A multicentre randomised controlled trial of an intelligent system to support decision making in the management of labour using the cardiotocogram

Training Booklet

for Midwives and Doctors

Version 6 May 2012

Contents

1. Introduction to the INFANT study

The INFANT (INtelligent Fetal AssessmeNT Monitoring) study commenced recruitment in January 2010. It is a multicentre randomised controlled trial which is taking place throughout the United Kingdom and Ireland. The study is being co-ordinated by a team at the UCL Clinical Trials Unit, based in London and local hospital based obstetricians and midwives. The study is funded by the UK Department of Health through the National Institute for Health Research, Health Technology Assessment Programme (NIHR HTA).

The aim of the study is to determine if the addition of an "intelligent" (decision-support) software giving real time analysis of cardiotocographs (CTG) to midwives and obstetricians reduces the incidence of intrapartum neonatal mortality and morbidity. The "intelligent" computer system is a piece of software that runs on the Guardian® labour system. In real time it looks for baseline rate, fetal heart rate variability, accelerations, type and timing of decelerations, short term variability rate, the quality of the signal and the contraction pattern. If the software detects an abnormal fetal heart rate (FHR) or contraction pattern, these should be highlighted on the screen.

The software has been designed by K2 Medical Systems and currently only runs on the Guardian® labour system, which is currently in use within this hospital.

The objectives of the INFANT study are to determine if the decision-support software compared to current practice will:

- Result in fewer "poor neonatal outcomes"
- Identify more clinically significant heart rate abnormalities
- Result in more prompt and timely action on clinically significant heart rate abnormalities
- Change the incidence of operative interventions

The study aims to recruit at least 46,000 women over 36 months across 10-12 sites in the UK and Ireland. Women will be split into 2 groups of 23,000. One group will receive the "intelligent" software program also known as decision-support (intervention arm) whilst the other group will be monitored conventionally and not have the decision-support software program (control arm). As this study is a randomised controlled trial, the woman, midwife or obstetrician will not have any control over what group/arm a woman gets entered into - it is a random allocation made by a computer server.

2. How will women know about the INFANT study?

There are three leaflets about research and the INFANT study that we are asking maternity sonographers and community/hospital based midwives to give to women at booking appointments, 20 week scans, 34 week midwife appointments and also when admitted in early/established labour.

Leaflet 1 – "Clinical Trials & Research in Pregnancy" (A4 – Trifold leaflet) – should be given out at the booking visit.

Leaflet 2 – "INFANT Study - Antenatal Information for Women" (A4 – Trifold leaflet) – should be given out at the 20 week anomaly scan.

Leaflet 3 – "INFANT Study – Participant Information Leaflet" (A5 booklet) – should be given out at the 34 week midwife visit, and when admitted for induction or in labour. However it can be given out at anytime during pregnancy.

Women who meet the inclusion criteria (listed below) should always be asked upon admission to delivery suite whether they have received any information about the study. If they have not, they should be given leaflet 3. (The National Childbirth Trust and other recognised antenatal tutors are also asked to help inform women about the INFANT study).

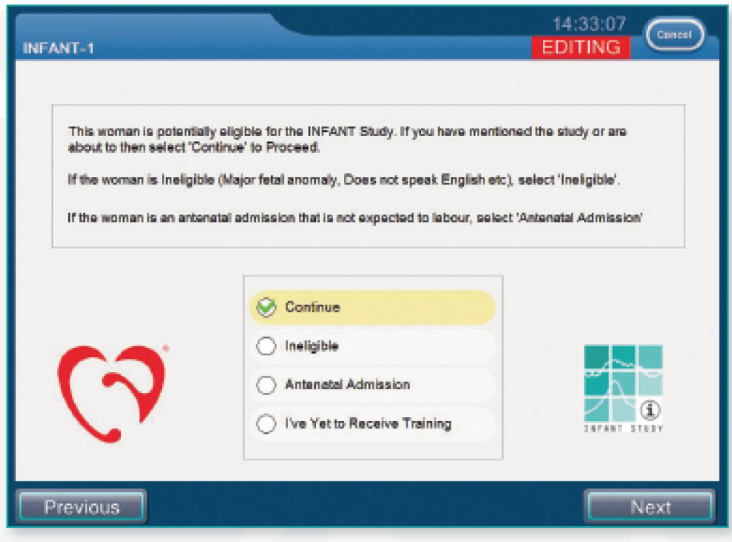
3. Who is included in the INFANT study?

All women admitted in labour who fit the following criteria:

- Singleton or twins
- ≥ 35+0 weeks gestation
- ≥ 16 years old
- No major fetal antenatal anomalies including cardiac arrhythmias such as heart block
- Able to give consent to participate in the study

All women who fit the above criteria should be approached for their consent to take part in the study whether they require continuous electronic fetal monitoring (EFM) or not. Whenever the Guardian® labour monitor is switched on and the usual admission screens entered (woman's ID, parity etc), the system will identify whether a woman is eligible for the INFANT study and prompt you to ask the woman about the study.

