**CAREmaps**
M.A.P.S. is an acronym for Morphokinetic Algorithms to Predict Success. Based on the research by CARE scientists we have developed a specific programme, using time lapse imaging, that related the morphokinetics (the developmental pattern/shape [morpho]; over time [kinetics]) of thousands of embryos to their viability (their chance of becoming a baby). This enabled us to develop models, or algorithms, to predict y which embryos have the best chance of resulting in birth, and to use these models in our clinics[1,2].

**Background**
Routine IVF involves culturing (growing) fertilised eggs and embryos in incubators with precise temperature and gas control. Our standard incubators, used for routine IVF, are monitored continuously to ensure that these conditions remain optimal and stable.
In order to assess for fertilisation and to record embryo development, the culture dishes, containing the developing embryos, are removed daily from the incubators to enable the embryologist to perform these checks. The embryologist works quickly to ensure that the dishes are outside of the incubation conditions for only a short time. The microscope stages are heated and the dishes are covered with oil to help keep the conditions as stable as possible during these times.

**Time lapse incubation and monitoring of embryos**
CARE offers patients an alternative and advanced type of embryo culture environment and monitoring. Routine culture is still available as the main method of incubation at CARE but we also offer time lapse culture (using an 'EmbryoScope™') which does not involve removing embryos from the incubators but allows the embryologist to look at time lapse videos of the developing embryos. It gives improved pregnancy and birth rates compared to standard incubation as embryos are selected using CAREmaps.[2,3,4] CARE was the first in the UK to offer this advanced method of embryo culture and our embryologists have more experience using this technology that any other UK clinic; and as such we have undertaken considerable research and moved this technology forward for the advantage of patients choosing to use it.

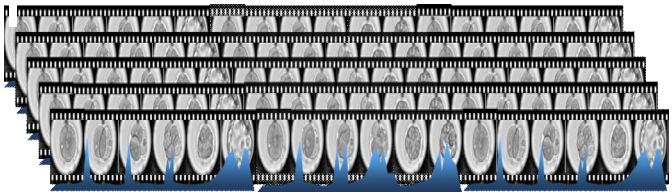
**Embryo selection**
Conventionally, embryologists select embryos for transfer based primarily on how they look (morphology) and on the sequence of 3 or 4 observations that they have recorded over the period since the eggs were collected and inseminated (IVF or ICSI). However, time lapse images taken every few minutes provide the embryologist with dramatically more information on which to base this critical decision. Typically, the embryologists obtain more than 5000 images which they study as a video, recording the specific times or each developmental event as well as the morphology (this together is called 'morphokinetics').

**CAREmaps is a whole system designed by CARE to maximise the chances of success in IVF.**
CAREmaps includes three important variables which, when used together, enable CARE embryologists to select the most viable embryo to give you the very best chance of a baby. These three variables are,

1. Closed incubation system (EmbryoScope)
   CAREmaps uses a "High Tech" incubator (the EmbryoScope™) which contains a microscope, camera and highly sophisticated computer software system. It gives 'continuous monitoring' of embryo development using time lapse microscopy in multiple focal planes (focuses through different sections of the embryo's cells). The embryologist can view these images and focus through levels of the oocyte or embryo to record and study the timing and nature of developmental events, without the need to remove the embryos from the incubator.
2. Time Lapse Imaging
3. Specific, CARE-designed morphokinetic algorithms - calculations about what the embryo should be doing at specific points in time





A series of time lapse images from the EmbryoScope.

**How effective is CAREmaps?**

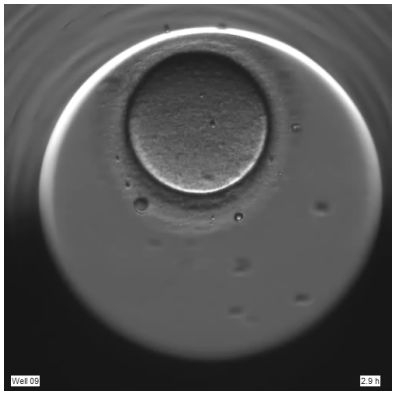
Embryologists in conventional IVF practice use morphology (how the embryo looks), to choose the one (or two) for transfer which they think has the best chance of resulting in a baby. CAREmaps adds dramatically more information for the embryologist to help choose the best embryo.

