Time to publication for NIHR HTA Programme-funded research: a cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004121
Article Type:	Research
Date Submitted by the Author:	25-Sep-2013
Complete List of Authors:	Chinnery, Fay; University of Southampton, NETSCC Young, Amanda; University of Southampton, NETSCC Goodman, Jennie; University of Southampton, NETSCC Ashton-Key, Martin; University of Southampton, NETSCC Milne, Ruairidh; University of Southampton, Wessex Institute
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Medical publishing and peer review
Keywords:	STATISTICS & RESEARCH METHODS, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Information management < BIOTECHNOLOGY & BIOINFORMATICS

Time to publication for NIHR HTA Programme-funded research: a cohort study

Fay Chinnery, Amanda Young, Jennie Goodman, Martin Ashton-Key, Ruairidh Milne

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Fay Chinnery
Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Amanda Young
Senior Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Jennie Goodman
Programme Manager

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Martin Ashton-Key
Consultant in Public Health Medicine / Consultant Advisor

Wessex Institute, University of Southampton, Southampton, Hampshire, SO16 7NS, UK
Ruairidh Milne
Professional Fellow in Public health

Correspondence to:
Fay Chinnery
F.Chinnery@soton.ac.uk
Tel: 023 8059 5548

Key words
Publication; Time to publication; Clinical trial; Health Technology Assessment (HTA) Programme

Word Count
2600

Contributors
The study was designed by RM, M A-K, FC and AY. FC, AY, JG and M A-K performed data extraction, FC and AY conducted the data analyses. FC drafted the manuscript, guided by M A-K, RM and AY. All authors have read and approved the final manuscript.

Data sharing statement
There are no additional data available.

Time to publication for NIHR HTA Programme-funded research: a cohort study

ABSTRACT

Objective: To assess the time to publication of primary research and evidence syntheses funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme in *Health Technology Assessment* (the peer reviewed journal for the NIHR HTA Programme, known as the monograph series) and in an external journal in the wider biomedical literature.

Study design: Retrospective cohort study.

Setting: Primary research and evidence synthesis projects funded by the HTA Programme were included in the cohort if they were registered in the NIHR research programmes database and planned to submit their draft final report for publication in *Health Technology Assessment* on or before 9 December 2011.

Main outcome measures: The median time to publication and publication at 30 months in both *Health Technology Assessment* and in an external journal, as determined by searching the NIHR research programmes database and HTA Programme website.

Results: Of 458 included projects, 184 (40.2%) were primary research projects and 274 (59.8%) were evidence syntheses. Of the 155 primary research projects with a completion date, the median time to publication was 23 months (26.5 and 35.5 months to publish a monograph and to publish in an external journal, respectively). 56.1% published a monograph by 30 months, but only 42.6% had published externally. The median time to publication of HTA-funded trials was 24 months and 67.5% published by 30 months. Among the evidence syntheses with a protocol online date (n=223), the median time to publication was 25.5 months, (28 months to publication in the monograph), but fewer than half of evidence synthesis projects publish in an external journal. 65% of evidence synthesis studies publish by 30 months (54.7% had produced a monograph but only 23.3% had published elsewhere).

Conclusion: Research funded by the HTA Programme publishes promptly. The importance of *Health Technology Assessment* was highlighted as the median time to publication was nine months shorter for the monograph than an external journal, and publication at 30 months was higher in the monograph than for other peer-reviewed journals.

Strengths and limitations of this study

- The study involves a large cohort, representing almost 20 years of research funded on behalf of the NHS.
- This report complements previous work which has shown that 98% of HTA projects funded since 2002 will publish a monograph.
- This project relied heavily on the NIHR research programmes database and some data were not available for analyses.

INTRODUCTION

In order for research to help patients and aid clinicians in their decision-making it must be published in full and made available in a timely fashion. However, it is estimated that over 50% of studies are never published completely, and studies with disappointing (non-significant) results may not be published at all.[1,2] Non-publication is believed to be primarily due to failure to write-up and submit research, rather than manuscripts being rejected.[3] Studies with null or negative findings take longer to be published than those with positive results,[4,5] and this publication bias may invalidate a meta-analysis, leading to overestimation of treatment effects. As a result, new interventions may be adopted without suitable evidence to support them.

In addition to publication bias, selective outcome reporting may also lead to overestimation of the effectiveness of the treatment, emphasising the need for rigorous reporting of research. Trials funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (which produces research evidence on behalf of the NHS) that only publish in *Health Technology Assessment* (the peer reviewed journal for the HTA Programme, known as the monograph series) tend to have a higher *P*-value for the main outcome compared to those that also have a publication in another journal. The full HTA monograph generally contains more outcomes than the main trial publication and journal articles tend to report a higher proportion of statistically significant outcomes. Consequently, researchers including HTA-funded trials in their systematic reviews are recommended to use information from the monograph and not the associated journal article.[6]

Turner *et al*.[7] have shown that 98% of projects funded by the HTA Programme in the last 10 years will publish in the HTA journal series. In contrast, Ross *et al*.[8] found that only 68% of clinical trials funded by the US National Institutes of Health (NIH) publish, with 46% publishing within 30 months of trial completion. Tricco *et al*.[9] established that Cochrane reviews have a median time to publication of 2.4 years, but only 80% of Cochrane protocols are published overall. Given the importance of publishing promptly and the recommendation that researchers use data from the monograph of a project, rather than its journal article; the aim of this study was to determine the time to publication for HTA-funded primary research and evidence synthesis projects in *Health Technology Assessment* and biomedical literature, and to compare time to publication with other public sector funders.

METHODS

Data source

Health Technology Assessment (http://www.hta.ac.uk/research/htajournal.shtml) is the peer reviewed journal for the NIHR HTA Programme. The HTA journal series publishes scientifically rigorous reports arising from work funded by the HTA Programme and all HTA research is expected to publish in the journal series. Approximately 50 reports are published in the series every year and over 600 issues have been published since its first volume in 1997.

The HTA Programme website states that *Health Technology Assessment* is indexed on MEDLINE, CINAHL, EMBASE, the Cochrane Library and the ISI Science Citation Index and assessed for inclusion in the Centre for Reviews and Dissemination (CRD) Database of Abstracts of Reviews of Effectiveness (DARE). The journal is ranked fourth (out of 76 titles) in the 'Health Care Sciences & Services' category of the Thomson Reuters 2011 Journal Citation Reports (Science Edition) and has a five-year impact factor of 5.596.

Cohort sample

The cohort in this project is derived from the NIHR research programmes database. It is a sub sample of the data set used by Turner *et al*.[7] and includes projects that planned to submit their draft final report on or before 9th December 2011. Based on project classification in the database, the cohort was divided into two main categories: primary research and evidence synthesis, primary research was subdivided further into trials (as defined by Ross *et al*.[8]) and the remainder were categorised as 'others'.

Data extracted from the database included the project reference number, its publication date in the HTA journal series and the date when the evidence syntheses protocols were made available online. The HTA journal (or draft final report or external publication if the project did not have a published monograph) was hand-searched for the end of recruitment date and length of follow-up in order to calculate the study conclusion date for the primary research projects. We also hand searched the HTA journal website for the online publication date of the first report for all projects in an external journal. We took a pragmatic approach and excluded protocols, background papers and systematic reviews that may have been conducted before the research began. We included the first report that used clinical data from the project, and excluded cost-effectiveness analyses (unless the project report specifically stated that it was an economic evaluation).

Time to publication

For primary research, the time to publication was determined by calculating the number of months from when the study concluded (i.e. end of follow-up, using the same methodology as Ross *et al*.[8]) to when the monograph was first published online and to when the first external publication was available online. For evidence syntheses, we followed the protocol of Tricco *et al*.[9] Time to publication was measured as the number of months from when the protocol was first made available online to the online publication date of the monograph and to the online availability of the study in an external journal.

Data analysis

Kaplan-Meier survival curves were produced for primary research and evidence synthesis projects and the cumulative percentage of HTA-funded studies published in the HTA journal series was compared to other peer reviewed journals, time to any publication was also plotted. We calculated the median (time for 50% of funded studies to publish) time to publication in *Health Technology Assessment*, elsewhere and for the first output for primary research, trials, and evidence syntheses.

Ross *et al*.[8] have emphasised the need for timely publication and have stated a cut-off of 30 months for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at 30 months and the total percentage published, both in the monograph and elsewhere.

The Anderson-Darling normality test in Minitab was used to establish distribution of the data subsets and any statistical difference between the times to publication was determined using the Mann-Whitney U test.

RESULTS

We identified 458 projects for inclusion in our analyses (figure 1).

Figure 1: Flow diagram of projects in this study.

INSERT FIGURE 1 HERE

Primary research

The primary research subset contains 184 projects; however, 29 of these did not state an end of recruitment date, or it was not possible to determine length of follow-up. Consequently, it was not possible to calculate the last point of data collection for 15.8% of HTA programme-funded primary research, even though many of these studies do have a publication.

Of the 155 primary research projects with a completion date, the median time to publication (time for 50% of the funded studies to publish) was 23 months, 26.5 months to the monograph and 35.5 months to publication in an external journal, but this difference was not statistically significant (P=0.149).

Sixty-nine per cent of all primary research funded by the HTA programme is published by 30 months, but only 56.1% of monographs are produced within this time. Limiting the analysis to trials, directly comparable to the work of Ross *et al*.[8], 67.5% publish within 30 months and have a median time to publication of 24 months (table 1). Overall publication rates are 92.9% for any publication, 88.4% in the monograph and 62.6% in an external journal (table 1, figure 2).

INSERT TABLE 1 HERE

Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the HTA monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

INSERT FIGURE 2 HERE

Evidence synthesis

Of the 274 evidence syntheses, the database did not record a protocol online date for 51 (18.6%) projects and so these could not be included in further analyses. Of the remaining projects, the median time to publication was 25.5 months. The monograph is published after 28 months on average but, unlike primary research, fewer than 50% of evidence synthesis projects publish in other peer-reviewed journals (table 2, figure 3). Evidence syntheses publish in a timely fashion, with 65% of studies publishing within 30 months and 93.3% publish overall.

INSERT TABLE 2 HERE

Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in the HTA monograph versus other peer reviewed biomedical journals and to the first publication anywhere.

INSERT FIGURE 3 HERE

DISCUSSION

Using the standard of Ross *et al*.,[8] HTA-funded research publishes promptly; 69% of primary research projects publish by 30 months, with a median time to publication of 23 months. Sixty-five per cent of evidence synthesis projects publish by 30 months and the median time to publication was 25.5 months.

Strengths and limitations

The main strength of this study is that it involves a large cohort, representing almost 20 years of research funded on behalf of the NHS. This report complements previous work which has shown that 98% of HTA projects funded since 2002 will publish a monograph.[7] This project used a subsample of the dataset of Turner et al.[7] with the intention to determine the time to publication of all of the primary

research and evidence synthesis projects that do publish. However, a major limitation of this project is the large amount of data missing from the analyses. It was not possible to determine the end-of-follow up for over 15% of primary research projects, and over 18% of the evidence synthesis studies did not have a recorded protocol online date, so they were not included in the analyses. Since data-recording was poorer in earlier years (unpublished data), we have disproportionately excluded more of the older projects. Consequently, since older projects take longer to publish on average (unpublished data), we may be underestimating how long HTA-funded studies take to publish overall.

This project relied heavily on data from the NIHR research programmes database and the HTA journal website to determine if a study has published elsewhere, which in turn depends on self-declarations from the principle investigators (PIs), as per contractual obligations. Preliminary work in an internal NETSCC report found that PIs were under-reporting their external publications by 15.8% and so the overall external publication rate is likely to be higher and we are overestimating the median time to publication in an external journal. In addition, the under-reporting may also be affecting the "Any publication" Kaplan-Meier curve and so influencing the median time to the first publication as well.

Comparison with other studies

Ross et al.[8] highlighted the need for the publication process to be prioritised in order to shorten the time taken for research findings to be available to the public. Their work found that the median time to publication of clinical trials funded by the US NIH and registered with ClinicalTrials.gov (and completed by 31st December 2008) was 23 months. However, this is only the median of the trials that published, not the whole cohort (i.e. the trials that were funded) and so it is underestimating the time to publication. Funders and researchers should aspire to publish all of their research, so the time taken for 50% of studies to publish is the appropriate median time to publication. Arguably, the 30 month publication rate may be the truly important measure of timeliness to publication.

It takes ~32 months for half of the clinical trials funded by the US NIH to publish; only 46% were published within 30 months of trial completion, with an overall publication rate of 68%. In comparison, the median time to publication of HTA Programme-funded trials is 24 months, 67.5% publish by 30 months, and 93.7% publish overall. The HTA figures also compare very favourably with results from industry sponsored trials; trials conducted by GlaxoSmithKline in Spain between 2001 and 2006 had a publication rate of 61% and a median time to publication of 28.4 months. However, it was not clear whether this was the median of the published trials or of the funded ones.[10] The median time to publication of more recent NIH clinical trials (those with a ClinicalTrials.gov identifier, published during 2009 and indexed in MEDLINE) is 21 months,[11] but the study did not comment on how long it took for 50% of the trials to publish. Lastly, Sixty-eight per cent of NIH-funded studies publish overall and 62.6% of HTA-funded primary research publishes externally. This highlights the importance of the HTA journal series as it provides a means of publication for those projects that would not otherwise reach the public domain.

HTA-funded evidence syntheses are also produced in a timely manner, with a median time to publication of 25.5 months and 65.0% of studies being published by 30 months (93.3% publishing overall). In comparison, Cochrane reviews have a median time to publication is 29 months, with only 80.9% publishing in full after eight years of follow-up.

Implications

The median time to publication in the monograph and an external journal could only be compared for primary research (as over half of the evidence syntheses do not have a recorded external publication); here the monograph is produced nine months earlier. Publication rate, for both types of research, was considerably higher in the monograph than for other peer reviewed biomedical journals. The shorter time to publication and high publication rate in the monograph is laudable; ensuring information from

research is easily accessible and widely available is important because it facilitates its use, increases its impact and consequently its value to society. Unpublished data may also invalidate conclusions from meta-analyses, and systematic reviews. These are not just a valuable source of information for health care professionals and researchers, but definitive conclusions about an intervention also prevent putting more patients at risk in further unneeded trials or depriving them of the correct treatment. Having the HTA journal is clearly important for dissemination of research to the public in a timely fashion and ensures that data are not lost as a result of publication bias. US federal requirements[12] call for "results of an Applicable Clinical Trial of a drug, biologic, or device that is approved, licensed, or cleared by FDA must be submitted by the Responsible Party no later than 12 months after the Completion Date". There is an important distinction between the user's (HTA Programme, clinicians and patients, NICE, etc.) perspective and the researcher's perspective of the process. Once they have submitted the draft final report, aside from editing the researcher may assume their task is finished, but the users are more concerned with when the research is in the public domain.

Conclusion and recommendations

Research funded by the HTA Programme publishes in a timely fashion; where a comparison was possible, time to publication was nine months shorter for the monograph than an external journal and publication rate was considerably higher in this than for other peer-reviewed journals. HTA trials publish more promptly than those funded by the NIH and industry and HTA evidence syntheses are produced sooner than Cochrane reviews. This current study highlighted the importance of HTA research being funded via a contract (researchers are contractually obliged to publish their findings in full) as well as the value of the HTA journal series and its rigorous editorial procedure.