Example of "prompt screen"



4. How will women be entered into the INFANT study?

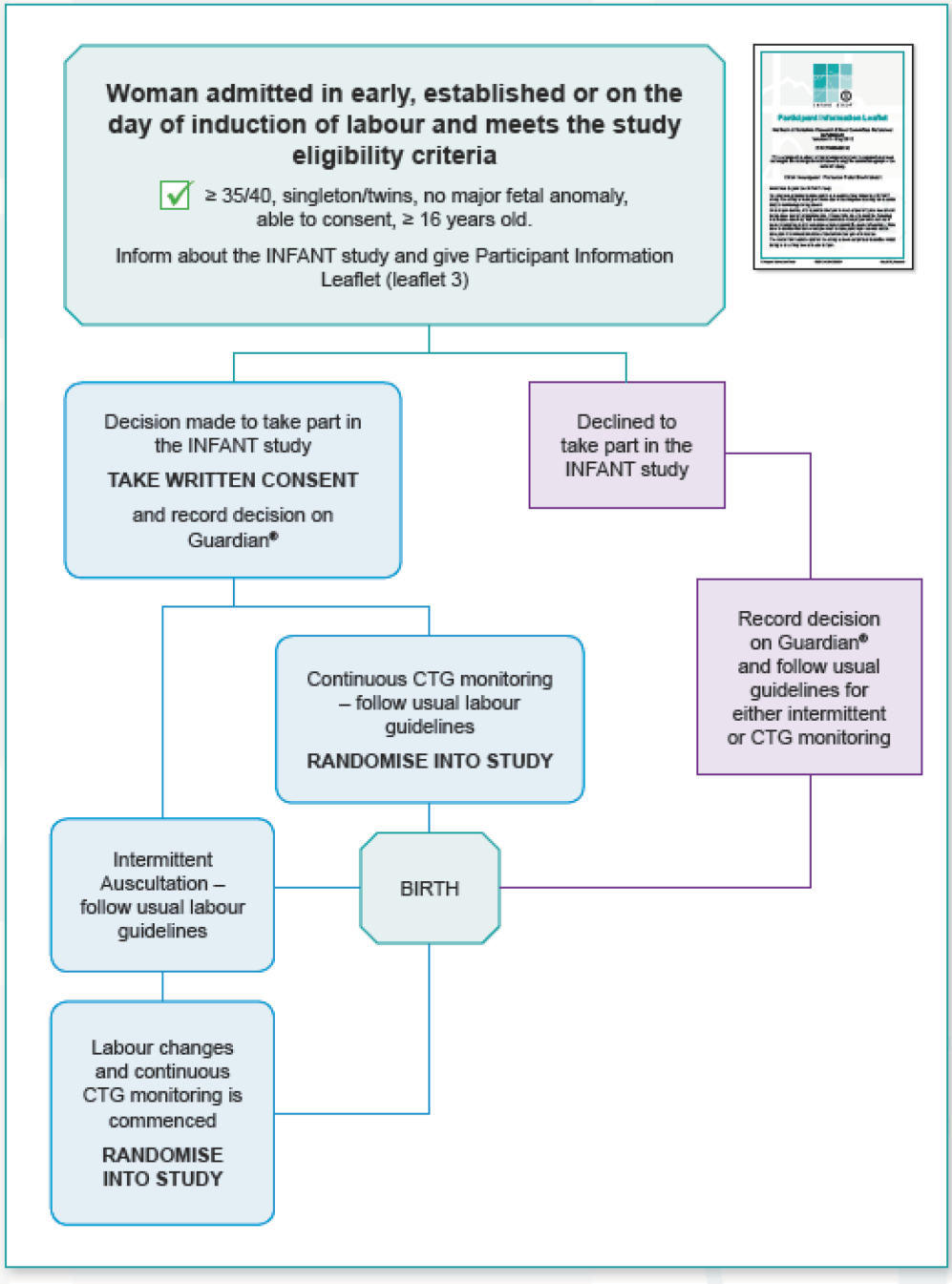
It is important that women are asked about participation in the study **as soon as they are admitted** in early or established labour, or on the day of induction of labour. This gives them the opportunity to read the "Participant Information Leaflet" and decide whether or not they wish to take part in the study. A simple explanation of what the study involves should be given by the primary midwife carer alongside the leaflet and any questions the woman has should be answered. Important points to note:-

a) If a woman does not wish to take part in the study, their care will not be altered in any way and the midwife should follow local guidelines for labour monitoring and no consent paperwork needs to be completed. However it is important that "No" to participating in the study is ticked on the admission screens so that the woman's decision is recorded on Guardian®.

b) If a woman agrees to take part in the study then the midwife/doctor must ask them to sign a study consent form (see pages 3-5 for consent guidance) and record this decision on Guardian®.

c) **It is important that all women who consent to take part in the study sign a consent form, even if they are going to be monitored intermittently. This means that the consent is already gained, and if later on in labour they are judged to require and accept continuous CTG monitoring they can be automatically entered into the study.**

Figure 1: Approach and randomisation for the INFANT Study



5. Taking informed consent for research

What is informed consent?

