

WAR IN THE BLOOD

Press Summary

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THE  TIMES

Car-T therapy saved me from leukaemia

When other treatments failed, this woman's own immune cells were weaponised to fight cancer

Peta Bee

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Tanya Hill had Car-T therapy two years ago. The procedure, described as a type of 'living drug', is complex

CHRIS MCANDREW FOR THE TIMES

Tanya Hill is sipping a latte and discussing arrangements for her wedding with the owner of the café in Biggleswade, Bedfordshire, where we meet. She is bouncing with excitement, her words spilling into each other as she outlines the plans for tomorrow's nuptials in Cambridge and a ten-week honeymoon to Australia with her new husband, Brendon. She has the bridal glow, the gleaming hair and the manicure booked. Never in a million years would you imagine that the big day is, as she puts it, to be "about so much more than the wedding". Yet for the 28-year-old, it will also be an occasion to mark 26

months in remission from leukaemia, after revolutionary Car-T therapy as part of a trial at University College London Hospitals (UCLH). Car-T is the subject of a BBC documentary, *War in the Blood*. “The day will be a celebration of everything,” Hill says. “It’s to say, ‘We’re here and I am still alive.’”

Four years ago Hill’s life was panning out almost perfectly. She had recently completed a master’s degree in crime and forensic science, and had taken the summer off “to go to festivals and join the gym”. In the autumn of 2015 she was preparing to send out her CV in an attempt to get “a hotshot job in London” when, after a weekend away to celebrate her 25th birthday, her world fell apart. She had been taking the drug Roaccutane, an acne treatment that required routine blood tests to check for side-effects such as liver problems. One morning she had a missed call from the GP who she usually called to check her results. “I remember the day like it was yesterday,” she says. “We had got up to go the gym when I saw the doctor’s number on my phone. Brendon insisted I call back and with that call everything changed.”

Diagnosed with acute lymphoblastic leukaemia — an aggressive cancer of the white blood cells — her life became an endless round of hospital visits and treatments. Three rounds of chemotherapy were unsuccessful and by May 2016 she was told she needed a stem cell transplant. One of her brothers was a 100 per cent match, but the procedure didn’t work and in 2017 she relapsed. “I then went on a new drug called inotuzumab that targets cancer cells, but leaves healthy cells alone, and that got me into remission,” she says. “But I was told that was temporary and there was no guarantee it wouldn’t come back.” It was at that point that her consultant at Addenbrooke’s Hospital in Cambridge recommended her for a clinical trial at UCLH using Car-T therapy (chimeric antigen receptor), a ground-breaking type of immunotherapy that involves using a patients’ immune cells to treat their condition.

In what sounds like a sci-fi experiment, the procedure — sometimes described as a type of “living drug” — is highly complex. Millions of a patient’s T-cells, the fighters of the immune system, are extracted from their blood and genetically reprogrammed to attack cancer cells, multiplied and, when turbocharged, reintroduced to the patient’s veins over several days.

“The T-cells in our bodies work like little robots looking for infected cells and killing them,” says Dr Martin Pule, a senior lecturer in haematology at UCLH’s Cancer Institute, where Hill was treated. “But they don’t normally find cancer cells because they come from within our own bodies.”

The T-cells can be taken from the body with no ill effect. “Our job is to reprogramme them with an artificial gene that means they can detect cancer cells in the body,” he says. “They then hunt around as normal looking for the cancer cells to kill and the T-cells start to make copies of themselves.”

With T-cells circulating in their bloodstream like cancer serial killers, patients who have exhausted other treatments and medical options often see a staggering change in their prognosis. A single genetically altered T-cell can destroy up to 100,000 cancer cells. Pule, who has headed the largest European clinical trials into immune cells, says it is an area of medical research that has exploded in the past decade. “It has gone from being considered this slightly eccentric area — there was nothing like it in oncology — to one that has produced particular success in childhood leukaemia,” he says. When it is successful it can bring remission that lasts for many years.

Car-T therapy has been found to work only for certain types of blood cancers — it is already provided on the NHS for children and young adults with B-cell acute

lymphoblastic leukaemia, and the National Institute for Health and Care Excellence recommends it for adults with B-cell lymphoma — but the potential is huge. Early studies suggest it could be used to treat solid tumours that are notoriously hostile and difficult for the body's T-cells to attack. "The most promising data is on leukaemia, but exploration is under way at UCL to look at the effects of solid cancers, and other researchers are looking at how it works with brain cancer," Pule says. "There also has been early success with bone marrow cancer."

