How has your professional and academic background led you to the field of HIV research and prevention?

I have been working with HIV patients since 1986, at which time it was a fatal disease and all we could really do was to make people comfortable. After 10 years of HIV research, we had an amazing breakthrough, combining three drugs. Suddenly, a fatal condition became one that we could treat.

I moved into clinical research in 1994, and was initially involved in an early-phase trial of an HIV vaccine while completing a Master’s degree in Communicable Disease Epidemiology.

Can you tell us about your preventive HIV trial in sub-Saharan Africa using vaginal gel? What was the outcome of this study, and how does it compare to similar studies in the region?

Our large microbicide gel study in Tanzania, Uganda, Zambia and South Africa took several years to prepare for, and unfortunately we found that the gel didn’t work. However, shortly afterwards, another research group reported that a gel had reduced HIV. The CAPRISA trial used tenofovir gel, which had a more potent drug in it - one that we use for treatment. Because it is absorbed by the body it could be accurately traced, so adherence to gel could be measured objectively. As confirmation in a second trial is always needed, the South African researchers went on to conduct the FACTS trial. Results were announced in February and unfortunately did not confirm benefit.

The FACTS team recruited young, single women as we know the rate of HIV is high in this group, however, on the back of being young and single, they mainly lived with their families and rarely had sex at home, so were unable to use the gel consistently. Two other studies into women in sub-Saharan African have encountered adherence challenges - one assessed tablets and a gel, while the other solely assessed tablets. The reasons are complex, including fear of side effects, and concerns that taking HIV treatment would lead others to believe they had HIV. The constant reminder that they could be on placebo gel is also demotivating as it is made clear to women that they should not expect any benefit from the product they are being asked to use.

Are there any advantages to using the vaginal gel as HIV protection?

In addition to its microbicidal properties, the gel acts as a lubricant. We received positive feedback from our large trial that both women and their partners liked this characteristic. Moreover, for women in sub-Saharan Africa, their greatest risk for catching HIV may come from their main partner. They can’t go to the man with whom they have children and on whom they depend and suggest he uses a condom because they suspect he has HIV. It’s an impossible negotiation for women in any setting, but particularly in one where there is gender inequality. Suggesting the gel for pleasure as opposed to HIV prevention is a much easier and more acceptable way for women to introduce the gel to their main partner.

The ‘Pre-exposure Option for Reducing HIV in the UK: Immediate or Deferred’ (PROUD) study – which examined the impact of Pre-Exposure Prophylaxis (PrEP) on acquiring HIV – showed an 86 per cent reduction of HIV when using PrEP. Can you discuss your fantastic results in more detail?

The PROUD study has been amazing. We had a much larger number of infections than we expected in those not on PrEP, and a very small number in the men using PrEP – two defaulted from the clinic and likely ran out of PrEP when they caught HIV, and one who we believe caught HIV a week before he started. We have clear evidence from PROUD of a much higher risk for HIV than we anticipated, and an extremely effective intervention – a terribly exciting result that suggests PrEP could make a major impact on this epidemic among gay men.

Where do you see your research into HIV going in the future?

The Microbicides Development Programme partnership still believes that tenofovir vaginal gel is a useful preventive strategy for women, that could have an impact on the epidemic, and so we’re keen to confirm its effectiveness. A lot of public investment has gone into the microbicide research, and it is frustrating to see how the FACTS result has put donors off. If we could raise funds, we would conduct an open-label trial, like PROUD, where the confusion of the placebo is removed. Women who know they are at risk of HIV will want to use a product to reduce that risk.
Researchers at the Medical Research Council Clinical Trials Unit in University College London, UK, are working among diverse demographics throughout the world to improve HIV prevention and treatment strategies.

HIV IMPAIRS THE function of immune system cells, resulting in their progressive deterioration and, without treatment, eventually leads to ‘immune deficiency’. According to estimates from the World Health Organization (WHO), some 35 million people across the globe were living with HIV by the end of 2013, while 2.1 million individuals became newly infected with the virus that same year. Clearly, despite therapeutic advances, HIV still represents a major public health problem and, unfortunately, little progress has been made in reducing the rate of transmission.

Many clinical trials testing different forms of interventions have been launched in recent years; however, they tend to be large and costly, and it can be incredibly difficult to interpret their results. Professor Sheena McCormack is one prominent researcher who is seeking to address this challenge. As the lead for HIV prevention trials at the Medical Research Council (MRC)’s Clinical Trials Unit (CTU) at University College London (UCL), she is passionate about developing and implementing biomedical interventions that prevent or reduce the risk of acquiring HIV.

Having worked in the field for the past three decades, McCormack has a wealth of experience conducting HIV trials among complex and diverse demographics and, during this time, she has witnessed enormous changes in the disease landscape. Indeed, thanks to the introduction of antiretroviral treatment in 1996, HIV has changed from being a fatal disease to one in which its sufferers have a relatively normal life expectancy.