Informed consent is the process by which a woman voluntarily confirms her willingness to participate/allow their inclusion in something that is asked of them. Women must be informed of the benefits and risks of taking part in any study or procedure that they consent to, and they MUST be given the opportunity to ask questions about the topic concerned.

When and where should consent be taken?

When admitting a woman to delivery suite, the INFANT Participant Information Leaflet (leaflet 3) should be given to all eligible women along with a brief introduction to the study. (It is hoped that for the majority of women this will not be the first time that the INFANT study is mentioned).

Who should take consent in the INFANT study?

Consent can be taken by any health care professional who has received training from an INFANT local co-ordinating midwife (LCM) in taking consent for the INFANT study and has signed the study delegation log. If you are unsure whether you are able to take consent, you should contact your INFANT LCM.

When taking consent you should use language which is easy to understand and which is free from jargon. It is important to ensure that open and approachable body language is used. There should not be a time pressure put on the woman to make a choice as she needs to make an informed decision. Finally, the woman should understand that by not giving consent it will **not** affect the standard of care that she or her baby/babies receive.

NOTE WOMEN ARE ONLY RANDOMISED INTO THE INFANT STUDY WHEN IT HAS BEEN DECIDED TO UNDERTAKE CONTINUOUS CTG MONITORING – THEREFORE THERE WILL BE A LARGE PROPORTION OF WOMEN WHO GIVE SIGNED CONSENT THAT NEVER BECOME FULLY ELIGIBLE FOR THE STUDY.

Eight point consent checklist for taking informed consent

1. Have you given the woman an opportunity to read the INFANT Participant Information Leaflet?
2. Have you explained, and has the woman understood, the aim of the INFANT study?

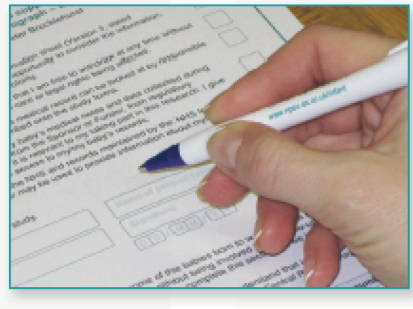
   To see if the addition of a software program can increase the number of babies born without difficulties.
3. Have you explained what the study entails – including a description of the software and that they might or might not have it. Also that all women are being approached on admission to the unit and only if continuous CTG monitoring commences will they actually be eligible – they will then be asked again verbally if they are happy to take part.

   We are always looking for ways we can improve the way we monitor babies heart rates in labour. Half of those who take part will have the computer program and half will not. We are asking all potentially eligible women in case they become eligible in the course of their labour – this would be if continuous CTG monitoring is started. However there will be a significant proportion of women who consent who never become eligible for randomisation.
4. Have you explained what a 'randomised controlled study' is?

   A study in which people are allocated at random (by chance alone) to receive one of several inteventions, in this case the decision-support software or not.
5. Have you explained the potential benefits and risks of taking part in the INFANT study?

   The benefits are that a computer will be constantly looking at the CTG as well as a midwife if the decision-support software is turned on. If the woman is allocated to no software they will still receive the same high level of care as is usual within the UK and Ireland. The potential risks of the study are minimal. It is possible that the use of decision-support software may change the number of procedures in labour, however a pilot study in Plymouth did not show any rise in caesarean section or instrumental births.
6. Have you explained that the woman is free to withdraw at any time without having to give a reason and without affecting her midwifery/obstetric care?
7. Have you explained the purpose of the 2 year follow-up?

   This is to determine if the software affects babies and their mothers in the longer term. Not all of those that agree to be followed up will be contacted, only 8,400 women and their babies will be followed up.
8. Does the woman consider they have had enough opportunity to ask questions?



If a woman agrees to take part in the study – ensure that a consent form is signed and dated by the woman and also the person taking consent *(see consent form example below).*

Guidelines on what to do when:

A woman declines to give consent: There should be no consent form completed. On the Guardian® platform the option "No" should be ticked to the question of would the woman like to take part in the INFANT study.