It doesn't work for everyone (some studies suggest it is successful in less than 50 per cent of patients) and there can be side-effects, including brain swelling and toxicity.

"Sometimes when it doesn't work, the T-cells are unable to see the leukaemia any more," Pule says. "In general, the experience depends on how much disease is on board and, on average, people undergoing it have a bad case of a flu-like syndrome with a high temperature and shaking." Hill had none of that. When she went to UCLH for her Car-T therapy, she says it didn't feel as though she was having cancer treatment at all. "I got a little bit tired and my feet were swollen one day, but other than that it felt like an eight-day holiday in London," she says. "Compared to everything else I had been through, I felt at that point that I was getting better."

Nearly two years on she has had no side-effects and has been reduced to three-monthly check-ups. She has been told these could be cut to six-monthly appointments after she returns from her honeymoon in October. "My energy is returning to the levels I had before cancer," Hill says. "And while my body has changed — I am more sensitive to everything and I've found I've got allergies that I never previously had — I don't think I look much different." She works out daily at the gym attached to the café, has run a marathon and is working as a dog walker, although she hopes to use her degree in the future. "I had chemo brain for a long time and it leaves you confused and sensitive to noise, unable to string words together," she says. "But that has got much better."

Could Car-T eventually replace chemo as a treatment for cancer? Pule says the field is still young, but with hundreds of clinical trials under way, that possibility is real. "It's challenging to reach that point, but we are closer," he says. "There's a lot of regulatory stuff and technical bureaucracy to get through and an overwhelming amount of work to be done." His inspiration comes from the patients. "We heard from one of them just the other day and they had run a marathon," Pule says. "These people are amazing."

Hill is undoubtedly one of them. She and Brendon are planning a move to the coast, and eventually hope to have children with the nine embryos they stored before she underwent some of her treatment. "I wouldn't wish cancer on anyone, but it's almost easier having the disease than being the person close to you without it," she says. "I'm the one with the cancer, so I can be proactive and do what I want, feel how I want about it. Your family and people close to you have a much harder time. It has completely changed my perspective on everything. And right now, life is very good."

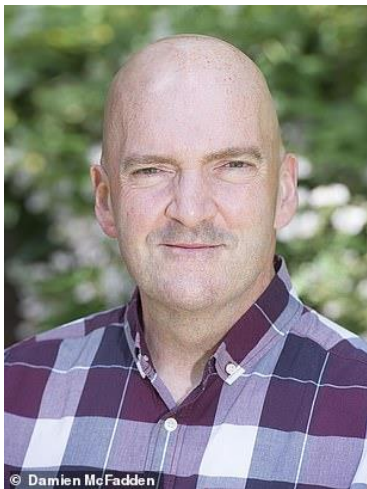
***War in the Blood* is on BBC Two at 9pm on July 7**

Miraculous children's therapy that could finally save adults with cancer

- Scott Davies, a driving instructor from Nottingham, had a form of blood cancer
- Acute lymphoblastic leukaemia affects 650 UK adults and children each year
- A new therapy, called CAR T-cell, has transformed survival rates for children
- Now, it is being used to help adults - and is responsible for Mr Davies' recovery

By [Caroline Scott for the Daily Mail](#)

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Fight: Scott Davies, a driving instructor from Nottingham, had a form of blood cancer
As Scott Davies sat down for his appointment with a haematology consultant, he glanced at the clock. It was 3pm.

‘When I looked again, it was ten past,’ says Scott, ‘but it could have been a lifetime, because in those few minutes my entire world was turned upside down.’

For in those ten minutes, the consultant had told Scott, now 52, a driving instructor from Nottingham, that the results of tests he’d had 48 hours earlier showed that he had an aggressive form of blood cancer, acute lymphoblastic leukaemia (ALL), which affects 650 adults and children in the UK each year.

‘My wife was crying; I was in shock,’ says Scott. ‘But I decided there and then that I was not going to die at the age of 47, I had to fight like hell.’

