreds and thousands of people get debilitating side-effects – but we just don’t know that.

There’s a larger body of opinion around over-medicalisation, and whether we should be relying on drugs to prevent heart disease when the true causes could be addressed through public health measures, such as stopping smoking and better diets. I’ve got a lot of sympathy with them, so I can understand people being a little bit sceptical about wider and wider use of statins.

**Q. Why are statins the most commonly prescribed medication in the UK?**

The simple reason is because they are very effective at preventing heart attacks. At the very least, they reduce your risk by 20 per cent – and probably by quite a lot more than that. That goes for people at high risk of heart disease who haven’t already got it, but it’s also very true for people who have heart disease and have had a heart attack. So because heart disease is so common and so many people are at increased risk, statins became very commonly prescribed.

**Q. What are the current recommendations for statin use?**

A. Some of the statin sceptics slightly misrepresent NICE guidance, which clearly says that lifestyle change, a healthy diet and stopping smoking are the key things to focus on to prevent heart disease. People who have tried those measures should also be offered the opportunity to take statins if their vascular risk remains above this 10 per cent threshold.

The guidance always makes clear it’s a patient decision. And it is a big decision taking a tablet every day, so it’s not going to be for everyone.

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A. The simple reason is because they are very effective at preventing heart attacks. At the very least, they reduce your risk by 20 per cent – and probably by quite a lot more than that. That goes for people at high risk of heart disease who haven’t already got it, but it’s also very true for people who have heart disease and have had a heart attack. So because heart disease is so common and so many people are at increased risk, statins became very commonly prescribed.

**Q. What would you advise people considering using statins?**

A. They’re contraindicated in people with active liver disease – that’s the main problem. Beyond that, it’s quite an individual decision, I think.

If I had a heart attack or a stroke, I’d be straight on a statin. Your risk of having another event is very high, and statins are particularly effective among people who have already had a vascular event.

Liam Smeeth is professor of clinical epidemiology at the London School of Hygiene and Tropical Medicine.
Non-medical staff are often under-represented in medical specialities, but this year – for the first time – two have been appointed to academic public health fellow posts in the West Midlands.

And, following a strenuous application process, one of the posts has gone to the former Central and North West London NHS Foundation Trust (CNWL) researcher Antiopi Ntouva, whose role will alternate between academic work and service training.

Ntouva, who is training to be a consultant in public health, is currently immersed in the academic aspect at the University of Birmingham. The next stage will involve service work at Worcester county council.

The post provides the opportunity to add new expertise to the varied abilities and experiences possessed by non-medics.

“There are all sorts of placements you can do for short periods of time to gain the different types of skills that are required for the post,” Ntouva says.

HAPPINESS IS A HEALTHY START FOR CHILDREN

Growing concern about child mental health problems led to 100 professionals being brought together in London by Noclor to hear some of the most influential voices in the fields of attachment and child mental health.

Behavioural problems affect 5%-10% of children in the UK, harming health and social development from childhood into adult life.

To identify and implement the interventions needed to give children the best start to life, a dialogue is required between communities, service providers, researchers and policymakers – which is why the subject was a fitting choice for the latest in a series of Noclor’s Healthy Conversations.

The event was held in September in collaboration with the Healthy Start Happy Start study – an Imperial College London project established to test the effectiveness of a brief parenting intervention in preventing enduring behavioural problems in at-risk children aged 12-36 months.

Professor Pasco Fearon, professor of developmental psychopathology at University College London, opened with a talk on the effects of intergenerational transmission and disorganised attachment in the long-term development of a child.

Professor Stephen Scott, professor of child health and behaviour at the Institute of Psychiatry at King’s College London, then discussed attachment beyond infancy and how parenting habits can affect future habits, emotional issues, and social and learning skills. Marian Bakermans-Kranenburg and Marinus van IJzendoorn, experts from the Netherlands, rounded off the event by describing their work on the attachment-focused, home-based programme at the core of the HSHS study.