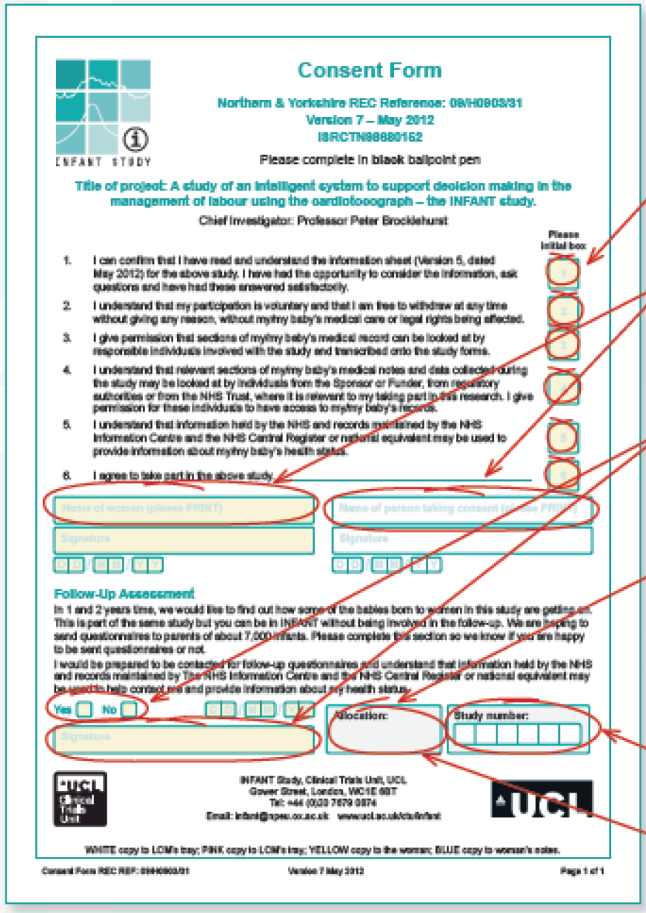
A woman consents but is not randomised: If at the end of labour a woman who consented to the study **DID NOT** undergo continuous CTG monitoring and thereby did not become fully eligible and was not randomised, "No CTG" should be written in the allocation box. The top and pink copy of the consent form should be put in the INFANT local co-ordinating midwife's tray; the yellow copy given to the woman and the blue copy should be filed in the notes.

A woman is randomised: Make sure the 6 digit study number for the woman and the allocation, either conventional or decision-support as stated on the Guardian® platform, is written on the consent form. The top and pink copy of the consent form should be put in the INFANT local co-ordinating midwife's tray; the yellow copy given to the woman and the blue copy should be filed in the notes.

A woman is not eligible: There should be no consent form completed.

A woman changes her mind once randomised: If this happens the midwife should write "withdrawn from the study" on the consent form, and then press the "INFANT admin" button which will give the option to withdraw the women from the study. Labour care should continue as normal.

Example of an INFANT study consent form



Consent Form

Northern & Yorkshire REC Reference: 08/H0803/31
Version 7 – May 2012
ISRCTN98880162

INFANT STUDY

Please complete in black ballpoint pen

Title of project: A study of an intelligent system to support decision making in the management of labour using the cardiotocograph – the INFANT study.

Chief Investigator: Professor Peter Brocklehurst

Please initial box

1. I can confirm that I have read and understand the information sheet (Version 5, dated May 2012) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my/my baby's medical care or legal rights being affected.
3. I give permission that sections of my/my baby's medical record can be looked at by responsible individuals involved with the study and transcribed onto the study forms.
4. I understand that relevant sections of my/my baby's medical notes and data collected during the study may be looked at by individuals from the Sponsor or Funder, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my/my baby's records.
5. I understand that information held by the NHS and records maintained by the NHS Information Centre and the NHS Central Register or national equivalent may be used to provide information about my/my baby's health status.
6. I agree to take part in the above study.

Name of woman (please PRINT) | Name of person taking consent (please PRINT)

Signature | Signature

Date | Date

Follow-Up Assessment

In 1 and 2 years time, we would like to find out how some of the babies born to women in this study are getting on. This is part of the same study but you can be in INFANT without being involved in the follow-up. We are hoping to send questionnaires to parents of about 7,000 infants. Please complete this section so we know if you are happy to be sent questionnaires or not.

I would be prepared to be contacted for follow-up questionnaires and understand that information held by the NHS and records maintained by The NHS Information Centre and the NHS Central Register or national equivalent may be used to help contact me and provide information about my health status.

Yes ☐ No ☐

Signature | Allocation: | Study number:

INFANT Study, Clinical Trials Unit, UCL
Gower Street, London, WC1E 6BT
Tel: +44 (0)20 7679 0374
Email: infant@npeu.ox.ac.uk www.ucl.ac.uk/ctu/infant

WHITE copy to LCMs tray; PINK copy to LCMs tray; YELLOW copy to the woman; BLUE copy to woman's notes.

Consent Form REC REF: 08/H0803/31 | Version 7 May 2012 | Page 1 of 1

Filling in the consent form accurately

Ensure all 6 statements are initialled **NOT ticked** by the woman

The woman and the person taking consent must print their names, sign and date the form

The follow up assessment must be ticked yes or no, signed and dated by the woman

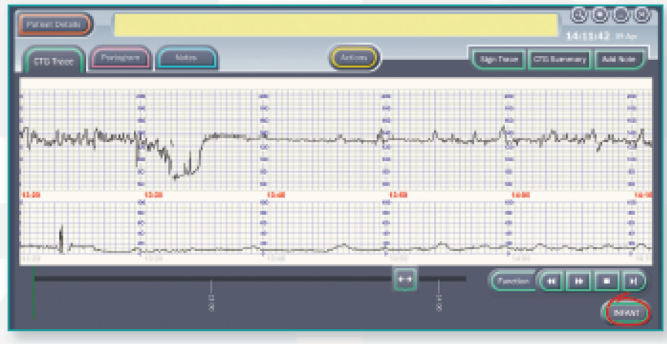
Clearly write the words decision-support OR conventional as stated on the Guardian® platform in the allocation box