Recommendations include encouraging other funding organisations to make it a condition for their investigators to publish final project results in full, within a set time, and to support this practice, regardless of whether findings are significant or not. In the UK, the Health Research Authority (HRA) is responsible for protecting and promoting the interests of patients and the public in health research. It plays a key leadership role in promoting transparency and has made a number of commitments to ensure the publication and dissemination of health research results.[13]

Future work should investigate the time to publication for other funders and ways in which delays can be reduced without compromising quality. Regardless of the funder, all trials should be registered and the methods and results reported in full and in a timely fashion.

ACKNOWLEDGEMENTS

The authors would like to thank Sheila Turner for providing the reference numbers of the projects and their publication date in the monograph; Stephen Lemon for his advice about data extraction from the NIHR research programmes database and Jo Merritt for sharing her data concerning authors not reporting projects that publish in an external journal. We would also like to acknowledge the Metadata team for providing their database and trial details used in the study.

COMPETING INTERESTS

FC has worked for the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) since February 2012; AY is an employee of NETSCC which hosts the Research on Research Programme, from where this work originated; JG worked for NETSCC from January 2006 to April 2013; M A-K is currently an editor for the Health Technology Assessment journal and a full-time employee of NETSCC; RM is employed as the Head of NETSCC and has worked for NETSCC (and its

predecessor organisation) in senior roles on and off since 1996. He was an editor of the Health Technology Assessment journal (1997-2005) and a founder editor for other journals in the new NIHR Journals Library (2011-12).

FUNDING

This research was supported by the NIHR Evaluation, Trials and Studies Coordinating Centre through its Research on Research programme. The views and opinions expressed are those of the authors and do not necessarily reflect those of the Department of Health or of NETSCC.

Table 1: Publication characteristics of HTA Programme-funded primary research and trials (studies with a completion date).

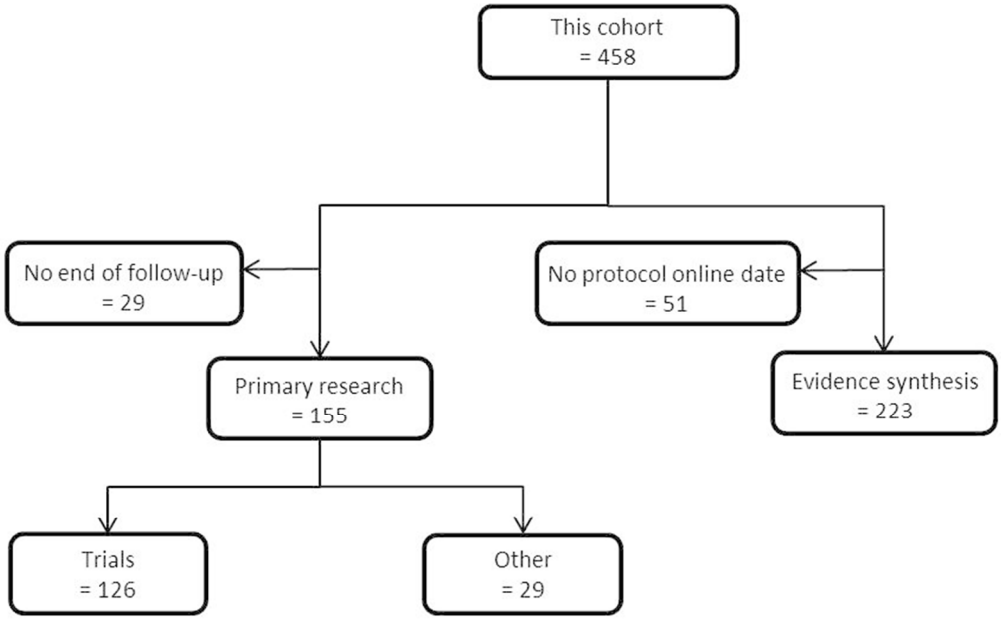
	Primary research			Trials
	Any publication	HTA Monograph	External journal	Any publication
Number of studies (in the cohort)	155	155	155	126
Published (n)	144	137	97	118
Published (%)	92.9	88.4	62.6	93.7
Time for 50% to publish (months)	23	26.5	35.5	24
Published at 30 months (n)	107	87	66	85
Published at 30 months (%)	69.0	56.1	42.6	67.5

Table 2: Publication characteristics of HTA Programme-funded evidence synthesis (studies with a protocol online date).

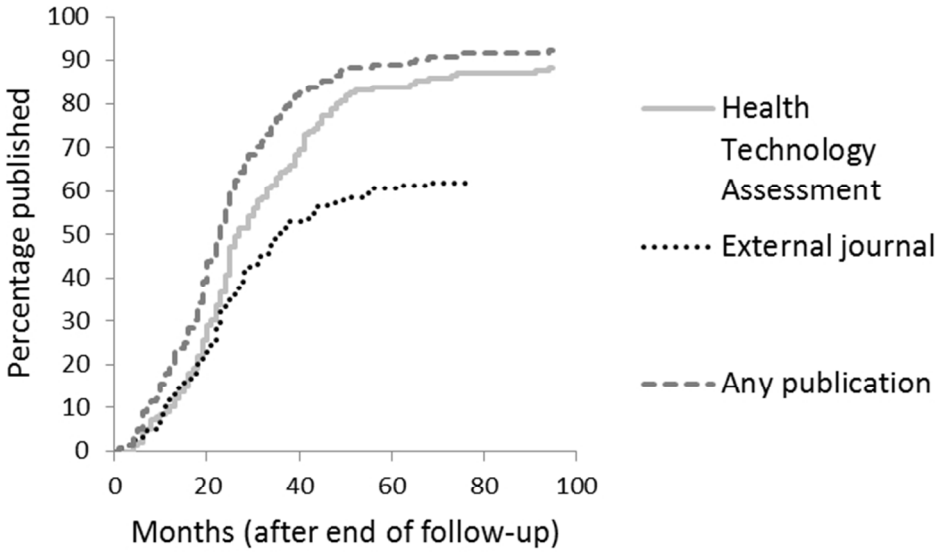
	Any publication	HTA Monograph	External Journal
Number of studies (in the cohort)	223	223	223
Published (n)	208	207	99
Published (%)	93.3	92.3	44.4
Time for 50% to publish (months)	25.5	28	-
Published at 30 months (n)	145	122	52
Published at 30 months (%)	65.0	54.7	23.3

REFERENCES

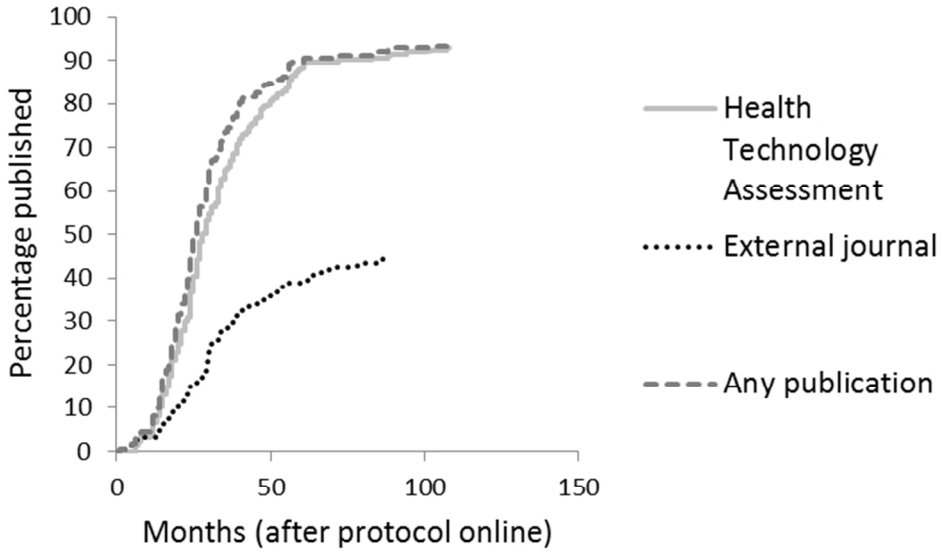
1. Scherer RW, Langenberg P, von Elm E. Full publication of results initially presented as abstracts. Cochrane Database Syst Rev 2007; Issue 2: MR000005
2. Chalmers I and Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009; **374**: 86-89
3. Dickersin K, Chan S, Chalmers TC, Sacks HS, Smith H Jr. Publication bias and clinical trials. Control Clin Trials. 1987; **8(4)**:343-53.
4. Song F, Parekh S, Hooper L, Loke YK, Ryder J, Sutton AJ, Hing C, Kwok CS, Pang C, Harvey I. Dissemination and publication of research findings: an updated review of related biases. Health Technol Assess. 2010; **14(8)**:iii, ix-xi, 1-193.
5. Suñé P, Suñé JM, Montoro JB. Positive outcomes influence the rate and time to publication, but not the impact factor of publications of clinical trial results. PLoS One. 2013; **8(1)**:e54583.
6. Matthews GA, Dumville JC, Hewitt CE, Torgerson DJ. Retrospective cohort study highlighted outcome reporting bias in UK publicly funded trials. J Clin Epidemiol. 2011; **64(12)**:1317-24
7. Turner S, Wright, D, Maeso B, Cook A, Milne R. Publication rate for funded studies from a major UK health research funder: a cohort study. BMJ Open 2013; **3(5)**. pii: e002521.
8. Ross JS, Tse T, Zarin D, Xu H, Zhou L, Krumholz HM. Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. BMJ 2012; **344**;d7292
9. Tricco AC, Brehaut J, Chen MH, Moher D. Following 411 Cochrane protocols to completion: a retrospective cohort study. PLoS One 2008; **3(11)**: e3684
10. Dal-Ré R, Pedromingo A, García-Losa M, Lahuerta J, Ortega, R. Are results from pharmaceutical company-sponsored studies available to the public? Eur J Clin Pharmacol 2010; **66**:1081-1089
11. Ross JS, Mocanu M, Lampropulos JF, Tse T, Krumholz HM. Time to Publication Among Completed Clinical Trials. JAMA Intern Med. 2013; **173(9)**:825-8.
12. Food and Drug Administration Amendments Act (FDAAA) of 2007 - Section 801.
13. http://www.hra.nhs.uk/hra-news-and-announcements/transparent-research/



143x88mm (150 x 150 DPI)



127x76mm (150 x 150 DPI)



127x76mm (150 x 150 DPI)

BMJ open

Time to publication for NIHR HTA Programme-funded research: a cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004121.R1
Article Type:	Research
Date Submitted by the Author:	09-Oct-2013
Complete List of Authors:	Chinnery, Fay; University of Southampton, NETSCC Young, Amanda; University of Southampton, NETSCC Goodman, Jennie; University of Southampton, NETSCC Ashton-Key, Martin; University of Southampton, NETSCC Milne, Ruairidh; University of Southampton, Wessex Institute
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Medical publishing and peer review
Keywords:	STATISTICS & RESEARCH METHODS, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Information management < BIOTECHNOLOGY & BIOINFORMATICS

Time to publication for NIHR HTA Programme-funded research: a cohort study

Fay Chinnery, Amanda Young, Jennie Goodman, Martin Ashton-Key, Ruairidh Milne

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Fay Chinnery
Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Amanda Young
Senior Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Jennie Goodman
Programme Manager

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Martin Ashton-Key
Consultant in Public Health Medicine / Consultant Advisor

Wessex Institute, University of Southampton, Southampton, Hampshire, SO16 7NS, UK
Ruairidh Milne
Professional Fellow in Public health

Correspondence to:
Fay Chinnery
F.Chinnery@soton.ac.uk
Tel: 023 8059 5548

Key words
Publication; Time to publication; Clinical trial; Health Technology Assessment (HTA) Programme

Word Count
2600

Contributors
The study was designed by RM, M A-K, FC and AY. FC, AY, JG and M A-K performed data extraction, FC and AY conducted the data analyses. FC drafted the manuscript, guided by M A-K, RM and AY. All authors have read and approved the final manuscript.

Data sharing statement
There are no additional data available.

Time to publication for NIHR HTA Programme-funded research: a cohort study

ABSTRACT

Objective: To assess the time to publication of primary research and evidence syntheses funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme published as a monograph in *Health Technology Assessment* and as a journal article in the wider biomedical literature.

Study design: Retrospective cohort study.

Setting: Primary research and evidence synthesis projects funded by the HTA Programme were included in the cohort if they were registered in the NIHR research programmes database and planned to submit their draft final report for publication in *Health Technology Assessment* on or before 9 December 2011.

Main outcome measures: The median time to publication and publication at 30.0 months in both *Health Technology Assessment* and in an external journal, as determined by searching the NIHR research programmes database and HTA Programme website.

Results: Of 458 included projects, 184 (40.2%) were primary research projects and 274 (59.8%) were evidence syntheses. 155 primary research projects had a completion date, the median time to publication was 23.0 months (26.5 and 35.5 months to publish a monograph and to publish in an external journal, respectively) and 69.0% had published by 30.0 months. The median time to publication of HTA-funded trials (n=126) was 24.0 months and 67.5% published by 30.0 months. Among the evidence syntheses with a protocol online date (n=223), the median time to publication was 25.5 months, (28.0 months to publication as a monograph), but only 44.4% of evidence synthesis projects publish in an external journal. 65.0% of evidence synthesis studies publish by 30.0 months.

Conclusion: Research funded by the HTA Programme publishes promptly. The importance of *Health Technology Assessment* was highlighted as the median time to publication was nine months shorter for a monograph than an external journal article.

~~**Objective**: To assess the time to publication of primary research and evidence syntheses funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme in *Health Technology Assessment* (the peer reviewed journal for the NIHR HTA Programme, known as the monograph series) and in an external journal in the wider biomedical literature.~~

~~**Study design**: Retrospective cohort study.~~

~~**Setting**: Primary research and evidence synthesis projects funded by the HTA Programme were included in the cohort if they were registered in the NIHR research programmes database and planned to submit their draft final report for publication in *Health Technology Assessment* on or before 9 December 2011.~~

~~**Main outcome measures**: The median time to publication and publication at 30 months in both *Health Technology Assessment* and in an external journal, as determined by searching the NIHR research programmes database and HTA Programme website.~~

~~**Results**: 458 projects were included. Of the 155 primary research projects with a completion date, the median time to publication was 23 months (26.5 and 35.5 months to publish a monograph and to publish in an external journal, respectively). 56.1% published a monograph by 30 months, but only 42.6% had published externally. The median time to publication of HTA-funded trials was 24 months and 67.5% published by 30 months. Among the evidence syntheses with a protocol online date (n=223), the median time to publication was 25.5 months, (28 months to publication in the~~

Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold, Italic
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold, Italic
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold, Italic
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold, Italic
Formatted: Font: Not Bold
Formatted: Font: Not Bold

monograph), but fewer than half of evidence synthesis projects publish in an external journal. 65% of evidence synthesis studies publish by 30 months (54.7% had produced a monograph but only 23.3% had published elsewhere).

Conclusion: Research funded by the HTA Programme publishes promptly. The importance of *Health Technology Assessment* was highlighted as the median time to publication was nine months shorter for the monograph than an external journal, and publication at 30 months was higher in the monograph than for other peer-reviewed journals.

