

Trial Scenarios: Monitoring

5. Trial of fish oil supplementation in normal pregnancy¹

Background:	Gestational age and birthweight are strong predictors of a baby's survival. Observational evidence suggests that women with a high dietary intake of oily fish have long pregnancies and babies with high birthweights.
Design:	RCT
Setting:	A single large antenatal clinic
Study population:	600 healthy pregnant women attending for routine week-30 antenatal visit.
Eligibility criteria:	Normal pregnancy at 30 weeks gestation based on ultrasound or LMP Exclusions – multiple pregnancy, bleeding in pregnancy, previous placental abruption, allergy to fish, regular fish oil supplementation.
Intervention:	Group 1 – 4g fish oils in capsule daily Group 2 – 4g olive oil in capsule daily Group 3 – no oil supplement
Randomisation:	Sealed opaque envelopes in antenatal clinic containing a number that corresponding to a treatment pack or indicating no supplementation.
Trial supplies:	Pre-numbered boxes of oil capsules given to the women at each visit
Outcomes:	Duration of pregnancy, birth weight and length
Other data:	Participant interviews about lifestyle factors relevant to pregnancy outcome, compliance, food frequency questionnaire
Data management:	Paper CRF. Data entry at coordinating centre.
Experience:	Experienced coordinators; clinic staff little trial experience

What are the particular hazards of the trial?

This is a low-risk trial – a single-centre trial to assess of the impact of two different oils present in a normal diet on the outcome of normal, low-risk pregnancies.

The particular concerns are:

¹ This scenario was based on a trial report by Olsen S, Sorensen N, Hedgaard M, Henriksen T, Hansen H, Grant A, Randomised controlled trial of effect of fish-oil supplementation on pregnancy duration. (*Lancet* 1992; 339:1003), but some of the details have been altered or invented

- 1 Randomisation process – use of sealed envelopes in an open trial makes the study vulnerable to the random allocation of treatment being compromised – either through ignorance or intentionally. Centralised process should be used if at all possible.
- 2 Although the women are not a vulnerable population, their babies are and their safety is of particular concern – both the risks and benefits of treatment should be carefully monitored.

Suggested Approaches to Monitoring

Trial Oversight:

- A trial management group, **and**
- An independent DMC (unless the recruitment phase will be so short that no information on pregnancy outcomes would be available on the first patients randomised in time to prevent some of the patients being recruited unnecessarily should a benefit be detected).

Before the start of recruitment:

Because it is a large antenatal clinic a large number of midwives and obstetricians will be involved in the study and they have little experience of trials.

An investigators' meeting or a site visit is recommended to ensure that all staff are clear about the trial procedures, in particular the randomisation process.

During the trial

Because the trial is being conducted in a single hospital, visiting the clinics periodically is likely to be an efficient way of monitoring the trial. The following could be checked

- Signed consent forms
- Adherence to randomisation process
- Patient eligibility (most of the panel would do this in a small sample)

Outcomes data could be checked either against the clinic records or by collecting a copy of the birth record.

At the end of the trial

Record of destruction of unused treatment packs.