The 6 digit study number will be given by Guardian® when a woman is randomised and should be written in the study number box by the midwife/ doctor. If the woman was monitored intermittently the words "NO CTG" should be written in the allocation box at the end of labour

6. How does randomisation actually take place?

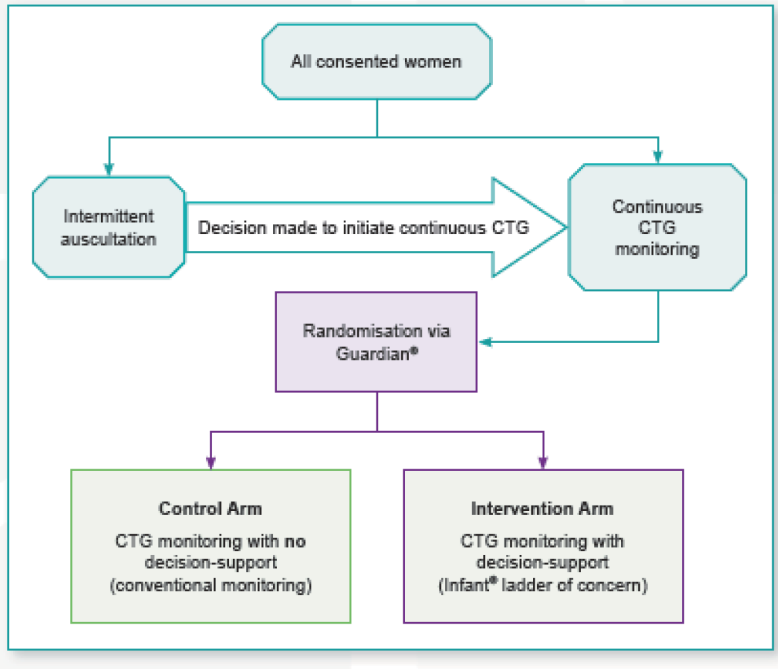
The Guardian® labour platform will prompt the midwife to record whether or not a woman has given consent to take part in the Study. Once the button of consent is pressed, there will be a series of prompts that will allow the midwife to easily randomise a woman into the INFANT study if continuous CTG monitoring is being undertaken. She/he will reach a page that will give a six digit randomisation number (generated automatically by Guardian®) and the woman's allocation. **It is very important to write this number on the bottom of the consent form in the study number box and document the woman's allocation, decision-support or conventional monitoring, in the allocation box.**

If the woman has been allocated to the control arm (conventional monitoring), the Guardian® monitor will display the CTG as usual with only the INFANT button showing in the bottom right hand of the screen. This can be pressed if a woman wishes to withdraw from the study at any point in their labour.



If a woman has been allocated to the intervention arm (where the decision-support software is active) the Infant® ladder of concern (see page 7) will appear at the right hand side of the woman's details situated at the top of the screen. The midwife should briefly inform the woman not to be anxious if she hears any "alerts or voice prompts" that the software may produce. The woman must be reassured that if a midwife is out of the room at anytime she should call via the call bell system and someone will review the rationale of the alert as soon as possible.

Figure 2: The process of randomisation into the control or intervention arms



7. How to use the Infant® Software on the Guardian® labour platform

The main identifier of the Infant® software on the Guardian® labour platform is the Infant® ladder of concern. This ladder is positioned next to the patient details and will indicate a colour coded system identifying any concern that it may have and highlight what the concern is. Below are examples of the ladder's colour codes.

GREEN (Level 4) – Indicates that the software has **no concerns** with the CTG

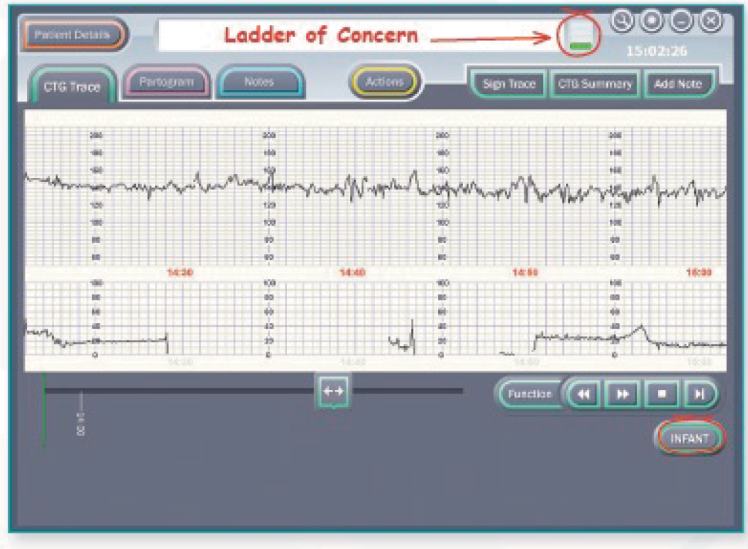
BLUE (Level 3) – Indicates that the software has **minor concerns** with the CTG

YELLOW (Level 2) – Indicates that the software has **serious concerns** with the CTG