Strengths and limitations of this study

- The study involves a large cohort, representing almost 20 years of research funded on behalf of the NHS.
- This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.
- This project relied heavily on the NIHR research programmes database and some data were not available for analyses.

INTRODUCTION

In order for research to help patients and aid clinicians in their decision-making it must be published in full and made available in a timely fashion. However, it is estimated that over 50.0% of studies are never published completely, and studies with disappointing (non-significant) results may not be published at all.[1,2] Non-publication is believed to be primarily due to failure to write-up and submit research, rather than manuscripts being rejected.[3] Studies with null or negative findings take longer to be published than those with positive results,[4,5] and this publication bias may invalidate a meta-analysis, leading to overestimation of treatment effects. As a result, new interventions may be adopted without suitable evidence to support them.

In addition to publication bias, selective outcome reporting may also lead to overestimation of the effectiveness of the treatment, emphasising the need for rigorous reporting of research. *Health Technology Assessment* (also known as the monograph series) is the peer reviewed journal for the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (which produces research evidence on behalf of the NHS). Trials funded by the ~~National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (which produces research evidence on behalf of the NHS)~~ NIHR HTA Programme that only publish in *Health Technology Assessment* ~~(the peer reviewed journal for the HTA Programme, known as the monograph series)~~ tend to have a higher *P*-value for the main outcome compared to those that also have a publication in another journal. The full *Health Technology Assessment* ~~HTA~~ monograph generally contains more outcomes than the main trial publication and journal articles tend to report a higher proportion of statistically significant outcomes. Consequently, researchers including HTA-funded trials in their systematic reviews are recommended to use information from the monograph and not the associated journal article.[6]

Turner *et al*.[7] have shown that 98.0% of projects funded by the HTA Programme in the last 10 years will publish in the monograph ~~HTA journal~~ series. In contrast, Ross *et al*.[8] found that only 68.0% of clinical trials funded by the US National Institutes of Health (NIH) publish, with 46.0% publishing within 30.0 months of trial completion. Tricco *et al*.[9] established that Cochrane reviews have a median time to publication of 2.4 years (~29.0 months), but only 80.9% of Cochrane protocols are published overall. Given the importance of publishing promptly and the recommendation that researchers use data from the monograph of a project, rather than its journal article; the aim of this study was to determine the time to publication for HTA-funded primary research and evidence synthesis projects in *Health Technology Assessment* and biomedical literature, and to compare time to publication with other public sector funders.

METHODS

~~**Data source**~~

~~*Health Technology Assessment* (http://www.hta.ac.uk/research/htajournal.shtml) is the peer reviewed journal for the NIHR HTA Programme. The HTA journal series publishes scientifically rigorous reports arising from work funded by the HTA Programme and all HTA research is expected to publish in the journal series. Approximately 50 reports are published in the series every year and over 600 issues have been published since its first volume in 1997.~~

~~The HTA Programme website states that *Health Technology Assessment* is indexed on MEDLINE, CINAHL, EMBASE, the Cochrane Library and the ISI Science Citation Index and assessed for inclusion in the Centre for Reviews and Dissemination (CRD) Database of Abstracts of Reviews of Effectiveness (DARE). The journal is ranked fourth (out of 76 titles) in the 'Health Care Sciences &~~

Formatted: Font: Italic

Formatted: Font: Italic

Formatted: Not Superscript/ Subscript

~~Services' category of the Thomson Reuters 2011 Journal Citation Reports (Science Edition) and has a five year impact factor of 5.596.~~

Cohort sample

The cohort in this project is derived from the NIHR research programmes database. It is a sub sample of the data set used by Turner *et al*.[7] and includes projects that planned to submit their draft final report on or before 9th December 2011 (as recorded in the NIHR research programmes database). Based on project classification in the database, the cohort was divided into two main categories: primary research and evidence synthesis, primary research was subdivided further into trials (as defined by Ross *et al*.[8]) and the remainder were categorised as 'others'.

Data extracted from the database included the project reference number, its publication date in ~~the~~ *Health Technology Assessment* ~~HTA journal series~~ and the date when the evidence syntheses protocols were made available online. The *Health Technology Assessment* monograph ~~HTA journal~~ (or draft final report or external publication if the project did not have a published monograph) was hand-searched for the end of recruitment date and length of follow-up in order to calculate the study conclusion date for the primary research projects. We also hand searched the *Health Technology Assessment* ~~*HTA*~~ journal website for the online publication date of the first report for all projects in an external journal. We took a pragmatic approach and excluded protocols, background papers and systematic reviews that may have been conducted before the research began. We included the first report that used clinical data from the project, and excluded cost-effectiveness analyses (unless the project report specifically stated that it was an economic evaluation).

Time to publication

For primary research, the time to publication was determined by calculating the number of months from when the study concluded (i.e. end of follow-up, using the same methodology as Ross *et al*.[8]) to when the monograph was first published online and to when the first external publication was available online. For evidence syntheses, we followed the protocol of Tricco *et al*.[9] Time to publication was measured as the number of months from when the protocol was first made available online to the online publication date of the monograph and to the online availability of the study in an external journal.

Three researchers (FC, M A-K and JG) conducted data extraction for the primary research dataset and any disagreement was resolved in discussion. Two researchers (FC and JG) extracted the data for the evidence synthesis projects. Again, any disagreement was settled in discussion.

Data analysis

Kaplan-Meier survival curves were produced for primary research and evidence synthesis projects, ~~and~~ the ~~cumulative~~ percentage of HTA-funded studies published in the monograph ~~HTA journal~~ series was compared to other peer reviewed journals., ~~time to any publication was also plotted.~~ We calculated the median (time for 50.0% of funded studies to publish) time to publication in *Health Technology Assessment*, elsewhere and for the first output for primary research, trials, and evidence syntheses.

Ross *et al*.[8] have emphasised the need for timely publication and have stated a cut-off of 30.0 months for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at 30.0 months and the total percentage published, both in the monograph series and elsewhere.

Formatted: Font: Not Italic

Formatted: Font: Italic

Formatted: No underline

Formatted: No underline

The Anderson-Darling normality test in Minitab was used to establish distribution of the data subsets (Anderson-Darling normality test) and the interquartile ranges (IQR) were also determined. Any and any statistical difference between the median times to publication was established determined using the Mann-Whitney -U test.

RESULTS

We identified 458 projects for inclusion in our analyses (figure 1).

Figure 1: Flow diagram of projects in this study.

INSERT FIGURE 1 HERE

Primary research

The primary research subset contains 184 projects; however, 29 of these did not state an end of recruitment date, or it was not possible to determine length of follow-up. Consequently, it was not possible to calculate the last point of data collection for 15.8% of HTA Pprogramme-funded primary research, even though many of these studies do have a publication.

Of the 155 primary research projects with a completion date, the median time to any publication (time for 50% of the funded studies to publish) was 23.0 months (IQR 19.0 months), 26.5 months (IQR 20.5 months) for publication as a to the monograph in *Health Technology Assessment* and 35.5 months (IQR 19.0 months) to for publication in any other an external journal, but this difference was not statistically significant (P=0.149).

Formatted: Font: Italic

Sixty-nine per cent of all primary research funded by the HTA Pprogramme is published by 30.0 months, but only 56.1% of monographs are produced within this time. Limiting the analysis to trials, directly comparable to the work of Ross *et al.*[8], 67.5% publish within 30.0 months and have a median time to publication of 24.0 months (IQR 15.3 months) (table 1). Overall publication rates are 92.9% for any publication, 88.4% in the monograph and 62.6% in an external journal (table 1, figure 2).

INSERT TABLE 1 HERE

Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the *Health Technology AssessmentHTA* monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

Formatted: Font: Italic

INSERT FIGURE 2 HERE

Evidence synthesis

Of the 274 evidence syntheses, the database did not record a protocol online date for 51 (18.6%) projects and so these could not be included in further analyses. Of the remaining projects, the median time to any publication was 25.5 months (IQR 16.0 months). The and the median time to publication of a monograph is published after 28.0 months (IQR 19.0 months) on average but, unlike primary research, fewer than 50.0% of evidence synthesis projects publish in other peer-reviewed journals (table 2, figure 3), so it was not possible to test for statistical significance. Evidence syntheses publish in a timely fashion, with 65.0% of studies publishing within 30.0 months and 93.3% publish overall.

INSERT TABLE 2 HERE

Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in the *Health Technology Assessment* ~~*HTA*~~ monograph versus other peer reviewed biomedical journals and to the first publication anywhere.

INSERT FIGURE 3 HERE

DISCUSSION

Using the standard of Ross *et al*.,[8] HTA-funded research publishes promptly; 69.0% of primary research projects publish by 30.0 months, with a median time to publication of 23.0 months. Sixty-five per cent of evidence synthesis projects publish by 30.0 months and the median time to publication was 25.5 months.

Strengths and limitations

The main strength of this study is that it involves a large cohort, representing almost 20 years of research funded on behalf of the NHS. This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.[7] This project used a subsample of the dataset of Turner et al.[7] with the intention to determine the time to publication of all of the primary research and evidence synthesis projects that do publish. However, a major limitation of this project is the ~~large~~ amount of data missing from the analyses. It was not possible to determine the end-of-follow up for over 15.0% of primary research projects, and over 18.0% of the evidence synthesis studies did not have a recorded protocol online date, so they were not included in the analyses. Since data-recording was poorer in earlier years (unpublished data), we have disproportionately excluded more of the older projects. Consequently, since older projects generally ~~take~~ took longer to publish ~~on average~~ (unpublished data), we may be underestimating how long HTA-funded studies take to publish overall.

This project relied heavily on data from the NIHR research programmes database and the *Health Technology Assessment* ~~*HTA*~~ journal website to determine if a study has published elsewhere, which in turn depends on self-declarations from the principle investigators (PIs), as per contractual obligations. Preliminary work in an internal NETSCC report found that PIs were under-reporting their external publications by 15.8% and so the overall external publication rate is likely to be higher and we are overestimating the median time to publication in an external journal. In addition, the under-reporting may also be affecting the "Any publication" Kaplan-Meier curve and so influencing the median time to the first publication as well.

Comparison with other studies

Ross et al.[8] highlighted the need for the publication process to be prioritised in order to shorten the time taken for research findings to be available to the public. Their work found that the median time to publication of clinical trials funded by the US NIH and registered with ClinicalTrials.gov (and completed by 31st December 2008) was 23.0 months. However, this is only the median of the trials that published, not the whole cohort (i.e. the trials that were funded) and so it is underestimating the time to publication. Funders and researchers should aspire to publish all of their research, so the time taken for 50.0% of all funded studies to publish is the appropriate median time to publication. Arguably, the 30.0 month publication rate may be the truly important measure of timeliness to publication.

It takes ~32.0 months for half of the clinical trials funded by the US NIH to publish; only 46.0% were published within 30.0 months of trial completion, with an overall publication rate of 68.0%. In comparison, the median time to publication of HTA Programme-funded trials is 24.0 months, 67.5% publish by 30.0 months, and 93.7% publish overall. The *Health Technology Assessment* ~~*HTA*~~ figures also compare very favourably with results from industry sponsored trials; trials conducted by GlaxoSmithKline in Spain between 2001 and 2006 had a publication rate of 61.0% and a median time

Formatted: Font: Italic

Formatted: Font: Italic

Formatted: Font: Italic

to publication of 28.4 months. However, it was not clear whether this was the median of the published trials or of the funded ones.[10] The median time to publication of more recent NIH clinical trials (those with a ClinicalTrials.gov identifier, published during 2009 and indexed in MEDLINE) is 21.0 months,[11] but the study did not comment on how long it took for 50.0% of the funded trials to publish. Lastly, ~~Sixty-eight per cent~~68.0% of NIH-funded studies publish overall and 62.6% of HTA-funded primary research publishes externally. This highlights the importance of the monograph series ~~HTA journal series~~ as it provides a means of publication for those projects that would not otherwise reach the public domain.

HTA-funded evidence syntheses are also produced in a timely manner, with a median time to publication of 25.5 months and 65.0% of studies being published by 30.0 months (93.3% publishing overall). In comparison, Cochrane reviews have a median time to publication of~~is~~ ~~~29.0 months, with only 80.99% publishing in full after eight years of follow-up.

Implications

The median time to publication in the monograph series and an external journal could only be compared for primary research (as over half of the evidence syntheses do not have a recorded external publication); here a ~~the~~ monograph is produced nine months earlier. Publication rate, for both types of research, was considerably higher in the monograph series than for other peer reviewed biomedical journals. The shorter time to publication and high publication rate in *Health Technology Assessment* ~~the monograph~~ is laudable; ensuring information from research is easily accessible and widely available is important because it facilitates its use, increases its impact and consequently its value to society. Unpublished data may also invalidate conclusions from meta-analyses, and systematic reviews. These are not just a valuable source of information for health care professionals and researchers, but definitive conclusions about an intervention also prevent putting more patients at risk in further unneeded trials or depriving them of the correct treatment. Having ~~the~~ *Health Technology Assessment* ~~HTA journal~~ is clearly important for dissemination of research to the public in a timely fashion and ensures that data are not lost as a result of publication bias. US federal requirements[12] call for "results of an Applicable Clinical Trial of a drug, biologic, or device that is approved, licensed, or cleared by FDA must be submitted by the Responsible Party no later than 12 months after the Completion Date". There is an important distinction between the user's (HTA Programme, clinicians and patients, NICE, etc.) perspective and the researcher's perspective of the process. Once they have submitted the draft final report, aside from editing the researcher may assume their task is finished, but the users are more concerned with when the research is in the public domain.

Formatted: Font: Italic

Conclusion and recommendations

Research funded by the HTA Programme publishes in a timely fashion; where a comparison was possible, time to publication was nine months shorter for a ~~the~~ monograph than an external journal article and publication rate was considerably higher in *Health Technology Assessment* ~~this~~ than for other peer-reviewed journals. HTA-funded trials publish more promptly than those funded by the NIH and industry and HTA-funded evidence syntheses are produced sooner than Cochrane reviews. This current study highlighted the importance of HTA Programme research being funded via a contract (researchers are contractually obliged to publish their findings in full) as well as the value of *Health Technology Assessment* ~~the HTA journal series~~ and its rigorous editorial procedure.

Recommendations include encouraging other funding organisations to make it a condition for their investigators to publish final project results in full, within a set time, and to support this practice, regardless of whether findings are significant or not. In the UK, the Health Research Authority (HRA) is responsible for protecting and promoting the interests of patients and the public in health research. It plays a key leadership role in promoting transparency and has made a number of commitments to ensure the publication and dissemination of health research results.[13]

Future work should investigate the time to publication for other funders and ways in which delays can be reduced without compromising quality. Regardless of the funder, all trials should be registered and the methods and results reported in full and in a timely fashion.

ACKNOWLEDGEMENTS

The authors would like to thank Sheila Turner for providing the reference numbers of the projects and their publication date in the monograph series; Stephen Lemon for his advice about data extraction from the NIHR research programmes database and Jo Merritt for sharing her data concerning authors not reporting projects that publish in an external journal. We would also like to acknowledge the Metadata team for providing their database and trial details used in the study.

COMPETING INTERESTS

FC has worked for the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) since February 2012; AY is an employee of NETSCC which hosts the Research on Research Programme, from where this work originated; JG worked for NETSCC from January 2006 to April 2013; M A-K is currently an editor for the Health Technology Assessment journal and a full-time employee of NETSCC; RM is employed as the Head of NETSCC and has worked for NETSCC (and its predecessor organisation) in senior roles on and off since 1996. He was an editor of the Health Technology Assessment journal (1997-2005) and a founder editor for other journals in the new NIHR Journals Library (2011-12).

