The Ocular Hypertension Treatment Study (OHTS): Do Site Visits Improve Participant Re-Engagement In Longitudinal Clinical Research?

Mathew S. Margolis; Patricia Morris; Deborah Dunn; Bradley Wilson; Michael A. Kass; Mae O. Gordon.

Introduction

The Ocular Hypertension Treatment Study (OHTS) was a treatment trial that randomized 1,636 participants with ocular hypertension in 32 clinical centers. Ocular hypertension, which can result in glaucomatous damage and vision loss, primarily affects adults over age 55.

Six years following study close-out, the NIH awarded funds for a 20-year follow-up to determine the clinical and QOL status of participants, now median age 78.

- OHTS study goal is to achieve 80% ascertainment of all randomized patients (n=1636).
  - Ascertainments are defined as the sum of the following mutually exclusive categories: core visits, telephone QOL surveys, declines, or confirmed deaths).
  - This goal was set to minimize bias due to sampling[1-3] and to protect statistical power[2, 4-7].

Despite the ubiquity of site visits in clinical research, little has been documented about their efficacy in participant re-engagement. Here we report the impact of site visits on completed core visits, telephone QOL surveys, and overall ascertainments.

Methods

- Clinics with <50% enrollment at a given date were site visited to increase participant ascertainment rate.
- A time period of five months pre- and post-site visit was selected to avoid bias from our annual coordinators meeting addressing re-engagement.
- Site visit costs were collected from central coordinating center records.

Results

	Absolute	Adjusted*
Number of Site Visits	11	-
Core visits		
Five months Pre-Site visit	33	37.1
Five months Post-Site visit	24	28.5
Telephone QOL surveys		
Five months Pre-Site visit	16	16.3
Five months Post-Site visit	19	20.3
Ascertainments		
Five months Pre-Site visit	90	110.0
Five months Post-Site visit	75	168.1

*Adjusted proportionally to account for the decreased participant pool over time; values represent the number of hypothetical outcomes if at any given time the participant pool was equal in size to that number at study onset.

- The absolute completion rate of core visits, telephone QOL surveys, and total ascertainments peaked shortly after site visits, but waned over the five-month post-site visit period with the exception of telephone QOL surveys.
- Proportional adjustment demonstrates a sustained increase in ascertainments and telephone QOL surveys in the five months following site visits; the increase in adjusted core visits was not sustained.
- The average cost per site visit was $2106, with a range of $960 to $2588.

References

1. Siddiqi AE, Sikorskii A, Given CW, Given B. Early participant attrition from clinical trials: role of trial design and logistics. *Clinical trials (London, England).* 2008;5(4):328-335.
2. Fewtrell MS, Kennedy K, Singhal A, et al. How much loss to follow-up is acceptable in long-term randomised trials and prospective studies? *Archives of disease in childhood.* Jun 2008;93(6):458-461.
3. Gupta A, Calfas KJ, Marshall SJ, et al. Clinical trial management of participant recruitment, enrollment, engagement, and retention in the SMART study using a Marketing and Information Technology (MARKIT) model. *Contemporary clinical trials.* May 2015;42:185-195.
4. Sterne JH, J.; Reeves, B. . A Cochrane Risk Of Bias Assessment Tool: for Non-Randomized Studies of Interventions (ACROBAT-NRSI). 2014; http://www.riskofbias.info.
5. Wells GS, B.; O'Connell, D., et al. The Newcastle-Ottawa Scale for assessing the quality of nonrandomised studies in meta-analysis. Accessed 8/2017.
6. Friedman LF, C.; DeMets, D. . Fundamentals of Clinical Trials. *New York: Springer- Verlag.* 1988.
7. S F. Managing attrition in clinical research. 1988;Clin Psychol Rev. (8):16.

Discussion

The OHTS faced the task of re-engaging participants (median age 78) six years after study close-out, and set an ambitious goal of an 80% ascertainment rate to protect study power and reduce bias.

To meet ascertainment goals, 11 underperforming sites were site visited. Our findings demonstrate the following:

- Site visits did not result in an absolute increase in ascertainments, however, they resulted in an absolute increase in telephone QOL of surveys and a proportional increase in ascertainments.
  - The absolute increase in telephone QOL surveys suggests site visits resulted in coordinators collecting alternative data when they could not secure core visits.
- Our results likely underestimate the effect of site visits as proportional adjustment is unable to account for the increasing difficulties in patient re-engagement over time.
- Timely increase in ascertainment status may decrease future spending for alternative retention efforts, and minimizes the probability for costly study extensions.

It is our opinion that site visits potentiate re-engagement efforts by individual sites, however, clinical coordinating centers must weigh the costs and benefits of using site visits as a tool for participant re-engagement.

Support & Acknowledgements

Supported by NIH [EY025180, EY025181, EY025182 and EY025183].

Washington University Ophthalmology & Visual Sciences NIH/NEI Core Grant #P30EY002687.

Washington University Ophthalmology & Visual Sciences Research to Prevent Blindness Unrestricted Grant.

Clinical and Translational Science Award (CTSA) Grant [UL1 TR000448].