RED (Level 1) – Indicates that the software has **urgent concerns** with the CTG

Example of Guardian® running with the Infant® software switched ON

Infant® GREEN LADDER OF CONCERN

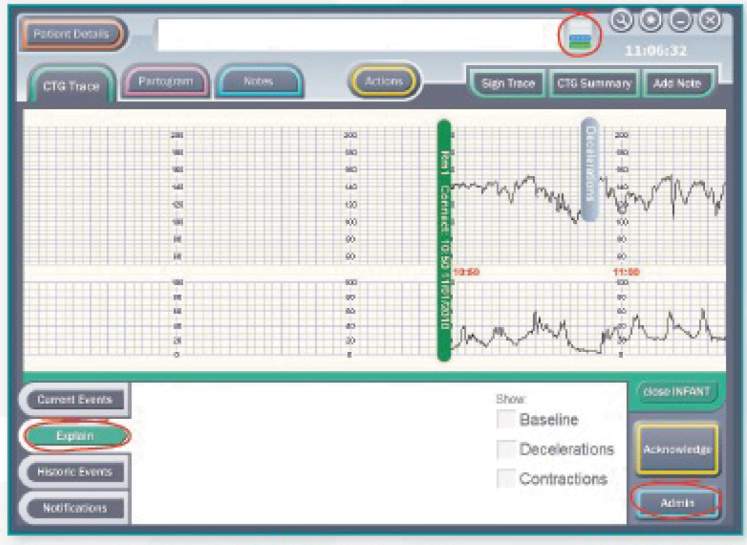


The midwife/doctor can recognise that the woman is in the intervention/decision-support arm of the study because the Infant® ladder of concern is present at the top of the screen, next to the woman's details.

In this example the level of concern showing on the ladder is **GREEN** indicating that the software has **NO CONCERNS**.

It is important to note that throughout the study all women who are monitored continuously will have the INFANT button displayed on the screen. This does NOT necessarily mean that the woman is in the study or the "intervention" arm. If the woman is not in the intervention arm or the study, this button acts as an administration button. If pressed it will allow you to enter the woman into the study if she is eligible, has given written consent, and has not been previously randomised.

Infant® BLUE LADDER OF CONCERN



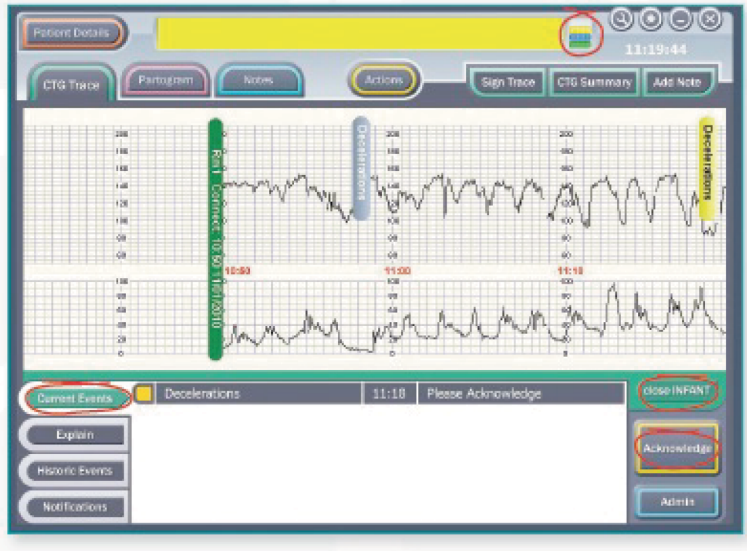
The Infant® ladder of concern is displaying **BLUE** indicating that there are now **MINOR CONCERNS**. The minor concern that it has noted is a deceleration.This is identified by a blue longitudinal marker (Infant® event marker) on the CTG.

Once a blue level of concern has occurred the software will only downgrade it to a green once the event is over and the CTG is reassuring. The midwife does not need to acknowledge any blue events on the Guardian® platform.

In this screen shot the "Explain" button has been opened. If any of the boxes entitled baseline, decelerations or contractions are ticked by the midwife/doctor, the software will show on the CTG trace where it has identified these i.e. if the baseline was ticked it would show in blue at 145 bpm (see page 10).

The "Admin" button, if pressed, will give options if the woman wishes to withdraw from the study. It is expected that this should be an extremely unusual event.

Infant® YELLOW LADDER OF CONCERN



Once the software has noted several incidents it will trigger a **YELLOW** alert, indicating **SERIOUS CONCERNS**. The ladder will now be "flashing" yellow. The bar with the woman's details will also turn yellow and the concern will be noted on the CTG by a yellow Infant® event marker. Alongside this visual display a tone will sound after **5 minutes and repeat at regular intervals** until it has been acknowledged by a midwife or doctor.