FUNDING

This research was supported by the NIHR Evaluation, Trials and Studies Coordinating Centre through its Research on Research programme. The views and opinions expressed are those of the authors and do not necessarily reflect those of the Department of Health or of NETSCC.

Table 1: Publication characteristics of HTA Programme-funded primary research and trials (studies with a completion date).

	Primary research			Trials
	Any publication	HTA Monograph	External journal	Any publication
Number of studies (in the cohort)	155	155	155	126
Published (n)	144	137	97	118
Published (%)	92.9	88.4	62.6	93.7
Time for 50% to publish (months)	23	26.5	35.5	24
Published at 30 months (n)	107	87	66	85
Published at 30 months (%)	69.0	56.1	42.6	67.5

	Primary research (n=155)			Trials (n=126)
	Any publication	*HTA* Monograph	External journal	Any publication
Number of studies published (%)	144 (92.9%)	137 (88.4%)	97 (62.6%)	118 (93.7%)
Median time to publication (months)	23.0	26.5	35.5	24.0
Number of studies published at 30 months (%)	107 (69.0%)	87 (56.1%)	66 (42.6%)	85 (67.5%)

Formatted: Font: Bold

Table 2: Publication characteristics of HTA Programme-funded evidence synthesis (studies with a protocol online date).

	Evidence syntheses (n=223)		
	Any publication	*HTA* Monograph	External journal
Number of studies published (%)	208 (93.3%)	207 (92.3%)	99 (44.4%)
Median time to publication (months)	25.5	28.0	-
Number of studies published at 30 months (%)	145 (65.0%)	122 (54.7%)	52 (23.3%)

Formatted: Font: Bold

REFERENCES

1. Scherer RW, Langenberg P, von Elm E. Full publication of results initially presented as abstracts. Cochrane Database Syst Rev 2007; Issue 2: MR000005
2. Chalmers I and Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009; **374**: 86-89
3. Dickersin K, Chan S, Chalmers TC, Sacks HS, Smith H Jr. Publication bias and clinical trials. Control Clin Trials. 1987; **8(4)**:343-53.

4. Song F, Parekh S, Hooper L, Loke YK, Ryder J, Sutton AJ, Hing C, Kwok CS, Pang C, Harvey I. Dissemination and publication of research findings: an updated review of related biases. Health Technol Assess. 2010; **14(8)**:iii, ix-xi, 1-193.
5. Suñé P, Suñé JM, Montoro JB. Positive outcomes influence the rate and time to publication, but not the impact factor of publications of clinical trial results. PLoS One. 2013; **8(1)**:e54583.
6. Matthews GA, Dumville JC, Hewitt CE, Torgerson DJ. Retrospective cohort study highlighted outcome reporting bias in UK publicly funded trials. J Clin Epidemiol. 2011; **64(12)**:1317-24
7. Turner S, Wright, D, Maeso B, Cook A, Milne R. Publication rate for funded studies from a major UK health research funder: a cohort study. BMJ Open 2013; **3(5)**. pii: e002521.
8. Ross JS, Tse T, Zarin D, Xu H, Zhou L, Krumholz HM. Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. BMJ 2012; **344**;d7292
9. Tricco AC, Brehaut J, Chen MH, Moher D. Following 411 Cochrane protocols to completion: a retrospective cohort study. PLoS One 2008; **3(11)**: e3684
10. Dal-Ré R, Pedromingo A, García-Losa M, Lahuerta J, Ortega, R. Are results from pharmaceutical company-sponsored studies available to the public? Eur J Clin Pharmacol 2010; **66**:1081-1089
11. Ross JS, Mocanu M, Lampropulos JF, Tse T, Krumholz HM. Time to Publication Among Completed Clinical Trials. JAMA Intern Med. 2013; **173(9)**:825-8.
12. Food and Drug Administration Amendments Act (FDAAA) of 2007 - Section 801.
13. http://www.hra.nhs.uk/hra-news-and-announcements/transparent-research/

Time to publication for NIHR HTA Programme-funded research: a cohort study

Fay Chinnery, Amanda Young, Jennie Goodman, Martin Ashton-Key, Ruairidh Milne

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Fay Chinnery
Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Amanda Young
Senior Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Jennie Goodman
Programme Manager

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Martin Ashton-Key
Consultant in Public Health Medicine / Consultant Advisor

Wessex Institute, University of Southampton, Southampton, Hampshire, SO16 7NS, UK
Ruairidh Milne
Professional Fellow in Public health

Correspondence to:
Fay Chinnery
F.Chinnery@soton.ac.uk
Tel: 023 8059 5548

Key words
Publication; Time to publication; Clinical trial; Health Technology Assessment (HTA) Programme

Word Count
2600

Time to publication for NIHR HTA Programme-funded research: a cohort study

ABSTRACT

Objective: To assess the time to publication of primary research and evidence syntheses funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme published as a monograph in *Health Technology Assessment* and as a journal article in the wider biomedical literature.

Study design: Retrospective cohort study.

Setting: Primary research and evidence synthesis projects funded by the HTA Programme were included in the cohort if they were registered in the NIHR research programmes database and planned to submit their draft final report for publication in *Health Technology Assessment* on or before 9 December 2011.

Main outcome measures: The median time to publication and publication at 30.0 months in both *Health Technology Assessment* and in an external journal, as determined by searching the NIHR research programmes database and HTA Programme website.

Results: Of 458 included projects, 184 (40.2%) were primary research projects and 274 (59.8%) were evidence syntheses. 155 primary research projects had a completion date, the median time to publication was 23.0 months (26.5 and 35.5 months to publish a monograph and to publish in an external journal, respectively) and 69.0% had published by 30.0 months. The median time to publication of HTA-funded trials (n=126) was 24.0 months and 67.5% published by 30.0 months. Among the evidence syntheses with a protocol online date (n=223), the median time to publication was 25.5 months, (28.0 months to publication as a monograph), but only 44.4% of evidence synthesis projects publish in an external journal. 65.0% of evidence synthesis studies publish by 30.0 months.

Conclusion: Research funded by the HTA Programme publishes promptly. The importance of *Health Technology Assessment* was highlighted as the median time to publication was nine months shorter for a monograph than an external journal article.

Strengths and limitations of this study

- The study involves a large cohort, representing almost 20 years of research funded on behalf of the NHS.
- This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.
- This project relied heavily on the NIHR research programmes database and some data were not available for analyses.

INTRODUCTION

In order for research to help patients and aid clinicians in their decision-making it must be published in full and made available in a timely fashion. However, it is estimated that over 50.0% of studies are never published completely, and studies with disappointing (non-significant) results may not be published at all.[1,2] Non-publication is believed to be primarily due to failure to write-up and submit research, rather than manuscripts being rejected.[3] Studies with null or negative findings take longer to be published than those with positive results,[4,5] and this publication bias may invalidate a meta-analysis, leading to overestimation of treatment effects. As a result, new interventions may be adopted without suitable evidence to support them.

In addition to publication bias, selective outcome reporting may also lead to overestimation of the effectiveness of the treatment, emphasising the need for rigorous reporting of research. *Health Technology Assessment* (also known as the monograph series) is the peer reviewed journal for the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (which produces research evidence on behalf of the NHS). Trials funded by the NIHR HTA Programme that only publish in *Health Technology Assessment* tend to have a higher *P*-value for the main outcome compared to those that also have a publication in another journal. The full *Health Technology Assessment* monograph generally contains more outcomes than the main trial publication and journal articles tend to report a higher proportion of statistically significant outcomes. Consequently, researchers including HTA-funded trials in their systematic reviews are recommended to use information from the monograph and not the associated journal article.[6]

Turner *et al*.[7] have shown that 98.0% of projects funded by the HTA Programme in the last 10 years will publish in the monograph series. In contrast, Ross *et al*.[8] found that only 68.0% of clinical trials funded by the US National Institutes of Health (NIH) publish, with 46.0% publishing within 30.0 months of trial completion. Tricco *et al*.[9] established that Cochrane reviews have a median time to publication of 2.4 years (~29.0 months), but only 80.9% of Cochrane protocols are published overall. Given the importance of publishing promptly and the recommendation that researchers use data from the monograph of a project, rather than its journal article; the aim of this study was to determine the time to publication for HTA-funded primary research and evidence synthesis projects in *Health Technology Assessment* and biomedical literature, and to compare time to publication with other public sector funders.

METHODS

Cohort sample

The cohort in this project is derived from the NIHR research programmes database. It is a sub sample of the data set used by Turner *et al*.[7] and includes projects that planned to submit their draft final report on or before 9th December 2011 (as recorded in the NIHR research programmes database). Based on project classification in the database, the cohort was divided into two main categories: primary research and evidence synthesis, primary research was subdivided further into trials (as defined by Ross *et al*.[8]) and the remainder were categorised as 'others'.

Data extracted from the database included the project reference number, its publication date in *Health Technology Assessment* and the date when the evidence syntheses protocols were made available online. The *Health Technology Assessment* monograph (or draft final report or external publication if the project did not have a published monograph) was hand-searched for the end of recruitment date and length of follow-up in order to calculate the study conclusion date for the primary research projects. We also hand searched the *Health Technology Assessment* journal website for the online publication date of the first report for all projects in an external journal. We took a pragmatic approach and excluded protocols, background papers and systematic reviews that may have been conducted

before the research began. We included the first report that used clinical data from the project, and excluded cost-effectiveness analyses (unless the project report specifically stated that it was an economic evaluation).

Time to publication

For primary research, the time to publication was determined by calculating the number of months from when the study concluded (i.e. end of follow-up, using the same methodology as Ross *et al*.[8]) to when the monograph was first published online and to when the first external publication was available online. For evidence syntheses, we followed the protocol of Tricco *et al*.[9] Time to publication was measured as the number of months from when the protocol was first made available online to the online publication date of the monograph and to the online availability of the study in an external journal.

Three researchers (FC, M A-K and JG) conducted data extraction for the primary research dataset and any disagreement was resolved in discussion. Two researchers (FC and JG) extracted the data for the evidence synthesis projects. Again, any disagreement was settled in discussion.

Data analysis

Kaplan-Meier survival curves were produced for primary research and evidence synthesis projects, the percentage of HTA-funded studies published in the monograph series was compared to other peer reviewed journals. We calculated the median (time for 50.0% of funded studies to publish) time to publication in *Health Technology Assessment*, elsewhere and for the first output for primary research, trials, and evidence syntheses.

Ross *et al*.[8] have emphasised the need for timely publication and have stated a cut-off of 30.0 months for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at 30.0 months and the total percentage published, both in the monograph series and elsewhere.

Minitab was used to establish distribution of the data subsets (Anderson-Darling normality test) and the interquartile ranges (IQR) were also determined. Any statistical difference between the median times to publication was established using the Mann-Whitney U test.

RESULTS

We identified 458 projects for inclusion in our analyses (figure 1).

Figure 1: Flow diagram of projects in this study.

INSERT FIGURE 1 HERE

Primary research

The primary research subset contains 184 projects; however, 29 of these did not state an end of recruitment date, or it was not possible to determine length of follow-up. Consequently, it was not possible to calculate the last point of data collection for 15.8% of HTA Programme-funded primary research, even though many of these studies do have a publication.

Of the 155 primary research projects with a completion date, the median time to any publication (time for 50% of the funded studies to publish) was 23.0 months (IQR 19.0 months), 26.5 months (IQR 20.5 months) for publication as a monograph in *Health Technology Assessment* and 35.5 months (IQR

19.0 months) for publication in any other external journal, but this difference was not statistically significant (P=0.149).

Sixty-nine per cent of all primary research funded by the HTA Programme is published by 30.0 months, but only 56.1% of monographs are produced within this time. Limiting the analysis to trials, directly comparable to the work of Ross *et al*.[8], 67.5% publish within 30.0 months and have a median time to publication of 24.0 months (IQR 15.3 months) (table 1). Overall publication rates are 92.9% for any publication, 88.4% in the monograph and 62.6% in an external journal (table 1, figure 2).

INSERT TABLE 1 HERE

Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

INSERT FIGURE 2 HERE

Evidence synthesis

Of the 274 evidence syntheses, the database did not record a protocol online date for 51 (18.6%) projects and so these could not be included in further analyses. Of the remaining projects, the median time to any publication was 25.5 months (IQR 16.0 months) and the median time to publication of a monograph is 28.0 months (IQR 19.0 months) but, unlike primary research, fewer than 50.0% of evidence synthesis projects publish in other peer-reviewed journals (table 2, figure 3), so it was not possible to test for statistical significance. Evidence syntheses publish in a timely fashion, with 65.0% of studies publishing within 30.0 months and 93.3% publish overall.

INSERT TABLE 2 HERE

Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed biomedical journals and to the first publication anywhere.

INSERT FIGURE 3 HERE

DISCUSSION

Using the standard of Ross *et al*.,[8] HTA-funded research publishes promptly; 69.0% of primary research projects publish by 30.0 months, with a median time to publication of 23.0 months. Sixty-five per cent of evidence synthesis projects publish by 30.0 months and the median time to publication was 25.5 months.

Strengths and limitations

The main strength of this study is that it involves a large cohort, representing almost 20 years of research funded on behalf of the NHS. This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.[7] This project used a subsample of the dataset of Turner et al.[7] with the intention to determine the time to publication of all of the primary research and evidence synthesis projects that do publish. However, a major limitation of this project is the amount of data missing from the analyses. It was not possible to determine the end-of-follow up for over 15.0% of primary research projects, and over 18.0% of the evidence synthesis studies did not have a recorded protocol online date, so they were not included in the analyses. Since data-recording was poorer in earlier years (unpublished data), we have disproportionately excluded more of the older projects. Consequently, since older projects generally took longer to publish (unpublished data), we may be underestimating how long HTA-funded studies take to publish overall.

This project relied heavily on data from the NIHR research programmes database and the *Health Technology Assessment* journal website to determine if a study has published elsewhere, which in turn depends on self-declarations from the principle investigators (PIs), as per contractual obligations. Preliminary work in an internal NETSCC report found that PIs were under-reporting their external publications by 15.8% and so the overall external publication rate is likely to be higher and we are overestimating the median time to publication in an external journal. In addition, the under-reporting may also be affecting the "Any publication" Kaplan-Meier curve and so influencing the median time to the first publication as well.

Comparison with other studies

Ross et al.[8] highlighted the need for the publication process to be prioritised in order to shorten the time taken for research findings to be available to the public. Their work found that the median time to publication of clinical trials funded by the US NIH and registered with ClinicalTrials.gov (and completed by 31st December 2008) was 23.0 months. However, this is only the median of the trials that published, not the whole cohort (i.e. the trials that were funded) and so it is underestimating the time to publication. Funders and researchers should aspire to publish all of their research, so the time taken for 50.0% of all funded studies to publish is the appropriate median time to publication. Arguably, the 30.0 month publication rate may be the truly important measure of timeliness to publication.