Scott, who has two grown-up children, was told that with the available treatments — chemotherapy, radiotherapy and a stem-cell transplant, where healthy stems cells are taken from a donor’s blood or bone marrow — there was only a 50 per cent chance he’d be alive in five years.

But against the odds, three years on, Scott has been cancer-free for a year and feels fitter than he's ever been, thanks to a groundbreaking trial of a treatment that harnesses patients' immune systems to fight off cancer.

Standard treatment for all is usually effective, initially at least, but 40 to 50 per cent of patients relapse within two years because it is so hard to eradicate completely. And those who relapse have a five-year survival rate of only 7 per cent.

But although the outlook for adults remains poor, a new therapy, called CAR T-cell, which harnesses the patient's own immune system to attack the cancer, has transformed survival rates for children and young adults with the condition.

CAR T-cell therapy is created by taking a patient's T cells — a key part of their immune system — and genetically modifying them in a laboratory so they produce special structures called chimeric antigen receptors or CARs, on their surface. This process takes around a month.

These CAR T-cells are then infused back into the patient's bloodstream, where the new receptors recognise specific proteins on the cancer cells' surface and kill them.

In a 2018 study of 75 children with ALL treated with CAR T-cell therapy, 93 per cent achieved remission — unprecedented results in a cancer trial — and 50 per cent were still in remission after a year, reported the New England Journal of Medicine.



Shocking: Mr Davies, who has two grown-up children, was told that with the available treatments — chemotherapy, radiotherapy and a stem-cell transplant — there was only a 50 per cent chance he'd be alive in five years

CAR T-cell therapy is now NICE-approved for ALL patients up to the age of 25. But despite the excitement over results with children, adults with ALL have not responded to CAR T-cell therapy in the same way

But the hope is that a new trial, the first outside the U.S., into CAR T-cell therapy in adults could change that. It involves around ten patients and is led by Dr Martin Pule, a clinical scientist at University College London Cancer Institute and Dr Claire Roddie, a consultant haematologist at University College Hospital, also in London.

The trial features in a powerful TV documentary, *War In The Blood*, that follows two patients, Mahmoud, 18, and Graham, 52, through their treatments. This groundbreaking therapy has the capacity to cure them — but could also trigger severe side-effects, ranging

from fever and breathing to heart problems and neurological damage so severe it could be fatal.

Dr Pule has spent the past ten years engineering CAR T-cells in the lab where they've overwhelmed cancer cells — both leukaemias and some solid tumours — in an incubator. However, there are no guarantees it will work in the same way in the complex environment of the adult patient. It's a biological battle Dr Pule is determined to win.

'Imagine immune cells as little robots hunting for and killing cells in our bodies infected with a virus,' he says. 'We take these immune cells and "re-programme" them to attack cancer cells instead.'

CAR T-cell therapy 'is the biggest development in haematology in my lifetime', adds Dr Roddie. The reaction in children in the 2018 Pennsylvania study, was, she admits, completely unexpected. 'You cannot imagine the excitement,' she says. 'But the problem in adults is that they are less able to tolerate the toxicity.'

'The approach can result in a high fever and chills, a racing heart and difficulty breathing. Neurological side-effects include headaches and confusion. But it's vital for us to study these effects so we can understand what patients can tolerate.' Scott, who does not appear in the documentary, was also one of the patients on the trial.

Before his diagnosis in 2016, he had been feeling exhausted for months and so saw his GP. 'On my first appointment, she looked at my notes and pointed out that I was usually so healthy, she hadn't seen me in five years,' he recalls.

'She thought I might be fighting a virus and ran some blood tests including a full blood count.'



Did you know? Acute lymphoblastic leukaemia affects 650 UK adults and children each year. This reveals the number of cells in the blood: it can detect infection, anaemia and some types of leukaemia, but Scott's GP, who hadn't seen a case of ALL in her 30 years as a doctor, thought his results were normal.

Six months later, Scott passed out during a speed awareness course, and his wife took him to hospital, where a haematologist re-examined his blood results and noticed he had a high number of abnormal white blood cells.

The consultant ordered a bone biopsy, where samples of white blood cells are taken, and this confirmed that Scott had ALL.

Immediately, he had chemotherapy over a six-month period, then radiotherapy to kill cancer cells in his brain and spinal fluid, followed by a stem-cell transplant from a bone marrow donor.