By comparing the detailed developmental patterns of thousands of transferred embryos – where we know whether they were successful in developing into a baby, wee have developed embryo selection models which ranks an embryo's chance of achieving a successful pregnancy and a baby, into categories; with the '"high potential" embryo having the highest potential to lead to a birth.
CARE Fertility's first embryo selection model was published in Reproductive Biomedicine on line and has been featured in newspapers, television and radio across the world. Since the publication of this model we have fine-tuned it and also developed further embryo selection models for specific scenarios, such as the day of embryo transfer and type of insemination (ICSI or IVF).

A very large independent data analysis, from 27 clinics outside of the UK, tested our published model for embryo selection. This analysis looked at the implantation outcome following the transfer of more than 500 IVF embryos and confirmed CARE Fertility's findings. Using time lapse technology, embryos categorised as having low implantation potential, based on CAREmaps, resulted in implantation rates of only 10%, whereas those categorised as having the highest potential resulted in implantation rates of 65% per embryo. CAREmaps will not change your embryos but it will help us choose the one which is most likely to result in success.

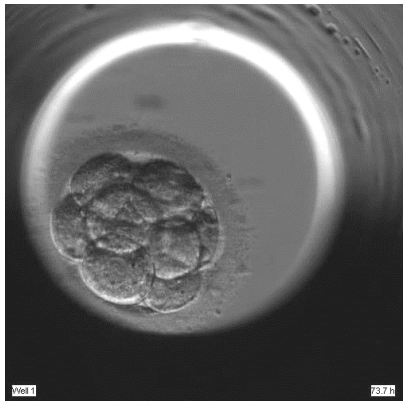
CAREmaps is only available at our clinics in the UK and Ireland and our on going research promises to further improve our models to give our patients the very best chance of success. Compared to standard methods, CAREmaps has resulted in significantly elevated birth rates. CAREmaps has resulted in higher birth rates compared to standard methodology and we have published our results and research to demonstrate this. It is important to note that there remains conflicting evidence on the efficacy of time lapse monitoring and that the HFEA have given it an amber rating which indicates that more evidence is required before it is considered proven.

During your consultation, your specific circumstances and medical history will be considered and your own estimated chance of success will be discussed with you.




The images show an egg in a patient's EmbryoScope dish (left) and the developing embryo (right).

Each dish or 'slide' contains 12 wells for individual embryo culture. The numbers on the bottom right of the images provide the embryologist the number of hours that have passed since the insemination (injection of the sperm using ICSI or the addition of sperm for IVF)



It is very important to understand that CAREmaps is **NOT a diagnostic** test of an embryo's viability or potential to make a baby. It is a non invasive test which helps CARE select the embryo with the highest potential.
Specific diagnostic chromosome testing is available at CARE – see separate Patient Information.

**Can CAREmaps be used for early stage – day 2/3 - embryo transfer as well as later – blastocyst stage?**
CARE was one of the first groups in the world to implement time lapse imaging for embryo assessment and has more experience than any other UK IVF centre. Our dedication to accurate analysis of the developmental patterns of embryos has led to the development of further and fine-tuned embryo selection models. CAREmaps is available for all patients and specific models are applied depending on the day of embryo transfer and insemination method (IVF or ICSI).

**Summary of advantages & applications of CAREmaps**
When considering CAREmaps, the advantages are as follows:
**Improved embryo culture and selection**
More information and a wealth of experience, allows embryologists at CARE to observe and select the developing embryos without removing them from their incubation environment. Embryos undergoing atypical or abnormal embryo development can be excluded from selection for embryo transfer or freezing. Suchphenomena cannot be identified with standard incubation methods and are associated with reduced implantation potential. CARE research has identified developmental patterns which are associated with embryo viability and CAREmaps is applied to rank embryos according to their chance of success.