It takes ~32.0 months for half of the clinical trials funded by the US NIH to publish; only 46.0% were published within 30.0 months of trial completion, with an overall publication rate of 68.0%. In comparison, the median time to publication of HTA Programme-funded trials is 24.0 months, 67.5% publish by 30.0 months, and 93.7% publish overall. The *Health Technology Assessment* figures also compare very favourably with results from industry sponsored trials; trials conducted by GlaxoSmithKline in Spain between 2001 and 2006 had a publication rate of 61.0% and a median time to publication of 28.4 months. However, it was not clear whether this was the median of the published trials or of the funded ones.[10] The median time to publication of more recent NIH clinical trials (those with a ClinicalTrials.gov identifier, published during 2009 and indexed in MEDLINE) is 21.0 months,[11] but the study did not comment on how long it took for 50.0% of the funded trials to publish. Lastly, 68.0% of NIH-funded studies publish overall and 62.6% of HTA-funded primary research publishes externally. This highlights the importance of the monograph series as it provides a means of publication for those projects that would not otherwise reach the public domain.

HTA-funded evidence syntheses are also produced in a timely manner, with a median time to publication of 25.5 months and 65.0% of studies being published by 30.0 months (93.3% publishing overall). In comparison, Cochrane reviews have a median time to publication of ~29.0 months, with only 80.9% publishing in full after eight years of follow-up.

Implications

The median time to publication in the monograph series and an external journal could only be compared for primary research (as over half of the evidence syntheses do not have a recorded external publication); here a monograph is produced nine months earlier. Publication rate, for both types of research, was considerably higher in the monograph series than for other peer reviewed biomedical journals. The shorter time to publication and high publication rate in *Health Technology Assessment* is laudable; ensuring information from research is easily accessible and widely available is important because it facilitates its use, increases its impact and consequently its value to society. Unpublished data may also invalidate conclusions from meta-analyses, and systematic reviews. These are not just a valuable source of information for health care professionals and researchers, but definitive conclusions about an intervention also prevent putting more patients at risk in further unneeded trials or depriving them of the correct treatment. Having *Health Technology Assessment* is clearly important for dissemination of research to the public in a timely fashion and ensures that data

are not lost as a result of publication bias. US federal requirements[12] call for "results of an Applicable Clinical Trial of a drug, biologic, or device that is approved, licensed, or cleared by FDA must be submitted by the Responsible Party no later than 12 months after the Completion Date". There is an important distinction between the user's (HTA Programme, clinicians and patients, NICE, etc.) perspective and the researcher's perspective of the process. Once they have submitted the draft final report, aside from editing the researcher may assume their task is finished, but the users are more concerned with when the research is in the public domain.

Conclusion and recommendations

Research funded by the HTA Programme publishes in a timely fashion; where a comparison was possible, time to publication was nine months shorter for a monograph than an external journal article and publication rate was considerably higher in *Health Technology Assessment* than for other peer-reviewed journals. HTA-funded trials publish more promptly than those funded by the NIH and industry and HTA-funded evidence syntheses are produced sooner than Cochrane reviews. This current study highlighted the importance of HTA Programme research being funded via a contract (researchers are contractually obliged to publish their findings in full) as well as the value of *Health Technology Assessment* and its rigorous editorial procedure.

Recommendations include encouraging other funding organisations to make it a condition for their investigators to publish final project results in full, within a set time, and to support this practice, regardless of whether findings are significant or not. In the UK, the Health Research Authority (HRA) is responsible for protecting and promoting the interests of patients and the public in health research. It plays a key leadership role in promoting transparency and has made a number of commitments to ensure the publication and dissemination of health research results.[13]

Future work should investigate the time to publication for other funders and ways in which delays can be reduced without compromising quality. Regardless of the funder, all trials should be registered and the methods and results reported in full and in a timely fashion.

ACKNOWLEDGEMENTS

The authors would like to thank Sheila Turner for providing the reference numbers of the projects and their publication date in the monograph series; Stephen Lemon for his advice about data extraction from the NIHR research programmes database and Jo Merritt for sharing her data concerning authors not reporting projects that publish in an external journal. We would also like to acknowledge the Metadata team for providing their database and trial details used in the study.

COMPETING INTERESTS

FC has worked for the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) since February 2012; AY is an employee of NETSCC which hosts the Research on Research Programme, from where this work originated; JG worked for NETSCC from January 2006 to April 2013; M A-K is currently an editor for the Health Technology Assessment journal and a full-time employee of NETSCC; RM is employed as the Head of NETSCC and has worked for NETSCC (and its predecessor organisation) in senior roles on and off since 1996. He was an editor of the Health Technology Assessment journal (1997-2005) and a founder editor for other journals in the new NIHR Journals Library (2011-12).

FUNDING

This research was supported by the NIHR Evaluation, Trials and Studies Coordinating Centre through its Research on Research programme. The views and opinions expressed are those of the authors and do not necessarily reflect those of the Department of Health or of NETSCC.

Contributors

The study was designed by RM, M A-K, FC and AY. FC, AY, JG and M A-K performed data extraction, FC and AY conducted the data analyses. FC drafted the manuscript, guided by M A-K, RM and AY. All authors have read and approved the final manuscript.

Data sharing statement

There are no additional data available.

Table 1: Publication characteristics of HTA Programme-funded primary research and trials (studies with a completion date).

	Primary research (n=155)			Trials (n=126)
	Any publication	*HTA* Monograph	External journal	Any publication
Number of studies published (%)	144 (92.9%)	137 (88.4%)	97 (62.6%)	118 (93.7%)
Median time to publication (months)	23.0	26.5	35.5	24.0
Number of studies published at 30 months (%)	107 (69.0%)	87 (56.1%)	66 (42.6%)	85 (67.5%)

Table 2: Publication characteristics of HTA Programme-funded evidence synthesis (studies with a protocol online date).

	Evidence syntheses (n=223)		
	Any publication	*HTA* Monograph	External journal
Number of studies published (%)	208 (93.3%)	207 (92.3%)	99 (44.4%)
Median time to publication (months)	25.5	28.0	-
Number of studies published at 30 months (%)	145 (65.0%)	122 (54.7%)	52 (23.3%)

REFERENCES

1. Scherer RW, Langenberg P, von Elm E. Full publication of results initially presented as abstracts. Cochrane Database Syst Rev 2007; Issue 2: MR000005
2. Chalmers I and Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009; **374**: 86-89
3. Dickersin K, Chan S, Chalmers TC, Sacks HS, Smith H Jr. Publication bias and clinical trials. Control Clin Trials. 1987; **8(4)**:343-53.
4. Song F, Parekh S, Hooper L, Loke YK, Ryder J, Sutton AJ, Hing C, Kwok CS, Pang C, Harvey I. Dissemination and publication of research findings: an updated review of related biases. Health Technol Assess. 2010; **14(8)**:iii, ix-xi, 1-193.
5. Suñé P, Suñé JM, Montoro JB. Positive outcomes influence the rate and time to publication, but not the impact factor of publications of clinical trial results. PLoS One. 2013; **8(1)**:e54583.
6. Matthews GA, Dumville JC, Hewitt CE, Torgerson DJ. Retrospective cohort study highlighted outcome reporting bias in UK publicly funded trials. J Clin Epidemiol. 2011; **64(12)**:1317-24
7. Turner S, Wright, D, Maeso B, Cook A, Milne R. Publication rate for funded studies from a major UK health research funder: a cohort study. BMJ Open 2013; **3(5)**. pii: e002521.

8. Ross JS, Tse T, Zarin D, Xu H, Zhou L, Krumholz HM. Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. BMJ 2012; **344**;d7292
9. Tricco AC, Brehaut J, Chen MH, Moher D. Following 411 Cochrane protocols to completion: a retrospective cohort study. PLoS One 2008; **3(11)**: e3684
10. Dal-Ré R, Pedromingo A, García-Losa M, Lahuerta J, Ortega, R. Are results from pharmaceutical company-sponsored studies available to the public? Eur J Clin Pharmacol 2010; **66**:1081-1089
11. Ross JS, Mocanu M, Lampropulos JF, Tse T, Krumholz HM. Time to Publication Among Completed Clinical Trials. JAMA Intern Med. 2013; **173(9)**:825-8.
12. Food and Drug Administration Amendments Act (FDAAA) of 2007 - Section 801.
13. http://www.hra.nhs.uk/hra-news-and-announcements/transparent-research/

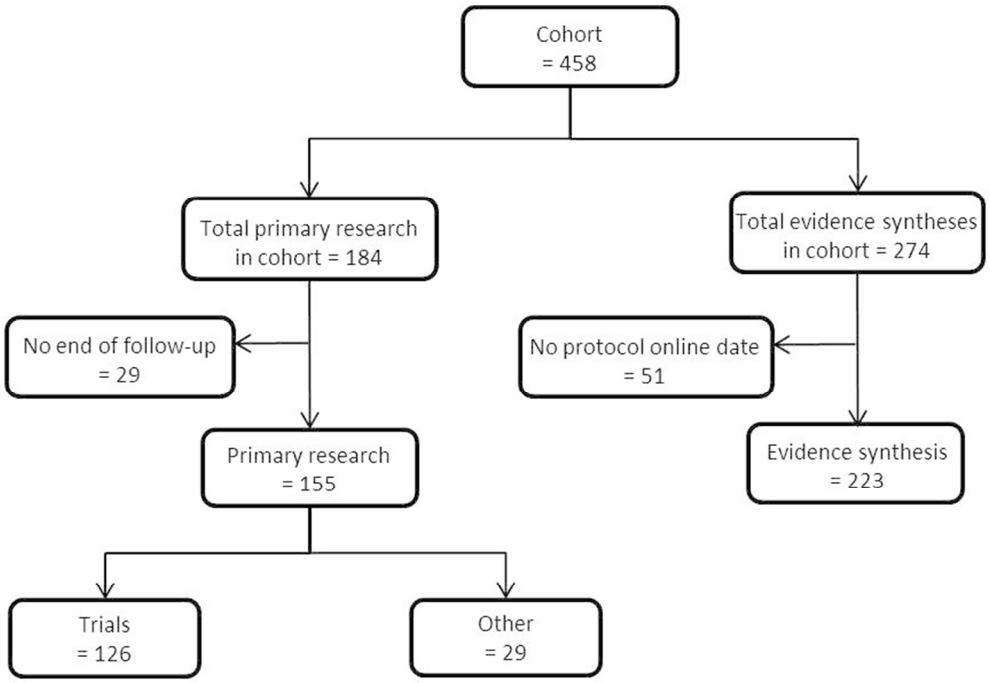


Figure 1: Flow diagram of projects in this study.
147x100mm (150 x 150 DPI)

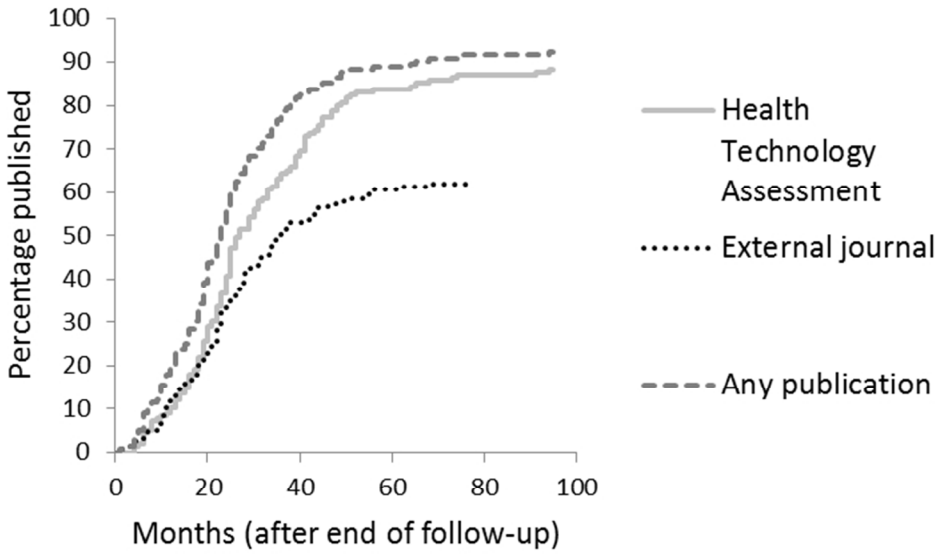


Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the Health Technology Assessment versus other peer reviewed biomedical journals and time to the first publication anywhere.
127x76mm (150 x 150 DPI)

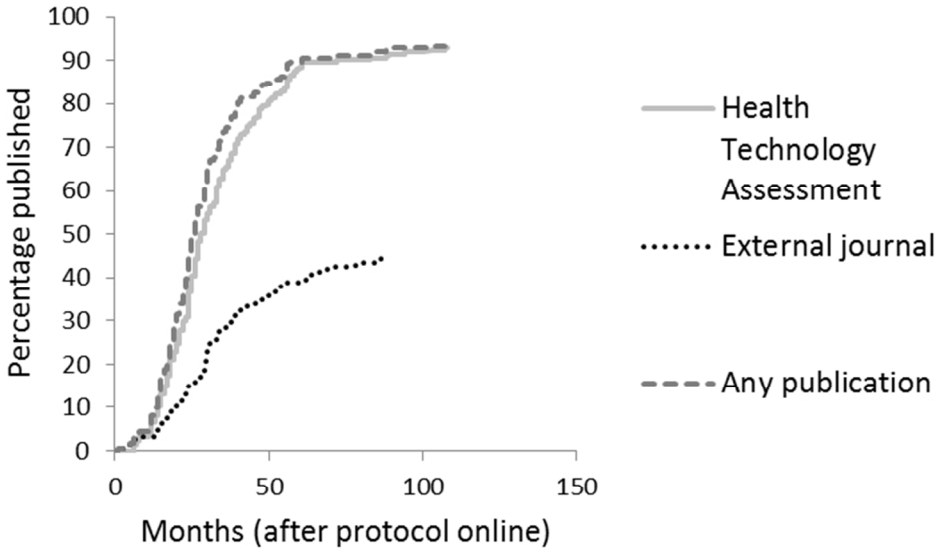


Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in Health Technology Assessment versus other peer reviewed biomedical journals and time to the first publication anywhere.
127x76mm (150 x 150 DPI)

Time to publication for NIHR HTA Programme-funded research: a cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004121.R2
Article Type:	Research
Date Submitted by the Author:	10-Oct-2013
Complete List of Authors:	Chinnery, Fay; University of Southampton, NETSCC Young, Amanda; University of Southampton, NETSCC Goodman, Jennie; University of Southampton, NETSCC Ashton-Key, Martin; University of Southampton, NETSCC Milne, Ruairidh; University of Southampton, Wessex Institute
Primary Subject Heading:	Research methods
Secondary Subject Heading:	Medical publishing and peer review
Keywords:	STATISTICS & RESEARCH METHODS, Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, Information management < BIOTECHNOLOGY & BIOINFORMATICS

Time to publication for NIHR HTA Programme-funded research: a cohort study

Fay Chinnery, Amanda Young, Jennie Goodman, Martin Ashton-Key, Ruairidh Milne

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Fay Chinnery
Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Amanda Young
Senior Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Jennie Goodman
Programme Manager

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Martin Ashton-Key
Consultant in Public Health Medicine / Consultant Advisor

Wessex Institute, University of Southampton, Southampton, Hampshire, SO16 7NS, UK
Ruairidh Milne
Professional Fellow in Public health

Correspondence to:
Fay Chinnery
F.Chinnery@soton.ac.uk
Tel: 023 8059 5548

Key words
Publication; Time to publication; Clinical trial; Health Technology Assessment (HTA) Programme

Word Count
2600

Time to publication for NIHR HTA Programme-funded research: a cohort study

ABSTRACT

Objective: To assess the time to publication of primary research and evidence syntheses funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme published as a monograph in *Health Technology Assessment* and as a journal article in the wider biomedical literature.

