

National, centralised hospital datasets can inform clinical trial outcomes in prostate cancer: a pilot study in the STAMPEDE trial.

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Introduction

Hospital Episode Statistics (HES) are routinely collected data describing National Health Service (NHS) hospital visits in England, with procedure and disease codes.¹ This study, embedded in STAMPEDE, aimed to build a model using HES, linked to primary medical records and trial case report forms (CRFs) to identify progressive disease events (PDEs), including skeletal-related events (SREs). STAMPEDE is the largest interventional prostate cancer trial in the world, testing multiple treatments alongside a control with its unique multi-arm multi-stage design.²

Methods

Analysis of 5 STAMPEDE patients in 2 stages (data to July 16). 1: Detailed manual note review of 3 patients' PDEs were compared to HES and CRFs to build model. 2: Used model to use HES to identify possible PDEs in 2 patients, verified by note review and compared to CRFs. We then created algorithm rules to identify PDEs per 8 week interval plus further analysis of HES coding to find SREs. We are now creating automated code to test this algorithm on a large set of patients.

Results

Prostate cancer PDEs coincided with clustering of HES events. HES found 4 PDEs omitted from CRFs but missed 2 (total PDEs: HES 10, CRFs 8). HES found a false positive CRF PDE. Compared with note review HES missed 4 PDEs (false negatives), with 2 missed and 2 upgraded to PDEs post-standard query procedures, plus HES found 3 false positives (1 STAMPEDE

treatment and 2 delayed treatments post-PDE). Hence HES found 71% of PDEs in note review (HES 10, note review 14). CRFs found 57% of PDEs compared to note review (CRFs 8, note review 14). Hence HES found 14% more PDEs than were recorded in CRFs compared to note review. HES identified 4 additional SREs not recorded in CRFs but missed 2. We will present additional preliminary data on a validation cohort of 50 trial patients.

Discussion

When clinical trials are undertaken and CRFs completed to collect outcomes there is often a huge challenge of long-term follow-up, particularly for events nearer end-of-life. One example of this is related to the docetaxel chemotherapy arm of STAMPEDE. We need to know what progression events happen as patients are lost to follow-up. Is the reduced number of PDEs seen on the docetaxel arm because there is a reduction of events due to the drug, or is it just that we have failed to capture them? Furthermore, reforms to the Cancer Drugs Fund in July 2016 required data on patients' outcomes to be collected but there is no current method to do so; hence a routine method of data collection is needed.³ The implications of identifying missed progression events would allow an increase in data quality, including prospectively in clinical trials.

This is the pilot feasibility study testing 5 patients. The stage 2 will involve 50 patients, which is currently being undertaken with an automated algorithm which is currently in development. The stage 3 involves 250 and stage 4, 9000 patients. Non-trial patients will then be tested and also will be tested for use in the new upcoming bladder cancer trial.

The HES data is linked to the STAMPEDE data via the clinical trial number which allows efficient and accurate linkage. Once the algorithm has been completed the output values will prompt data queries which in turn will allow population of trial CRFs or a cue to analyse the clinical portal for more information on the PDE. Automated linkage between CRF data and the output using the HES algorithm, is another step which will need to be designed to analyse vast numbers of patients.

Conclusion

Hospital record review revealed site staff may miss reporting major clinical efficacy outcome events on CRFs, especially nearer end-of-life. HES successfully identified most PDEs (often found as a cluster of SREs), plus additional trial events not reported on CRFs compared to note review and as predicted HES and CRFs found fewer PDEs. PDEs and SREs missed from CRF recording can be identified in HES. This confirmed use of HES to detect PDEs is feasible. HES-identified events have potential as a primary data source when subsequently verified by standard data queries. Future work will test this model prospectively in the forthcoming BladderPath trial. It may offer a superior, cost-effective method of primary data collection compared to traditional CRF recording.

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