A randomized clinical trial to compare early versus delayed endovenous treatment of superficial venous reflux in patients with chronic venous ulceration.

Economic analysis plan

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Does the early treatment of superficial venous reflux in addition to compression therapy improve wound healing and result in greater cost effectiveness in comparison to compression therapy alone in patients with chronic venous ulceration?

The economic evaluation will be based on a patient level in-trial analysis and a modeling exercise. The analyses will be performed from the perspective of the NHS and society. As a preliminary step, a literature review will be conducted to identify other economic analyses in these or similar patients E.g. REACTIV trial. .

In-trial analysis

Resource use items in hospital and community care will be recorded for each patient. They will be collected by case note review and questionnaires completed at baseline, 6 and 12-months. Standard NHS and other published UK unit costs will be multiplied by the resource use collected in the trial to calculate overall costs. A standard cost will be applied for each bandage change, although additional treatments administered for the treatment of symptoms or complications directly related to venous ulceration will be included. Health-related quality of life (utilities) will be calculated from generic QoL questionnaire (EQ-5D). These will be used to estimate quality-adjusted life years for each patient during the trial period (QALY). Cost effectiveness will be calculated as the incremental cost-effectiveness ratio (the difference in mean cost divided by the difference in mean QALY).

Economic decision model

The decision model has two primary objectives (i) to incorporate evidence from other trials, particularly meta-analyses of similar treatments in comparable populations (ii) to extrapolate outcomes beyond the 1-year trial reporting period.

Incorporating evidence from other trials

A clinical literature review will be conducted to identify other trials in comparable populations, e.g. updating Howard, 2008. The aim is to identify the relative effectiveness of all currently feasible treatment options for these patients, not just those evaluated in the EVRA trial. The comparators and treatments may include open surgery, early endovenous ablation (which may be implemented by different techniques, with or without compression bandaging), or compression bandaging with endovenous

ablation treatment once the ulcer has healed. If the data permit a new meta-analysis will be undertaken. This may be an indirect comparison or mixed comparison depending on the structure of the published data.

Extrapolating beyond the 12 month trial period

The second objective of the economic model is to estimate the overall net benefit of the treatments over the long term. It is possible that not all ulcers will have healed within 12 months. Furthermore, the ulcer may return, in some cases after the 12 month trial period. Formally quantifying these effects in each treatment option requires some kind of extrapolation. The data to support such extrapolation may be taken from the trial (e.g fitting parametric time-to-event functions to the trial data, and extending these beyond the trial) or may come from external sources (such as rates of events reported from longer term studies and observational data in the literature). NHS resource use and patient HRQOL associated with healed and unhealed leg ulcers will be taken from the EVRA trial and other literature.

The results of the analyses will be presented as estimates of mean incremental costs, effects, and, incremental cost per QALY. Sensitivity analysis will be conducted. The results of the base case and sensitivity analyses will be presented as mean estimates and as cost-effectiveness acceptability curves (CEACs).