Study design: Retrospective cohort study.

Setting: Primary research and evidence synthesis projects funded by the HTA Programme were included in the cohort if they were registered in the NIHR research programmes database and planned to submit their draft final report for publication in *Health Technology Assessment* on or before 9 December 2011.

Main outcome measures: The median time to publication and publication at 30.0 months in both *Health Technology Assessment* and in an external journal, as determined by searching the NIHR research programmes database and HTA Programme website.

Results: Of 458 included projects, 184 (40.2%) were primary research projects and 274 (59.8%) were evidence syntheses. 155 primary research projects had a completion date, the median time to publication was 23.0 months (26.5 and 35.5 months to publish a monograph and to publish in an external journal, respectively) and 69.0% had published by 30.0 months. The median time to publication of HTA-funded trials (n=126) was 24.0 months and 67.5% published by 30.0 months. Among the evidence syntheses with a protocol online date (n=223), the median time to publication was 25.5 months, (28.0 months to publication as a monograph), but only 44.4% of evidence synthesis projects publish in an external journal. 65.0% of evidence synthesis studies publish by 30.0 months.

Conclusion: Research funded by the HTA Programme publishes promptly. The importance of *Health Technology Assessment* was highlighted as the median time to publication was nine months shorter for a monograph than an external journal article.

Strengths and limitations of this study

- The study involves a large cohort, representing almost 20 years of research funded on behalf of the NHS.
- This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.
- This project relied heavily on the NIHR research programmes database and some data were not available for analyses.

INTRODUCTION

In order for research to help patients and aid clinicians in their decision-making it must be published in full and made available in a timely fashion. However, it is estimated that over 50.0% of studies are never published completely, and studies with disappointing (non-significant) results may not be published at all.[1,2] Non-publication is believed to be primarily due to failure to write-up and submit research, rather than manuscripts being rejected.[3] Studies with null or negative findings take longer to be published than those with positive results,[4,5] and this publication bias may invalidate a meta-analysis, leading to overestimation of treatment effects. As a result, new interventions may be adopted without suitable evidence to support them.

During 2011/12, the National Institute for Health Research (NIHR) invested £202.2 million in research across a broad range of programmes and initiatives. *Health Technology Assessment* (also known as the monograph series) is the peer reviewed journal for the NIHR Health Technology Assessment (HTA) Programme. Reports published in *Health Technology Assessment* provide a full account of the research project, including methods and a full description of the results. These full monographs complement shorter articles submitted for publication in other peer-review journals, which the NIHR actively encourages researchers to do as part of their dissemination strategy.

In addition to publication bias, selective outcome reporting may also lead to overestimation of the effectiveness of the treatment, emphasising the need for rigorous reporting of research. Trials funded by the NIHR HTA Programme that only publish in *Health Technology Assessment* tend to have a higher *P*-value for the main outcome compared to those that also have a publication in another journal. The full *Health Technology Assessment* monograph generally contains more outcomes than the main trial publication and journal articles tend to report a higher proportion of statistically significant outcomes. Consequently, researchers including HTA-funded trials in their systematic reviews are recommended to use information from the monograph and not the associated journal article.[6]

Turner *et al*.[7] have shown that 98.0% of projects funded by the HTA Programme in the last 10 years will publish in the monograph series. In contrast, Ross *et al*.[8] found that only 68.0% of clinical trials funded by the US National Institutes of Health (NIH) publish, with 46.0% publishing within 30.0 months of trial completion. Tricco *et al*.[9] established that Cochrane reviews have a median time to publication of 2.4 years (~29.0 months), but only 80.9% of Cochrane protocols are published overall. Given the importance of publishing promptly and the recommendation that researchers use data from the monograph of a project, rather than its journal article; the aim of this study was to determine the time to publication for HTA-funded primary research and evidence synthesis projects in *Health Technology Assessment* and biomedical literature, and to compare time to publication with other organisations that fund or evaluate research.

METHODS

Cohort sample

The cohort in this project is derived from the NIHR research programmes database. It is a sub sample of the data set used by Turner *et al*.[7] and includes projects that planned to submit their draft final report on or before 9th December 2011 (as recorded in the NIHR research programmes database). Based on project classification in the database, the cohort was divided into two main categories: primary research and evidence synthesis, primary research was subdivided further into trials (as defined by Ross *et al*.[8]) and the remainder were categorised as 'others'.

Data extracted from the database included the project reference number, its publication date in *Health Technology Assessment* and the date when the evidence syntheses protocols were made available

online. The *Health Technology Assessment* monograph (or draft final report or external publication if the project did not have a published monograph) was hand-searched for the end of recruitment date and length of follow-up in order to calculate the study conclusion date for the primary research projects. We also hand searched the *Health Technology Assessment* journal website for the online publication date of the first report for all projects in an external journal. We took a pragmatic approach and excluded protocols, background papers and systematic reviews that may have been conducted before the research began. We included the first report that used clinical data from the project, and excluded cost-effectiveness analyses (unless the project report specifically stated that it was an economic evaluation).

Time to publication

For primary research, the time to publication was determined by calculating the number of months from when the study concluded (i.e. end of follow-up, using the same methodology as Ross *et al*.[8]) to when the monograph was first published online and to when the first external publication was available online. For evidence syntheses, we followed the protocol of Tricco *et al*.[9] Time to publication was measured as the number of months from when the protocol was first made available online to the online publication date of the monograph and to the online availability of the study in an external journal.

Three researchers (FC, M A-K and JG) conducted data extraction for the primary research dataset and any disagreement was resolved in discussion. Two researchers (FC and JG) extracted the data for the evidence synthesis projects. Again, any disagreement was settled in discussion. In the case of primary research, the first output registered was often the protocol or a background paper; consequently, two researchers (AY and FC) hand-searched the HTA journal website to determine the publication date of the first report from a project and this date was confirmed in discussion.

Data analysis

Kaplan-Meier survival curves were produced for primary research and evidence synthesis projects, the percentage of HTA-funded studies published in the monograph series was compared to other peer reviewed journals. We calculated the median (time for 50.0% of funded studies to publish) time to publication in *Health Technology Assessment*, elsewhere and for the first output for primary research, trials, and evidence syntheses.

Ross *et al*.[8] have emphasised the need for timely publication and have stated a cut-off of 30.0 months for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at 30.0 months and the total percentage published, both in the monograph series and elsewhere.

Minitab was used to establish distribution of the data subsets (Anderson-Darling normality test) and the interquartile ranges (IQR) were also determined. Any statistical difference between the median times to publication was established using the Mann-Whitney U test.

RESULTS

We identified 458 projects for inclusion in our analyses (figure 1).

Figure 1: Flow diagram of projects in this study.

INSERT FIGURE 1 HERE

Primary research

The primary research subset contains 184 projects; however, 29 of these did not state an end of recruitment date, or it was not possible to determine length of follow-up. Consequently, it was not possible to calculate the last point of data collection for 15.8% of HTA Programme-funded primary research, even though many of these studies do have a publication.

Of the 155 primary research projects with a completion date, the median time to any publication (time for 50% of the funded studies to publish) was 23.0 months (IQR 19.0 months), 26.5 months (IQR 20.5 months) for publication as a monograph in *Health Technology Assessment* and 35.5 months (IQR 19.0 months) for publication in any other external journal, but this difference was not statistically significant (P=0.149).

Sixty-nine per cent of all primary research funded by the HTA Programme is published by 30.0 months, but only 56.1% of monographs are produced within this time. Limiting the analysis to trials, directly comparable to the work of Ross *et al*.[8], 67.5% publish within 30.0 months and have a median time to publication of 24.0 months (IQR 15.3 months) (table 1). Overall publication rates are 92.9% for any publication, 88.4% in the monograph and 62.6% in an external journal (table 1, figure 2).

INSERT TABLE 1 HERE

Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

INSERT FIGURE 2 HERE

Evidence synthesis

Of the 274 evidence syntheses, the database did not record a protocol online date for 51 (18.6%) projects and so these could not be included in further analyses. Of the remaining projects, the median time to any publication was 25.5 months (IQR 16.0 months) and the median time to publication of a monograph is 28.0 months (IQR 19.0 months) but, unlike primary research, fewer than 50.0% of evidence synthesis projects publish in other peer-reviewed journals (table 2, figure 3), so it was not possible to test for statistical significance. Evidence syntheses publish in a timely fashion, with 65.0% of studies publishing within 30.0 months and 93.3% publish overall.

INSERT TABLE 2 HERE

Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

INSERT FIGURE 3 HERE

DISCUSSION

Using the standard of Ross *et al*.,[8] HTA-funded research publishes promptly; 69.0% of primary research projects publish by 30.0 months, with a median time to publication of 23.0 months. Sixty-five per cent of evidence synthesis projects publish by 30.0 months and the median time to publication was 25.5 months.

Strengths and limitations

The main strength of this study is that it involves a large cohort, representing almost 20 years of research funded on behalf of the NHS. This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.[7] This project used a subsample of the dataset of Turner et al.[7] with the intention to determine the time to publication of all of the

primary research and evidence synthesis projects that do publish. However, a major limitation of this project is the amount of data missing from the analyses. It was not possible to determine the end-of-follow up for over 15.0% of primary research projects, and over 18.0% of the evidence synthesis studies did not have a recorded protocol online date, so they were not included in the analyses. Since data-recording was poorer in earlier years (unpublished data), we have disproportionately excluded more of the older projects. Consequently, since older projects generally took longer to publish (unpublished data), we may be underestimating how long HTA-funded studies take to publish overall.

This project relied heavily on data from the NIHR research programmes database and the *Health Technology Assessment* journal website to determine if a study has published elsewhere, which in turn depends on self-declarations from the principle investigators (PIs), as per contractual obligations. Preliminary work in an internal NETSCC report found that PIs were under-reporting their external publications by 15.8% and so the overall external publication rate is likely to be higher and we are overestimating the median time to publication in an external journal. In addition, the under-reporting may also be affecting the "Any publication" Kaplan-Meier curve and so influencing the median time to the first publication as well.

Comparison with other studies

Ross et al.[8] highlighted the need for the publication process to be prioritised in order to shorten the time taken for research findings to be available to the public. Their work found that the median time to publication of clinical trials funded by the US NIH and registered with ClinicalTrials.gov (and completed by 31st December 2008) was 23.0 months. However, this is only the median of the trials that published, not the whole cohort (i.e. the trials that were funded) and so it is underestimating the time to publication. Funders and researchers should aspire to publish all of their research, so the time taken for 50.0% of all funded studies to publish is the appropriate median time to publication. Arguably, the 30.0 month publication rate may be the truly important measure of timeliness to publication.

It takes ~32.0 months for half of the clinical trials funded by the US NIH to publish; only 46.0% were published within 30.0 months of trial completion, with an overall publication rate of 68.0%. In comparison, the median time to publication of HTA Programme-funded trials is 24.0 months, 67.5% publish by 30.0 months, and 93.7% publish overall. The *Health Technology Assessment* figures also compare very favourably with results from industry sponsored trials; trials conducted by GlaxoSmithKline in Spain between 2001 and 2006 had a publication rate of 61.0% and a median time to publication of 28.4 months. However, it was not clear whether this was the median of the published trials or of the funded ones.[10] The median time to publication of more recent NIH clinical trials (those with a ClinicalTrials.gov identifier, published during 2009 and indexed in MEDLINE) is 21.0 months,[11] but the study did not comment on how long it took for 50.0% of the funded trials to publish. Lastly, 68.0% of NIH-funded studies publish overall and 62.6% of HTA-funded primary research publishes externally. This highlights the importance of the monograph series as it provides a means of publication for those projects that would not otherwise reach the public domain.

HTA-funded evidence syntheses are also produced in a timely manner, with a median time to publication of 25.5 months and 65.0% of studies being published by 30.0 months (93.3% publishing overall). In comparison, Cochrane reviews have a median time to publication of ~29.0 months, with only 80.9% publishing in full after eight years of follow-up.

Implications

The median time to publication in the monograph series and an external journal could only be compared for primary research (as over half of the evidence syntheses do not have a recorded external publication); here a monograph is produced nine months earlier. Publication rate at 30.0 months and in total, for both types of research, was considerably higher in the monograph series than

for other peer reviewed biomedical journals. The shorter time to publication and high publication rate in *Health Technology Assessment* is laudable; ensuring information from research is easily accessible and widely available is important because it facilitates its use, increases its impact and consequently its value to society. Unpublished data may also invalidate conclusions from meta-analyses, and systematic reviews. These are not just a valuable source of information for health care professionals and researchers, but definitive conclusions about an intervention also prevent putting more patients at risk in further unneeded trials or depriving them of the correct treatment. Having *Health Technology Assessment* is clearly important for dissemination of research to the public in a timely fashion and ensures that data are not lost as a result of publication bias.

Conclusion and recommendations

Research funded by the HTA Programme publishes in a timely fashion; where a comparison was possible, time to publication was nine months shorter for a monograph than an external journal article and publication rate was considerably higher in *Health Technology Assessment* than for other peer-reviewed journals, both overall and at 30.0 months. HTA-funded trials publish more promptly than those funded by the NIH and industry and HTA-funded evidence syntheses are produced sooner than Cochrane reviews. This current study highlighted the importance of HTA Programme research being funded via a contract that obliges researchers to publish their findings in full.

Recommendations include encouraging other funding organisations to make it a condition for their investigators to publish final project results in full, within a set time, and to support this practice, regardless of whether findings are significant or not. In the UK, the Health Research Authority (HRA) is responsible for protecting and promoting the interests of patients and the public in health research. It plays a key leadership role in promoting transparency and has made a number of commitments to ensure the publication and dissemination of health research results.[12]

Future work should investigate the time to publication for other funders and ways in which delays can be reduced without compromising quality. Regardless of the funder, all trials should be registered and the methods and results reported in full, as called for by the AllTrials initiative,[13,14] in a timely fashion.

Table 1: Publication characteristics of HTA Programme-funded primary research and trials (studies with a completion date).

	Primary research (n=155)			Trials (n=126)
	Any publication	*HTA* Monograph	External journal	Any publication
Number of studies published (%)	144 (92.9%)	137 (88.4%)	97 (62.6%)	118 (93.7%)
Median time to publication (months)	23.0	26.5	35.5	24.0
Number of studies published at 30 months (%)	107 (69.0%)	87 (56.1%)	66 (42.6%)	85 (67.5%)

Table 2: Publication characteristics of HTA Programme-funded evidence synthesis (studies with a protocol online date).

	Evidence syntheses (n=223)		
	Any publication	*HTA* Monograph	External journal
Number of studies published (%)	208 (93.3%)	207 (92.3%)	99 (44.4%)
Median time to publication (months)	25.5	28.0	-
Number of studies published at 30 months (%)	145 (65.0%)	122 (54.7%)	52 (23.3%)

ACKNOWLEDGEMENTS

The authors would like to thank Sheila Turner for providing the reference numbers of the projects and their publication date in the monograph series; Stephen Lemon for his advice about data extraction from the NIHR research programmes database and Jo Merritt for sharing her data concerning authors not reporting projects that publish in an external journal. We would also like to acknowledge the Metadata team for providing their database and trial details used in the study.