There followed six months of remission, but in February 2017, a routine bone biopsy showed his leukaemia had come back.

'I was told that my chance of being alive in two years was down to 20 per cent, which was absolutely devastating,' he says. 'But in the next breath I was offered a chance to join the

CAR T-cell trial at University College Hospital in London. For me, it was a lifeline, and I didn't think for more than a second before accepting.'

Shortly after, he travelled to London to see Dr Roddie.

'She explained the process,' says Scott. 'After re-programming the cells, they would introduce them into my body via an intravenous drip which would take an hour.'

'Once they were in my bloodstream, the CAR T-cells would track down the cancer cells and kill them. It sounded like having an army in my blood 24/7, chasing down these baddies and taking them out.'

Scott had to wait until July last year to begin treatment as the T-cells were adapted in a lab. Then he spent three weeks at University College Hospital being monitored for side-effects, which usually occur within five days of the infusion.

'We've been able to collect data on only a small number of adult patients so far, but what we are seeing represents a real step change in cancer treatment,' says Dr Roddie.

'I believe we stand on the cusp of a breakthrough that could radically change the way we treat all cancers. We are trialling a range of different CAR T-cells targeting different leukaemias, lymphomas and even some solid cancers — in particular, adult and paediatric brain cancers.'

'One of the biggest frustrations for me is that I'm not able to offer patients with ALL further treatment after chemotherapy, when I know that in our lab we have pre-clinical therapies available [therapies which haven't undergone trials on humans].'

However, as the documentary's title suggests, progress does come at a price.

At one point, Graham, a 52-year-old wine merchant from Hertfordshire, was suffering from breathing so laboured due to the side-effects of CAR T-cell therapy that he needed an oxygen mask and was told he might die. A week later, he was back from the brink.

While the programme continues and her patients battle horrible side-effects, Dr Roddie grows paler.

'We get to know families so well and it's terribly hard when things don't go as we'd like, because this really is the last fireball, the last chance to get a patient into remission,' she says.

'But despite the difficult work, it's also immeasurably rewarding. As a team, we've given these patients another crack at life, and they've given us the extraordinary opportunity to learn what we could have done better.'

'We're incredibly close now to being able to target all cancers and that keeps me going.'

Results from the trial won't be available until next year and then there will need to be a bigger study before treatment could be licensed for use in the NHS.

Scott is relishing life and is planning to cycle from John O'Groats to Land's End next year.

'There are not many second chances in cancer treatment and if you're given one, you have to take it,' he says.

War In The Blood airs on BBC Two, 9pm, Sunday, July 7.

WHAT IS LEUKAEMIA?

Leukaemia is a cancer that starts in blood-forming tissue, usually the bone marrow.

It leads to the over-production of abnormal white blood cells, which fight off infections.

But a higher number of white blood cells means there is 'less room' for other cells, including red blood cells - which transport oxygen around the body - and platelets - which cause blood to clot when the skin is cut.

There are many different types of leukaemia, which are defined according to the immune cells they affect and how the disease progresses.

For all types combined, 9,900 people in the UK were diagnosed with leukaemia in 2015, Cancer Research UK statistics reveal.

And in the US, around 60,300 people were told they had the disease last year, according to the National Cancer Institute.

Most cases have no obvious cause, with the cancer not being contagious or inherited.

Leukaemia generally becomes more common with age - the exception being acute lymphoblastic leukemia, which peaks in children.

Other risk factors include being male, exposed to certain chemicals or radiation, and some bone-marrow disorders.

Symptoms are generally vague and get worse over time.

These can include:

- Tiredness
- Frequent infections
- Sweats
- Bruising
- Heavy periods, nose bleeds or bleeding gums
- Palpitations
- Shortness of breath

Acute leukaemia - which progresses rapidly and aggressively - is often curable via chemo, radiotherapy or a stem cell transplant.

Chronic forms of the disease - which typically progress slowly - tend to be incurable, however, these patients can often live with the disease.