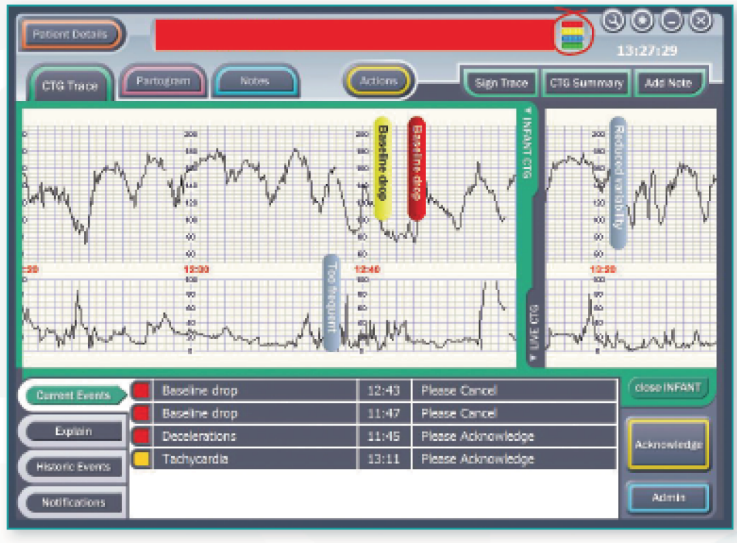
To acknowledge the alert, the acknowledge button must be pressed and the midwife/doctor must then "thumbprint" to complete the acknowledgment. Once this is done the ladder will remain a constant yellow until the software recognises that the incident is over. Only when the Infant® software recognises that the event is over will it downgrade the alert to a **BLUE**/**GREEN** status. The midwife's/doctor's name who acknowledged the alert will appear next to the description of the alert under the current events, to show that they were the person who acknowledged the alert.

NB: If this tone is not acknowledged **after 10 minutes,** a voice message stating "Warning, there are some anomalies with the trace, please acknowledge" will be sounded **at regular intervals** until it is acknowledged.

A yellow alarm automatically triggers the current events screen to open to show the detail of the concern i.e. decelerations so that the midwife/doctor can review and acknowledge the alert.

To return to the screen with no current events shown, all open current events must be acknowledged and the "close INFANT" button pressed. This will then stay closed until another level of concern is noted or until the INFANT button (shown on page 7) is pressed by the user. This does not turn the Infant® software off. If the screen displays an Infant® ladder of concern, the software is on.

Infant® RED LADDER OF CONCERN



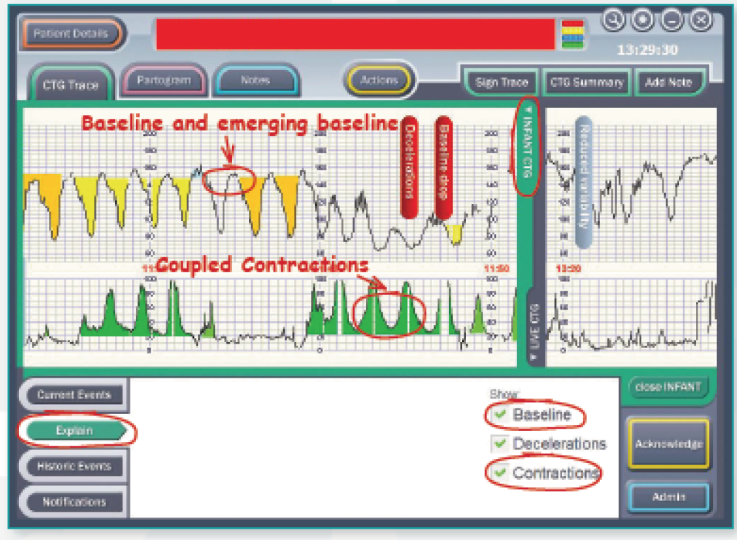
In the above screen shot the Infant® ladder of concern is **RED**. The ladder will now be "flashing" **RED** indicating **URGENT CONCERNS**. The bar with the woman's details will also be highlighted in red and the Infant® event marker on the CTG will be red.

An audible warning tone (slightly different to the yellow alert) will sound **after 2 minutes** and repeat at regular intervals to alert the midwife/doctor that the software has detected some **URGENT CONCERNS**. If the tone remains unacknowledged for a period of **2 minutes** a vocal warning stating "Warning, the trace is abnormal, senior review is urgently required" will sound at regular intervals until the midwife/doctor acknowledges the alert.

The alert is acknowledged by pressing the "acknowledge" button and using the thumbprint recognition. Once this has been acknowledged, the ladder will remain a constant **RED** until the software recognises that the incident is over and downgrades the level of concern to **YELLOW**, **BLUE** or **GREEN** if applicable.

When a RED concern is triggered, the midwife would be expected to not only acknowledge the alert with a thumbprint but to get a senior member of the labour ward team to review the CTG.

Infant® EXPLAIN ALERT FUNCTION



When an alert is noted by the colour change on the Infant® ladder of concern the midwife or doctor can question the decision-support software to observe three characteristics of the trace (baseline, decelerations, and contractions). This can be done anytime during the labour and not just when a concern state is triggered. This is done by pressing the "Explain" button and ticking the boxes of what you want to see. The decision-support software can highlight in different colours the various concerns. If you wanted to see the frequency of contractions, you would tick the contractions option and the contractions would be highlighted for you to clearly review.