COMPETING INTERESTS

FC has worked for the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) since February 2012; AY is an employee of NETSCC which hosts the Research on Research Programme, from where this work originated; JG worked for NETSCC from January 2006 to April 2013; M A-K is currently an editor for the Health Technology Assessment journal and a full-time employee of NETSCC; RM is employed as the Head of NETSCC and has worked for NETSCC (and its predecessor organisation) in senior roles on and off since 1996. He was an editor of the Health Technology Assessment journal (1997-2005) and a founder editor for other journals in the new NIHR Journals Library (2011-12).

FUNDING

This research was supported by the NIHR Evaluation, Trials and Studies Coordinating Centre through its Research on Research programme. The views and opinions expressed are those of the authors and do not necessarily reflect those of the Department of Health or of NETSCC.

Contributors

The study was designed by RM, M A-K, FC and AY. FC, AY, JG and M A-K performed data extraction, FC and AY conducted the data analyses. FC drafted the manuscript, guided by M A-K, RM and AY. All authors have read and approved the final manuscript.

Data sharing statement

There are no additional data available.

REFERENCES

1. Scherer RW, Langenberg P, von Elm E. Full publication of results initially presented as abstracts. Cochrane Database Syst Rev 2007; Issue 2: MR000005
2. Chalmers I and Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009; **374**: 86-89
3. Dickersin K, Chan S, Chalmers TC, et al. Publication bias and clinical trials. Control Clin Trials. 1987; **8(4)**:343-53.
4. Song F, Parekh S, Hooper L, et al. Dissemination and publication of research findings: an updated review of related biases. Health Technol Assess. 2010; **14(8)**:iii, ix-xi, 1-193.
5. Suñé P, Suñé JM, Montoro JB. Positive outcomes influence the rate and time to publication, but not the impact factor of publications of clinical trial results. PLoS One. 2013; **8(1)**:e54583.
6. Matthews GA, Dumville JC, Hewitt CE, et al. Retrospective cohort study highlighted outcome reporting bias in UK publicly funded trials. J Clin Epidemiol. 2011; **64(12)**:1317-24
7. Turner S, Wright, D, Maeso B, et al. Publication rate for funded studies from a major UK health research funder: a cohort study. BMJ Open 2013; **3(5)**. pii: e002521.
8. Ross JS, Tse T, Zarin D, et al. Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. BMJ 2012; **344**;d7292
9. Tricco AC, Brehaut J, Chen MH, et al. Following 411 Cochrane protocols to completion: a retrospective cohort study. PLoS One 2008; **3(11)**: e3684
10. Dal-Ré R, Pedromingo A, García-Losa M, et al. Are results from pharmaceutical company-sponsored studies available to the public? Eur J Clin Pharmacol 2010; **66**:1081-1089
11. Ross JS, Mocanu M, Lampropulos JF, et al. Time to Publication Among Completed Clinical Trials. JAMA Intern Med. 2013; **173(9)**:825-8.
12. http://www.hra.nhs.uk/hra-news-and-announcements/transparent-research/
13. http://www.alltrials.net/
14. http://www.bmj.com/content/346/bmj.f105

Time to publication for NIHR HTA Programme-funded research: a cohort study

Fay Chinnery, Amanda Young, Jennie Goodman, Martin Ashton-Key, Ruairidh Milne

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Fay Chinnery
Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Amanda Young
Senior Research Fellow

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Jennie Goodman
Programme Manager

National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton, Alpha House, Enterprise Road, Southampton, SO16 7NS, UK
Martin Ashton-Key
Consultant in Public Health Medicine / Consultant Advisor

Wessex Institute, University of Southampton, Southampton, Hampshire, SO16 7NS, UK
Ruairidh Milne
Professional Fellow in Public health

Correspondence to:
Fay Chinnery
F.Chinnery@soton.ac.uk
Tel: 023 8059 5548

Key words
Publication; Time to publication; Clinical trial; Health Technology Assessment (HTA) Programme

Word Count
2600

Contributors
The study was designed by RM, M A-K, FC and AY. FC, AY, JG and M A-K performed data extraction, FC and AY conducted the data analyses. FC drafted the manuscript, guided by M A-K, RM and AY. All authors have read and approved the final manuscript.

Data sharing statement
There are no additional data available.

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, a worldwide, licence, to the Publishers and its licensees in perpetuity (subject to the Reversion of Rights set out below), in all forms, formats and media (whether known now or created in the future), to i) publish, reproduce, distribute, display and store the Contribution, ii) translate the Contribution into other languages, create adaptations, reprints, include within collections and create summaries, extracts and/or, abstracts of the Contribution and convert or allow conversion into any format including without limitation audio, iii) create any other derivative work(s) based in whole or part on the Contribution, iv) to exploit all subsidiary rights that currently exist or as may exist in the future in the Contribution, v) the inclusion of electronic links from the Contribution to third party material where-ever it may be located; and, vi) licence any third party to do any or all of the above.

Time to publication for NIHR HTA Programme-funded research: a cohort study

ABSTRACT

Objective: To assess the time to publication of primary research and evidence syntheses funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme published as a monograph in *Health Technology Assessment* and as a journal article in the wider biomedical literature.

Study design: Retrospective cohort study.

Setting: Primary research and evidence synthesis projects funded by the HTA Programme were included in the cohort if they were registered in the NIHR research programmes database and planned to submit their draft final report for publication in *Health Technology Assessment* on or before 9 December 2011.

Main outcome measures: The median time to publication and publication at 30.0 months in both *Health Technology Assessment* and in an external journal, as determined by searching the NIHR research programmes database and HTA Programme website.

Results: Of 458 included projects, 184 (40.2%) were primary research projects and 274 (59.8%) were evidence syntheses. 155 primary research projects had a completion date, the median time to publication was 23.0 months (26.5 and 35.5 months to publish a monograph and to publish in an external journal, respectively) and 69.0% had published by 30.0 months. The median time to publication of HTA-funded trials (n=126) was 24.0 months and 67.5% published by 30.0 months. Among the evidence syntheses with a protocol online date (n=223), the median time to publication was 25.5 months, (28.0 months to publication as a monograph), but only 44.4% of evidence synthesis projects publish in an external journal. 65.0% of evidence synthesis studies publish by 30.0 months.

Conclusion: Research funded by the HTA Programme publishes promptly. The importance of *Health Technology Assessment* was highlighted as the median time to publication was nine months shorter for a monograph than an external journal article.

Strengths and limitations of this study

- The study involves a large cohort, representing almost 20 years of research funded on behalf of the NHS.
- This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.
- This project relied heavily on the NIHR research programmes database and some data were not available for analyses.

INTRODUCTION

In order for research to help patients and aid clinicians in their decision-making it must be published in full and made available in a timely fashion. However, it is estimated that over 50.0% of studies are never published completely, and studies with disappointing (non-significant) results may not be published at all.[1,2] Non-publication is believed to be primarily due to failure to write-up and submit research, rather than manuscripts being rejected.[3] Studies with null or negative findings take longer to be published than those with positive results,[4,5] and this publication bias may invalidate a meta-analysis, leading to overestimation of treatment effects. As a result, new interventions may be adopted without suitable evidence to support them.

~~In addition to publication bias, selective outcome reporting may also lead to overestimation of the effectiveness of the treatment, emphasising the need for rigorous reporting of research. *Health Technology Assessment* (also known as the monograph series) is the peer reviewed journal for the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (which produces research evidence on behalf of the NHS).~~

During 2011/12, the National Institute for Health Research (NIHR) invested £202.2 million in research across a broad range of programmes and initiatives. *Health Technology Assessment* (also known as the monograph series) is the peer reviewed journal for the NIHR Health Technology Assessment (HTA) Programme. Reports published in *Health Technology Assessment* provide a full account of the research project, including methods and a full description of the results. These full monographs complement shorter articles submitted for publication in other peer-review journals, which the NIHR actively encourages researchers to do as part of their dissemination strategy.

Formatted: Font: Italic

Formatted: Font: Italic

In addition to publication bias, selective outcome reporting may also lead to overestimation of the effectiveness of the treatment, emphasising the need for rigorous reporting of research. Trials funded by the NIHR HTA Programme that only publish in *Health Technology Assessment* tend to have a higher *P*-value for the main outcome compared to those that also have a publication in another journal. The full *Health Technology Assessment* monograph generally contains more outcomes than the main trial publication and journal articles tend to report a higher proportion of statistically significant outcomes. Consequently, researchers including HTA-funded trials in their systematic reviews are recommended to use information from the monograph and not the associated journal article.[6]

Turner *et al*.[7] have shown that 98.0% of projects funded by the HTA Programme in the last 10 years will publish in the monograph series. In contrast, Ross *et al*.[8] found that only 68.0% of clinical trials funded by the US National Institutes of Health (NIH) publish, with 46.0% publishing within 30.0 months of trial completion. Tricco *et al*.[9] established that Cochrane reviews have a median time to publication of 2.4 years (~29.0 months), but only 80.9% of Cochrane protocols are published overall. Given the importance of publishing promptly and the recommendation that researchers use data from the monograph of a project, rather than its journal article; the aim of this study was to determine the time to publication for HTA-funded primary research and evidence synthesis projects in *Health Technology Assessment* and biomedical literature, and to compare time to publication with other organisations that fund or evaluate research.~~other public sector funders.~~

METHODS

Cohort sample

The cohort in this project is derived from the NIHR research programmes database. It is a sub sample of the data set used by Turner *et al*.[7] and includes projects that planned to submit their draft final report on or before 9th December 2011 (as recorded in the NIHR research programmes database). Based on project classification in the database, the cohort was divided into two main categories:

primary research and evidence synthesis, primary research was subdivided further into trials (as defined by Ross *et al.*[8]) and the remainder were categorised as 'others'.

Data extracted from the database included the project reference number, its publication date in *Health Technology Assessment* and the date when the evidence syntheses protocols were made available online. The *Health Technology Assessment* monograph (or draft final report or external publication if the project did not have a published monograph) was hand-searched for the end of recruitment date and length of follow-up in order to calculate the study conclusion date for the primary research projects. We also hand searched the *Health Technology Assessment* journal website for the online publication date of the first report for all projects in an external journal. We took a pragmatic approach and excluded protocols, background papers and systematic reviews that may have been conducted before the research began. We included the first report that used clinical data from the project, and excluded cost-effectiveness analyses (unless the project report specifically stated that it was an economic evaluation).

Time to publication

For primary research, the time to publication was determined by calculating the number of months from when the study concluded (i.e. end of follow-up, using the same methodology as Ross *et al.*[8]) to when the monograph was first published online and to when the first external publication was available online. For evidence syntheses, we followed the protocol of Tricco *et al.*[9] Time to publication was measured as the number of months from when the protocol was first made available online to the online publication date of the monograph and to the online availability of the study in an external journal.

Three researchers (FC, M A-K and JG) conducted data extraction for the primary research dataset and any disagreement was resolved in discussion. Two researchers (FC and JG) extracted the data for the evidence synthesis projects. Again, any disagreement was settled in discussion. In the case of primary research, the first output registered was often the protocol or a background paper; consequently, two researchers (AY and FC) hand-searched the HTA journal website to determine the publication date of the first report from a project and this date was confirmed in discussion.

Data analysis

Kaplan-Meier survival curves were produced for primary research and evidence synthesis projects, the percentage of HTA-funded studies published in the monograph series was compared to other peer reviewed journals. We calculated the median (time for 50.0% of funded studies to publish) time to publication in *Health Technology Assessment*, elsewhere and for the first output for primary research, trials, and evidence syntheses.

Ross *et al.*[8] have emphasised the need for timely publication and have stated a cut-off of 30.0 months for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at 30.0 months and the total percentage published, both in the monograph series and elsewhere.

Minitab was used to establish distribution of the data subsets (Anderson-Darling normality test) and the interquartile ranges (IQR) were also determined. Any statistical difference between the median times to publication was established using the Mann-Whitney U test.

RESULTS

We identified 458 projects for inclusion in our analyses (figure 1).

Figure 1: Flow diagram of projects in this study.

INSERT FIGURE 1 HERE

Primary research

The primary research subset contains 184 projects; however, 29 of these did not state an end of recruitment date, or it was not possible to determine length of follow-up. Consequently, it was not possible to calculate the last point of data collection for 15.8% of HTA Programme-funded primary research, even though many of these studies do have a publication.

Of the 155 primary research projects with a completion date, the median time to any publication (time for 50% of the funded studies to publish) was 23.0 months (IQR 19.0 months), 26.5 months (IQR 20.5 months) for publication as a monograph in *Health Technology Assessment* and 35.5 months (IQR 19.0 months) for publication in any other external journal, but this difference was not statistically significant (P=0.149).

Sixty-nine per cent of all primary research funded by the HTA Programme is published by 30.0 months, but only 56.1% of monographs are produced within this time. Limiting the analysis to trials, directly comparable to the work of Ross *et al.*[8], 67.5% publish within 30.0 months and have a median time to publication of 24.0 months (IQR 15.3 months) (table 1). Overall publication rates are 92.9% for any publication, 88.4% in the monograph and 62.6% in an external journal (table 1, figure 2).

INSERT TABLE 1 HERE

Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

INSERT FIGURE 2 HERE

Evidence synthesis

Of the 274 evidence syntheses, the database did not record a protocol online date for 51 (18.6%) projects and so these could not be included in further analyses. Of the remaining projects, the median time to any publication was 25.5 months (IQR 16.0 months) and the median time to publication of a monograph is 28.0 months (IQR 19.0 months) but, unlike primary research, fewer than 50.0% of evidence synthesis projects publish in other peer-reviewed journals (table 2, figure 3), so it was not possible to test for statistical significance. Evidence syntheses publish in a timely fashion, with 65.0% of studies publishing within 30.0 months and 93.3% publish overall.

INSERT TABLE 2 HERE

Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

INSERT FIGURE 3 HERE

DISCUSSION

Using the standard of Ross *et al.*,[8] HTA-funded research publishes promptly; 69.0% of primary research projects publish by 30.0 months, with a median time to publication of 23.0 months. Sixty-five per cent of evidence synthesis projects publish by 30.0 months and the median time to publication was 25.5 months.

Strengths and limitations

The main strength of this study is that it involves a large cohort, representing almost 20 years of research funded on behalf of the NHS. This report complements previous work which has shown that 98.0% of HTA projects funded since 2002 will publish a monograph.[7] This project used a subsample of the dataset of Turner et al.[7] with the intention to determine the time to publication of all of the primary research and evidence synthesis projects that do publish. However, a major limitation of this project is the amount of data missing from the analyses. It was not possible to determine the end-of-follow up for over 15.0% of primary research projects, and over 18.0% of the evidence synthesis studies did not have a recorded protocol online date, so they were not included in the analyses. Since data-recording was poorer in earlier years (unpublished data), we have disproportionately excluded more of the older projects. Consequently, since older projects generally took longer to publish (unpublished data), we may be underestimating how long HTA-funded studies take to publish overall.