Source: [Leukaemia Care](#)

War in the Blood – BBC2

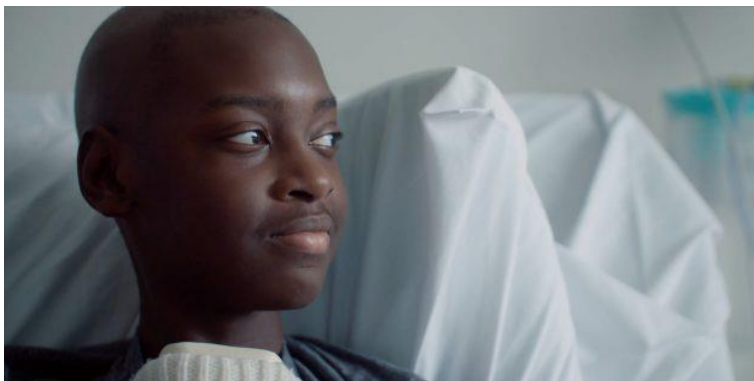
Airs at 9:00pm on Sunday 7 July 2019

Steve Morrissey Tue, July 2 12:01am



Could cancer be defeated with a single injection? In War in the Blood, we learn about a groundbreaking new treatment being put through its paces

War in the Blood is an extraordinary film about two cancer patients, Graham and Mahmoud, who are taking part in a new treatment trial to fight the devastating disease.



Hoping for the best: Mahmoud

CAR T-cell therapy is the last hope for terminally ill patients, who have exhausted all other current treatment options of surgery, chemotherapy and radiation.

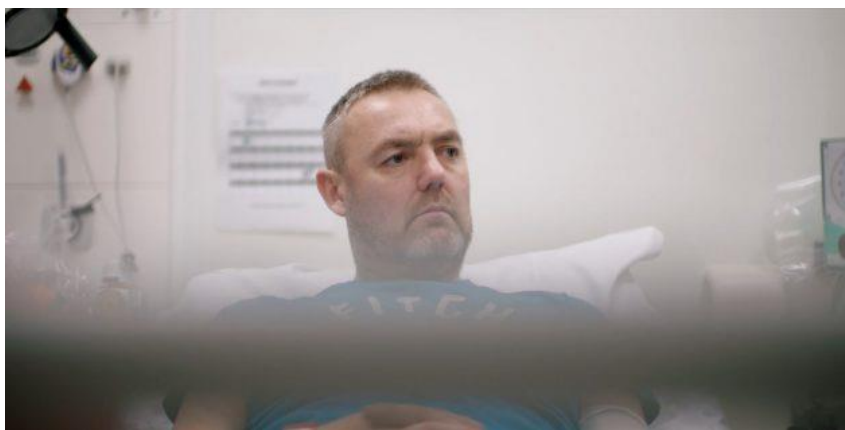
The new approach is being pioneered in the UK by **Dr Martin Pule**, and takes cells out of the body, modifies them in a lab to turn them into cancer-killing cells, then puts them back into the patient's body.

"Just five or six years ago, CAR-T therapy was only an academic discipline," says Dr Pule.

"But once the commercial pharma companies took an interest, this made people think this new technology could really take off."

is the first time this treatment has been tested on people in the UK, so it's risky and there are no guarantees it will work.

There are also a lot of concerns about the negative and possibly fatal side effects.



Ready for treatment: Graham

Graham and Mahmoud are heroic trailblazers, determined not only to do this for themselves but for every cancer patient who might need it in the future.

A beautiful, inspiring and deeply emotional film.

War in the Blood, a film about treating cancer patients with CAR T cell therapy

02 Jul 2019

A new BBC film looks at the work of scientists at UCL and clinicians at UCLH working together on groundbreaking ‘first in-human’ immunotherapy trials.



From left, Dr Claire Roddie and Dr Martin Pule.

These clinical trials are testing new treatments which ‘re-programme’ the immune system to recognise and kill cancer cells, providing a more efficient and less toxic way of treating cancer.

Between them, UCLH and UCL are leading the largest portfolio of CAR T cell studies in Europe with underpinning support from the [National Institute for Health Research](#) (NIHR) University College London Hospitals (UCLH) Biomedical Research Centre (BRC) and funding by several partners including the blood cancer charity Bloodwise, and the EU 7th Framework Programme.

[Dr Martin Pule](#) of the [UCL Cancer Institute](#), who leads the [UCL CAR T-cell programme](#) and whose work is the main focus of [the film](#), said: “CAR T-cell therapy can result in long lasting remissions in patients with blood cancers which have failed all standard treatments. CAR T-cell therapy is a revolutionary new approach in treating cancer.”