The Video-feedback Intervention to promote Positive Parenting and Sensitive Discipline (VIPP-SD) was developed in the Netherlands to improve parental sensitivity, and to make parents more responsive to the needs of children and more consistent in their parenting.

Profile: Antiopi Ntouva on becoming one of the first non-medical academic public health fellows in the West Midlands

Richard Watt named new CNWL research director

Prestigious breakthrough for former CNWL researcher

RICHARD WATT NAMED NEW CNWL RESEARCH DIRECTOR

Professor Richard Watt, one of the key figures in supporting the career of Antiopi Ntouva, has been appointed director of research, development and innovation at CNWL.

“He brings a wealth of experience and expertise to the role, and is well placed to develop our research strategy,” said medical director Dr Cornelius Kelly. “He has an enviable track record of commitment to the next generation of researchers, as well as supporting more established investigators.”

Professor Watt’s brief is to further develop research activity and capacity across the trust, in collaboration with CNWL’s university partners.

In addition to his new appointment, he is also Professor of Dental Public Health and head of the Department of Epidemiology and Public Health at University College London.
Pathways to training opportunities

Training courses

The following sessions are being hosted by Noclor and our associates. All the sessions are free and open to all staff who have an interest in research (including doctors, dentists, nurses, research assistants), and who are working in or associated with our partner Trusts.

- Good Clinical Practice
- Informed Consent
- Essential Skills in Research Delivery
- Trial Master File
- Principal Investigator Training
- Critical Appraisal of Quantitative Research Workshop
- Advanced Skills in Research Delivery
- Literature Searching Workshop
- Critical Appraisal of Qualitative Research

April

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<td>Essential Skills for Clinical Research Nurses</td>
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If there is a training subject that your research staff would benefit from that we do not currently offer, please do get in touch with us by emailing sadie.wilmarsh@nhs.net.

Finding research funding

It is possible to apply for funding from the following organisations. This is by no means an exhaustive list and deadlines have not been included. Refer directly to the organisation’s website for application deadlines.

- National Institute of Health Research: http://www.nihr.ac.uk
- Medical Research Council: http://www.mrc.ac.uk
- Wellcome Trust: http://www.wellcome.ac.uk
- Cancer Research UK: http://www.cancerresearchuk.org
- Diabetes UK: http://www.diabetes.org.uk
- Health Foundation: http://www.health.org.uk
- Kings Fund: http://www.kingsfund.org.uk
- The Association of Medical Research Charities: http://www.amrc.org.uk
- More general funding sources can be found at: http://www.refunding.org.uk

Please note that for assistance from the finance team, the researcher must contact Noclor within the timeframe given below:

| Programme Grants | 6 weeks prior to submission deadline |
| Research for Patient Benefits Grants | 4 weeks prior to submission deadline |
| Research Council Grants | 2 weeks prior to submission deadline |
| NIHR HTA Grants | 4 weeks prior to submission deadline |
| Research Council Grants (MRC, Economic & Social Research Council) | 3 weeks prior to submission deadline |

Contact the Noclor finance team at: finance.noclor@nhs.net

Twitter research accounts reach new milestones

The two Twitter accounts run by Noclor continue to extend their reach in the research community and beyond. The NHS research news account launched late last year, @NHSRes, now has 1,800 followers. The account automatically shares the latest news and updates on healthcare research through an internally-developed app.

Noclor’s own account, @NoclorResearch, has now hit 375 followers. Tweets sent from the account in October reached more than 4,000 people.

Promoting the best in research
Projects currently recruiting

ANTLER: A study investigating the use of citalopram, sertraline, fluoxetine and mirtazapine to prevent relapse in primary care patients taking long-term maintenance antidepressants, but now feel well enough to consider stopping. The programme is being compared to maintenance treatment to find out which types of patients can benefit from reduced drug treatment.

ENRICH: “Enhanced discharge from inpatient to community mental health care” is a programme of applied research to manualise, pilot and trial a peer worker intervention. Peer workers are trained to meet psychiatric service users on the ward, then continue to work with them in the crucial post-discharge period.

• For information on Noclor support: Primarycare.noclor@nhs.net