This project relied heavily on data from the NIHR research programmes database and the *Health Technology Assessment* journal website to determine if a study has published elsewhere, which in turn depends on self-declarations from the principle investigators (PIs), as per contractual obligations. Preliminary work in an internal NETSCC report found that PIs were under-reporting their external publications by 15.8% and so the overall external publication rate is likely to be higher and we are overestimating the median time to publication in an external journal. In addition, the under-reporting may also be affecting the "Any publication" Kaplan-Meier curve and so influencing the median time to the first publication as well.

Comparison with other studies

Ross et al.[8] highlighted the need for the publication process to be prioritised in order to shorten the time taken for research findings to be available to the public. Their work found that the median time to publication of clinical trials funded by the US NIH and registered with ClinicalTrials.gov (and completed by 31st December 2008) was 23.0 months. However, this is only the median of the trials that published, not the whole cohort (i.e. the trials that were funded) and so it is underestimating the time to publication. Funders and researchers should aspire to publish all of their research, so the time taken for 50.0% of all funded studies to publish is the appropriate median time to publication. Arguably, the 30.0 month publication rate may be the truly important measure of timeliness to publication.

It takes ~32.0 months for half of the clinical trials funded by the US NIH to publish; only 46.0% were published within 30.0 months of trial completion, with an overall publication rate of 68.0%. In comparison, the median time to publication of HTA Programme-funded trials is 24.0 months, 67.5% publish by 30.0 months, and 93.7% publish overall. The *Health Technology Assessment* figures also compare very favourably with results from industry sponsored trials; trials conducted by GlaxoSmithKline in Spain between 2001 and 2006 had a publication rate of 61.0% and a median time to publication of 28.4 months. However, it was not clear whether this was the median of the published trials or of the funded ones.[10] The median time to publication of more recent NIH clinical trials (those with a ClinicalTrials.gov identifier, published during 2009 and indexed in MEDLINE) is 21.0 months,[11] but the study did not comment on how long it took for 50.0% of the funded trials to publish. Lastly, 68.0% of NIH-funded studies publish overall and 62.6% of HTA-funded primary research publishes externally. This highlights the importance of the monograph series as it provides a means of publication for those projects that would not otherwise reach the public domain.

HTA-funded evidence syntheses are also produced in a timely manner, with a median time to publication of 25.5 months and 65.0% of studies being published by 30.0 months (93.3% publishing overall). In comparison, Cochrane reviews have a median time to publication of ~29.0 months, with only 80.9% publishing in full after eight years of follow-up.

Implications

The median time to publication in the monograph series and an external journal could only be compared for primary research (as over half of the evidence syntheses do not have a recorded external publication); here a monograph is produced nine months earlier. Publication rate~~,~~ at 30.0 months and in total, for both types of research, was considerably higher in the monograph series than for other peer reviewed biomedical journals. The shorter time to publication and high publication rate in *Health Technology Assessment* is laudable; ensuring information from research is easily accessible and widely available is important because it facilitates its use, increases its impact and consequently its value to society. Unpublished data may also invalidate conclusions from meta-analyses, and systematic reviews. These are not just a valuable source of information for health care professionals and researchers, but definitive conclusions about an intervention also prevent putting more patients at risk in further unneeded trials or depriving them of the correct treatment. Having *Health Technology Assessment* is clearly important for dissemination of research to the public in a timely fashion and ensures that data are not lost as a result of publication bias. ~~US federal requirements[12] call for "results of an Applicable Clinical Trial of a drug, biologic, or device that is approved, licensed, or cleared by FDA must be submitted by the Responsible Party no later than 12 months after the Completion Date". There is an important distinction between the user's (HTA Programme, clinicians and patients, NICE, etc.) perspective and the researcher's perspective of the process. Once they have submitted the draft final report, aside from editing the researcher may assume their task is finished, but the users are more concerned with when the research is in the public domain.~~

Conclusion and recommendations

Research funded by the HTA Programme publishes in a timely fashion; where a comparison was possible, time to publication was nine months shorter for a monograph than an external journal article and publication rate was considerably higher in *Health Technology Assessment* than for other peer-reviewed journals, both overall and at 30.0 months. HTA-funded trials publish more promptly than those funded by the NIH and industry and HTA-funded evidence syntheses are produced sooner than Cochrane reviews. This current study highlighted the importance of HTA Programme research being funded via a contract that obliges ~~(~~researchers ~~are contractually obliged~~ to publish their findings in full~~,)~~ ~~as well as the value of *Health Technology Assessment* and its rigorous editorial procedure.~~

Recommendations include encouraging other funding organisations to make it a condition for their investigators to publish final project results in full, within a set time, and to support this practice, regardless of whether findings are significant or not. In the UK, the Health Research Authority (HRA) is responsible for protecting and promoting the interests of patients and the public in health research. It plays a key leadership role in promoting transparency and has made a number of commitments to ensure the publication and dissemination of health research results.[1~~2~~~~3~~]

Future work should investigate the time to publication for other funders and ways in which delays can be reduced without compromising quality. Regardless of the funder, all trials should be registered and the methods and results reported in full, as called for by the AllTrials initiative,[13,14] ~~and~~ in a timely fashion.

Formatted: Superscript

ACKNOWLEDGEMENTS

The authors would like to thank Sheila Turner for providing the reference numbers of the projects and their publication date in the monograph series; Stephen Lemon for his advice about data extraction from the NIHR research programmes database and Jo Merritt for sharing her data concerning authors not reporting projects that publish in an external journal. We would also like to acknowledge the Metadata team for providing their database and trial details used in the study.

COMPETING INTERESTS

FC has worked for the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) since February 2012; AY is an employee of NETSCC which hosts the Research on Research Programme, from where this work originated; JG worked for NETSCC from January 2006 to April 2013; M A-K is currently an editor for the Health Technology Assessment journal and a full-time employee of NETSCC; RM is employed as the Head of NETSCC and has worked for NETSCC (and its predecessor organisation) in senior roles on and off since 1996. He was an editor of the Health Technology Assessment journal (1997-2005) and a founder editor for other journals in the new NIHR Journals Library (2011-12).

FUNDING

This research was supported by the NIHR Evaluation, Trials and Studies Coordinating Centre through its Research on Research programme. The views and opinions expressed are those of the authors and do not necessarily reflect those of the Department of Health or of NETSCC.

Table 1: Publication characteristics of HTA Programme-funded primary research and trials (studies with a completion date).

	Primary research (n=155)			Trials (n=126)
	Any publication	*HTA* Monograph	External journal	Any publication
Number of studies published (%)	144 (92.9%)	137 (88.4%)	97 (62.6%)	118 (93.7%)
Median time to publication (months)	23.0	26.5	35.5	24.0
Number of studies published at 30 months (%)	107 (69.0%)	87 (56.1%)	66 (42.6%)	85 (67.5%)

Table 2: Publication characteristics of HTA Programme-funded evidence synthesis (studies with a protocol online date).

	Evidence syntheses (n=223)		
	Any publication	*HTA* Monograph	External journal
Number of studies published (%)	208 (93.3%)	207 (92.3%)	99 (44.4%)
Median time to publication (months)	25.5	28.0	-
Number of studies published at 30 months (%)	145 (65.0%)	122 (54.7%)	52 (23.3%)

REFERENCES

1. Scherer RW, Langenberg P, von Elm E. Full publication of results initially presented as abstracts. Cochrane Database Syst Rev 2007; Issue 2: MR000005
2. Chalmers I and Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009; **374**: 86-89
3. Dickersin K, Chan S, Chalmers TC, Sacks HS, Smith H Jr. Publication bias and clinical trials. Control Clin Trials. 1987; **8(4)**:343-53.
4. Song F, Parekh S, Hooper L, Loke YK, Ryder J, Sutton AJ, Hing C, Kwok CS, Pang C, Harvey I. Dissemination and publication of research findings: an updated review of related biases. Health Technol Assess. 2010; **14(8)**:iii, ix-xi, 1-193.
5. Suñé P, Suñé JM, Montoro JB. Positive outcomes influence the rate and time to publication, but not the impact factor of publications of clinical trial results. PLoS One. 2013; **8(1)**:e54583.
6. Matthews GA, Dumville JC, Hewitt CE, Torgerson DJ. Retrospective cohort study highlighted outcome reporting bias in UK publicly funded trials. J Clin Epidemiol. 2011; **64(12)**:1317-24
7. Turner S, Wright, D, Maeso B, Cook A, Milne R. Publication rate for funded studies from a major UK health research funder: a cohort study. BMJ Open 2013; **3(5)**. pii: e002521.

8. Ross JS, Tse T, Zarin D, Xu H, Zhou L, Krumholz HM. Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis. BMJ 2012; **344**;d7292
9. Tricco AC, Brehaut J, Chen MH, Moher D. Following 411 Cochrane protocols to completion: a retrospective cohort study. PLoS One 2008; **3(11)**: e3684
10. Dal-Ré R, Pedromingo A, García-Losa M, Lahuerta J, Ortega, R. Are results from pharmaceutical company-sponsored studies available to the public? Eur J Clin Pharmacol 2010; **66**:1081-1089
11. Ross JS, Mocanu M, Lampropulos JF, Tse T, Krumholz HM. Time to Publication Among Completed Clinical Trials. JAMA Intern Med. 2013; **173(9)**:825-8.
~~12. Food and Drug Administration Amendments Act (FDAAA) of 2007 - Section 801.~~
12. http://www.hra.nhs.uk/hra-news-and-announcements/transparent-research/
13. http://www.alltrials.net/
14. http://www.bmj.com/content/346/bmj.f105
~~13.~~15.

Field Code Changed

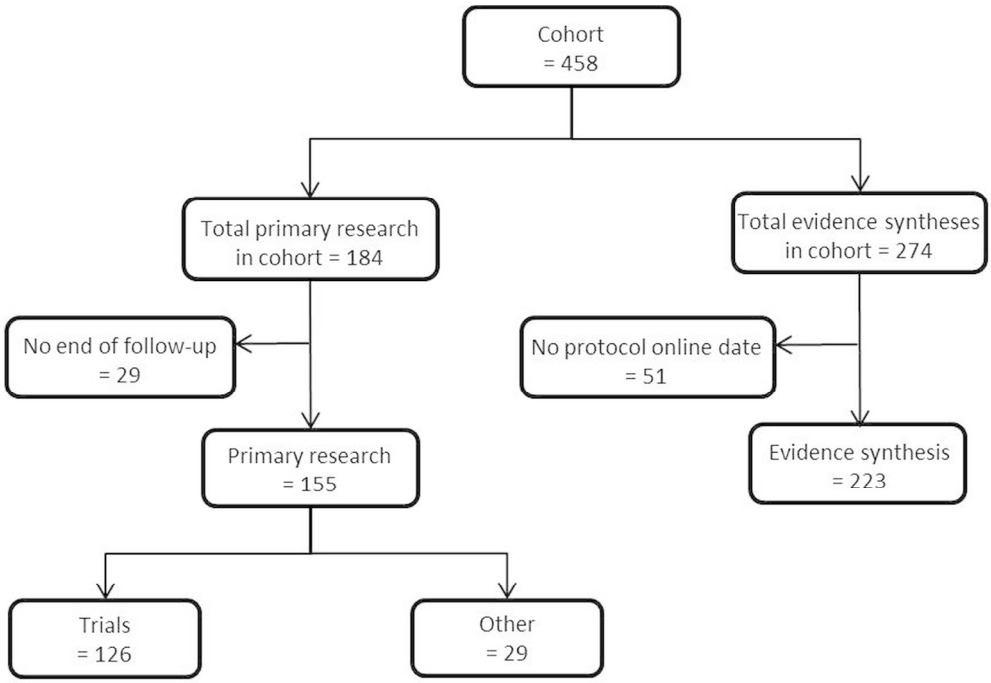


Figure 1: Flow diagram of projects in this study.
132x90mm (300 x 300 DPI)

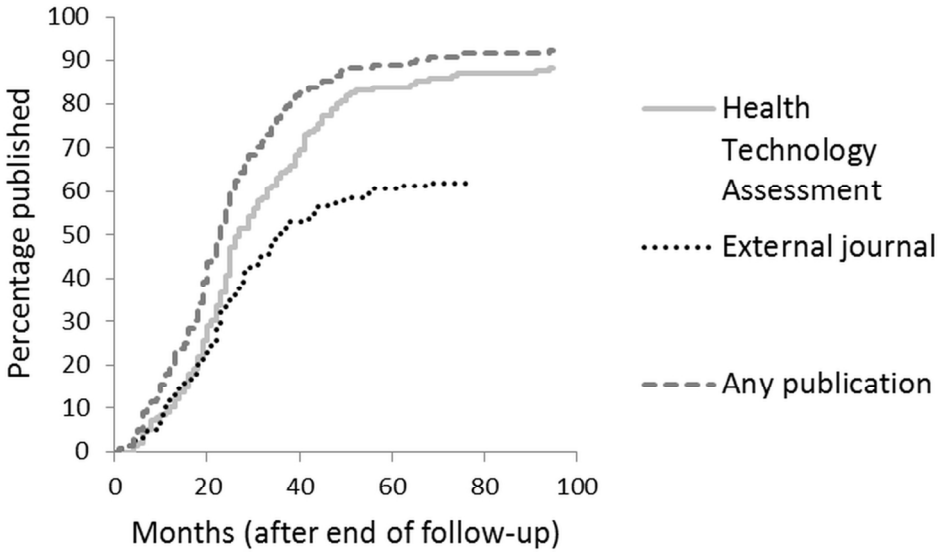


Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the Health Technology Assessment monograph series versus other peer reviewed biomedical journals and time to the first publication anywhere.
150x90mm (300 x 300 DPI)

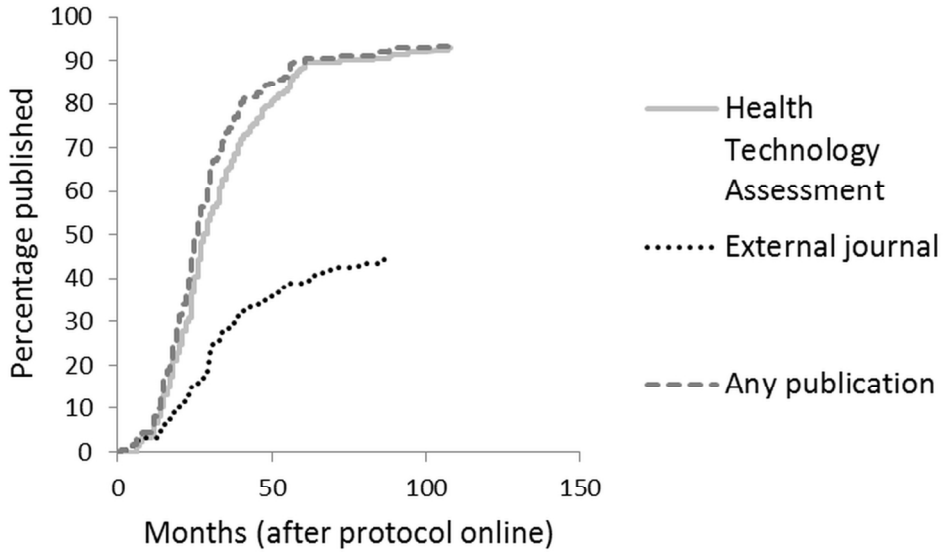


Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in the Health Technology Assessment monograph series versus other peer reviewed biomedical journals and time to the first publication anywhere.
150x90mm (300 x 300 DPI)