Treatments which use the immune system to fight cancer are different to conventional treatments. Our immune system can be much more selective in discriminating between normal and cancerous cells which means that many of the common side-effects of conventional therapies are avoided. Also, immune responses can last for many years, preventing relapse.

Most of the [BRC-supported](#) immunotherapy clinical trials focus on using an immune cell called [a T-cell to attack cancer](#). This cell can be imagined as a miniature robot which moves around our bodies, looking for infected cells and killing them. However, T-cells do not recognise most cancers, since cancers develop from our own tissues and appear normal to most T-cells. The main challenge with T-cell immunotherapy approaches is to find ways to direct T-cells to attack cancer cells.

CAR T-cell therapy directs T-cells to attack cancer cells by harvesting T-cells from blood and genetically engineering them outside the body so they are reprogrammed to kill cancer cells. Once they are infused back to the patient, these CAR T-cells act as miniature robot, and find and destroy cancer cells.

BRC director Professor Bryan Williams said the centre had supported the team from outset. He said: "We supported this work because we could see the potential for it to generate new and potentially life-saving treatments for cancer. It is truly remarkable to see the speed at which this has happened - it is an example of research in action in the NHS at its very best."

The BBC's intimate feature length documentary follows two patients through their treatment and the doctors battling to save their lives. Filmed over two years at University College Hospital and UCL, the 100-minute film *War in the Blood*, directed by Arthur Cary, is a powerful statement on the contribution of terminally ill patients to the world of clinical research.

Not allowed to meet and separated by two floors of a hospital, 53-year-old Graham and 18-year-old Mahmoud are nevertheless bound together by their commitment to the treatment and their faith in the science. Terminally ill, the trial represents their only option. How do their ages and life experiences affect their physical and emotional response?

For the scientists and clinicians working to develop this treatment, the responsibility of designing and testing new treatments in patients is both exciting and daunting. At the heart of this film is the complex relationship between scientists developing these treatments, the clinical team testing them and the patients receiving the experimental therapies.

The documentary is uncompromising and does not shy away from the experiences of patients with end-stage cancer and the complex motivations behind participating in an experimental clinical study.

UCLH consultant [haematologist](#) Claire Roddie said: "CAR T-cell therapy is a form of personalised treatment for patients who do not respond to standard anti-cancer treatments like chemotherapy and has been shown in trials to cure some patients with cancer, even those with advanced cancers. Most treatments used in patients with end-stage cancer extend life by a few months. For a good proportion of patients, CAR T-cells are resulting in cures. This is unprecedented."

CAR T-cell therapy has so far shown most promise for haematological (blood) cancers, and [Professor Emma Morris](#) of the UCL Division of Infection & Immunity says the therapy represents "a real step change in how we treat cancers. It represents a leap in medical therapies, from using small chemical molecules or proteins to using cells. The complexity of

cells means that they can be engineered in highly ingenious ways, leading to treatments with specificity and activity unimaginable in conventional treatments.”

UCLH is looking forward to opening the Sir Naim Dangoor Centre for Cellular Immunotherapy in 2020. This will be an eight-bed unit at UCLH within a new surgery and cancer building made possible by a generous gift of £1.6 million from the Exilarch’s Foundation, and will build on the world-renowned expertise and ground-breaking advances being made at UCLH to successfully treat cancer using cellular immunotherapy.

At UCLH, [Professor Karl Peggs](#) established the clinical translational side of the academic CAR T-cell programme and is now working on setting up Europe’s first dedicated cellular immunotherapy research and treatment centre.

The establishment of this centre will enable UCLH to focus research on advancing cellular immunotherapies. As Prof Peggs says: “While clinical translation of cellular immunotherapy research into blood cancers has already shown positive outcomes, more research is desperately needed. We anticipate that through this research, treatment for other types of cancer – such as skin, ovarian, liver and lung cancers – will be developed, meaning greater cancer survival rates. It is a very exciting development that could be a game changer for the treatment of cancer.”

[War in the Blood](#), produced by Minnow Films for BBC Two, and directed by Arthur Caryl, will air on Sunday 7 July at 9pm.