INTRODUCING VAGINAL GEL
Over the past 15 years, McCormack has been involved in two effectiveness studies. One was dedicated to testing a non-antiretroviral microbicide vaginal gel as a preventive measure against HIV for women in sub-Saharan Africa, and a second tested an antiretroviral tablet for reducing HIV amongst gay men and transgender women in the UK.

Unfortunately, the first study failed to show any advantage to using the gel; an outcome attributed to lack of potency. However, within a year, a research group based in South Africa reported a reduction in HIV using a vaginal gel that contained the antiretroviral drug tenofovir. Although a second trial conducted in South Africa was not able to confirm this – due to the fact that only a minority of women were able to use the gel consistently – McCormack remains an advocate of this method of HIV prevention.

“The evidence gained across several microbicide trials is that women and their partners enjoy sex with the gel,” she shares. “This is a much easier reason to provide when introducing the gel to their main partner, compared to trying to discuss it in the context of HIV prevention.”

PROUD AND POWERFUL
The second study – of which McCormack is also the Chief Investigator – is targeted at a completely different demographic and showed incredible results. Entitled ‘Pre-exposure Option for Reducing HIV in the UK: Immediate or Deferred’ (PROUD), this innovative study was launched in 2012 and the results were announced in February 2015 at the Conference on Retroviruses and Opportunistic Infections.
PROUD enrolled 545 HIV-negative men who have sex with men (MSM) and transgender women who reported engaging in high-risk sexual behaviours such as anal intercourse without a condom. The study tested the effectiveness of Pre-Exposure Prophylaxis (PrEP) as a preventive measure in the form of Truvada pills, which are identical to those taken by HIV-positive individuals. Provided by Gilead Sciences, participants were advised to take this prophylactic medication daily. As an open-label trial with no placebo, it mimicked routine drug delivery in order to ascertain ‘real life’ HIV protection and cost-effectiveness. One group took PrEP for the entire 24 months while the second only took PrEP in the latter 12-month period of the trial. The effectiveness was calculated as a ratio of the HIV incidence rates in the two groups during the first year of the study. Revealingly, these were 1.3 per 100 person years in those on PrEP and 8.9 per 100 person years in those not on PrEP.

The first step for a commissioning policy is to publish the results of PROUD and the accompanying cost-effectiveness models. Afterwards, the decision regarding PrEP will lie in the hands of various committees – firstly to assess its prioritisation and secondly its affordability. McCormack is confident about the outcome: “Of course, these committees may decide against PrEP, but as we practice evidence-based medicine, the PROUD result would make that hard to justify”.

HIV VACCINE/TREATMENT – A BROAD VIEW OF STUDIES AMONG DIFFERENT DEMOGRAPHICS

OBJECTIVE
To develop and implement biomedical interventions that prevent or reduce the risk of acquiring HIV.

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SHEENA MCCORMACK joined the Medical Research Council (MRC) Programme on HIV/AIDS in 1994, which was subsequently absorbed into the MRC Clinical Trials Unit, and completed an MSc in Communicable Disease Epidemiology at the London School of Hygiene and Tropical Medicine. She now works as co-Principal Investigator of the Microbicides Development Programme and serves as as the Executive Board of the UK HIV Vaccine Consortium. McCormack’s current trials include three early-phase HIV vaccine trials (two at St Mary’s Hospital), and PROUD, a pilot study of oral Pre-Exposure Prophylaxis for gay men and transgender women in the UK – a joint initiative with Public Health England.

VACCINATION ADVANCES
McCormack is also involved in the UK HIV Vaccine Consortium (UKHVC), bringing her clinical expertise to bear in the group. The results from recent trials have indicated that the key to a successful HIV vaccine lies in combining different immunogens; however, this has proved difficult due to the apparent unwillingness of different pharmaceutical companies to work with academics in this regard. Yet recent efforts to develop an Ebola vaccine to address the crisis in West Africa have challenged this – and attitudes appear to be changing.

Encouragingly, the Wellcome Trust has awarded the UKHVC funding to make its own vaccines – and McCormack has played a key role in fostering partnerships with research networks in African countries including Tanzania and Mozambique, as well as with Swedish, German and American collaborators. These associations have linked many vaccine trials – and the results have convinced the Consortium to apply for funding to test the latest combination for effectiveness. Once again, the fate of McCormack’s work in this area will lie with a committee.

REDUCING THE RISK
Currently, the cost of treating an HIV-positive individual with antiretrovirals throughout their lifetime is approximately £280-360,000 in the UK. HIV is clearly a health problem that puts a heavy economic burden on society – and in places such as sub-Saharan Africa, where it is not always possible to access the necessary antiretrovirals, it can represent a death sentence. In this context, McCormack’s research into effective preventive methods is vital. “My hope is that the results of these ambitious clinical trials will continue to forge advances in HIV prevention, making a real difference to the lives of people at risk of HIV in diverse demographics,” she concludes.

Having worked in the HIV field for the past three decades, McCormack has a wealth of experience conducting HIV trials among complex and diverse demographics.