The fetal heart rate/contractions are colour coded with the following colours:

Baseline: Blue

Emerging Baseline: Green

Decelerations: Shallow – Pink; Insignificant – Green; Moderate – Yellow; Severe – Orange

Contractions: Normal – Green; Coupled - Dark Green; Red – If they have pushing detected on them

In the above screen shot the left hand side of the trace is showing the Infant® review CTG. This trace will show the position of any Infant® event if selected from the current event list window or can be scrolled by the user to review the trace in its entirety.

The right hand side of the trace will show the latest 10 minutes of real time CTG data.

The dividing banner clearly defines the traces.

Please note, if a woman is randomised to the intervention arm (decision-support software turned on) this should not affect your care of the woman. You should still be manually reviewing the CTG as you would for a woman randomised to the control arm or not in the study. The decision-support software is meant to be an additional review and not a replacement.

8. Guardian® Central Station

The central station has been adapted to incorporate the Infant® study software. The above screen shot demonstrates how the CTGs will appear if they have the Infant® software running. The Infant® ladder of concern will show on the left hand side of the CTG if the woman is randomised into the decision-support arm. Rooms 1, 2 and 3 are displaying the Infant® ladder of concern whereas the trace in the bottom right hand corner from theatre 2 does not have the Infant® study software running alongside it. This woman is either in the control arm of the study or not in it at all.

At the top of the screen the delivery room boxes are highlighted to correlate with the colour coding on the Infant® ladder of concern. For example the Infant® study software in room 1 has noted that the trace is non-reassuring which has escalated the Infant® concern state to red, the room number at the top of the screen has also turned red. If the room number is flashing, this indicates that the alert has not yet been acknowledged. In the table at the bottom of the screen the end column is also displaying a red number 1 – this indicates that the Infant® software has been triggered to the highest concern state. Theatre 2 has a black box around it which indicates that the woman is in the control arm of the study. If there is not a black outline or a colour in these boxes the woman is not randomised into the study.

It is extremely important to note that a CTG can be running even if the room boxes are grey – a grey box only indicates that the Infant® study software is not running alongside the CTG. All CTGs must still be consistently reviewed by midwives and doctors.

NB: Central stations may not be available in all hospitals.

9. Articles/Journals of Interest

Altaf, S., C. Oppenheimer, et al. (2006). "Practices and views on fetal heart monitoring: a structured observation and interview study." *British Journal of Obstetrics and Gynaecology* 113(4): 409-18.

Amer-Wahlin, I., C. Hellsten, et al. (2001). "Cardiotocography only versus cardiotocography plus ST analysis of fetal electrocardiogram for intrapartum fetal monitoring: a Swedish randomised controlled trial." *Lancet* 358(9281): 534-8.

Ayres-de-Campos D., et., A randomised clinical trial of intrapartum fetal monitoring with computer analysis and alerts versus previously available monitoring. BMC Pregnancy Childbirth, 2010: 10:71

Ayres-de-Campos D., et al., Knowledge of adverse neonatal outcome alters clinicians' interpretation of the intrapartum cardiotocograph. BJOG, 2011: 118(8): 978-84.

Barber V.S., et al Computers and CTG: where are we at?. British Journal of Midwifery, 2010: 18(10): p. 644-649.

Chester, B. (1998). "Electronic Fetal Monitoring: A brief summary of its development, problems and prospects." *European Journal of Obstetrics and Gynaecology* 78: 133-40.

Costa A., et al., Access to computerised analysis of intrapartum cardiotocographs improves clinicians' prediction of newborn umbilical artery blood pH. BJOG, 2010; 117(10): 1288-93

Devoe, L. D. (2009). "The future of intrapartum care: navigating the perfect storm--an obstetrician's odyssey." *American Journal of Obstetrics and Gynecology* 201(1): 100-4.

Georgieva, A., S. J. Payne, et al. (2009). "Computerised electronic foetal heart rate monitoring in labour: automated contraction identification." *Medical Biological Engineering and Computing* 46(12): 1315-20.

Hindley, C. and A. M. Thomson (2005). "The rhetoric of informed choice: perspectives from midwives on intrapartum fetal heart rate monitoring." *Health Expectations* 8(4): 306-14.

Medicines and Healthcare products Regulatory Agency, Medical Device Alert (Action Update).Ref: MDA/2010/054.

Sameshima, H., T. Ikenoue, et al. (2004). "Unselected low-risk pregnancies and the effect of continuous intrapartum fetal heart rate monitoring on umbilical blood gases and cerebral palsy." *American Journal of Obstetrics and Gynecology* 190(1): 118-23.

Sinclair, M. (2001). "Midwives' attitudes to the use of the cardiotocograph machine." *Journal of Advanced Nursing* 35(4): 599-606.

Stout, M, et al., Electron Fetal Monitoring: Past, Present, and Future. Clin Perinatol, 2011: 38; 127-142.

Please note: The full text of the above journal papers can be located in the INFANT study resource file in Delivery suite, Community Office, Ultrasound Scan Department and the Antenatal Clinic.

A copy of the full INFANT study protocol can also be found in the resource files or ask your INFANT LCM for a copy. The protocol can also be found at www.npeu.ox.ac.uk/infant