**Downloadable Images**
As we are collecting images of each embryo every 10-20 minutes, these can be viewed by the embryologist as time-lapse video and used to gain detailed information on each embryo's development. We are able to send patients a link to the videos of your embryo(s) that was/were transferred and this can be viewed/downloaded from our unique CAREmaps portal.

**Further practical information**

**Routine IVF insemination does not take place in the EmbryoScope**
CARE practice, for IVF patients (as opposed to ICSI), is to aim to fertilise the eggs in standard incubators and place the fertilised eggs, the following day into the EmbryoScope. CAREmaps can still be applied in order to select the most viable embryo(s) for transfer, irrespective of insemination method. Patients may elect to have ICSI (fees apply) in order to utilise the EmbryoScope right from the point of insemination to acquire images and information relating to the fertilisation process. This should be discussed with CARE staff, if required.

**Delay in treatment start date**
Due to there being limited spaces in the EmbryoScope™, a booking system exists. When demand is high and all slots allocated, a patient's treatment start date may have to be delayed in order to ensure a position in the EmbryoScope™,. Alternatively, patients may elect to continue with standard incubation. Although we do our very best to accommodate all patients where possible, positions in the EmbryoScope™ are subject to availability. From time to time slots may unexpectedly become available (e.g. if a booked cycle is cancelled) and these can be offered to patients at short notice.

**Number of Embryos exceeds 12**
If more than 12 embryos develop, as there are 12 wells in an EmbryoScope™ dish, only 12 of the patient's embryos can be cultured in the EmbryoScope™. The rest are placed into our conventional incubators unless space allows – additional charges apply (see fees).

In the unlikely event of the imaging system within the EmbryoScope™ being unable to take a clear image of a developing embryo, video images may be unavailable or only available in part. If time lapse



culture or imaging is interrupted temporarily for necessary servicing or maintenance, such that the algorithms cannot be applied, you will be refunded the fee for CAREmaps and the embryologists will use alternative methods to select the embryo(s) for transfer.

**Culturing in the Embryoscope**

Embryo culture, as part of CAREmaps programing, will start following insemination (ICSI on day of egg collection – Day 0 – or after IVF fertilisation check on day 1) and continue until embryo transfer. After this point, any embryos kept for observation at patient request (e.g. assessment for possible freezing), will be moved to our standard incubation.

**Who may elect for CAREmaps?**

Anyone undergoing a cycle of self funded treatment, with mature eggs collected, subject to availability. The service may not be available for NHS funded cycles, depending upon the particular NHS provider.

**Fees**

There is an additional fee for CAREmaps. This fee is due at the start of treatment and will be refunded if there are no mature eggs placed into the EmbryoScope™ or if fertilisation fails. Downloadable images of transferred embryos are also available to those patients who wish to receive them. An e-mail address will be taken from you at egg recovery and a link sent to you shortly after embryo transfer. The fee for CAREmaps includes access to video images of transferred embryos and is detailed in CARE's price list, available from CARE Reception.

**Important note**

CAREmaps is a programme developed using CARE's entire specific culture environment – culture media, gases, etc. The development of an embryo in any particular laboratory is affected by these conditions; therefore CAREmaps programme may not apply to other clinics outside the CARE network as they may operate either subtle or substantially different conditions. The CAREmaps algorithms and the resultant increased success rates apply only to CARE clinics.

Where CAREmaps is used, embryos will be selected for embryo transfer or freezing based on the knowledge that we hold to date, in good faith and in the patients' best interest.
In some instances, there may be insufficient or only poorly developing embryos to allow selection by the embryologist to take place. In these cases, providing the embryo(s) is considered to give the patient a chance of pregnancy, albeit small, it may be transferred following discussion with the patient and clinician.

**References**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