



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

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

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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.

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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

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7 was poorer in earlier years (unpublished data), we have disproportionately excluded more of the older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 Consequently, since older projects take longer to publish on average (unpublished data), we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

10
11 This project relied heavily on data from the NIHR research programmes database and the HTA
12 journal website to determine if a study has published elsewhere, which in turn depends on self-
13 declarations from the principle investigators (PIs), as per contractual obligations. Preliminary work in
14 an internal NETSCC report found that PIs were under-reporting their external publications by 15.8%
15 and so the overall external publication rate is likely to be higher and we are overestimating the median
16 time to publication in an external journal. In addition, the under-reporting may also be affecting the
17 "Any publication" Kaplan-Meier curve and so influencing the median time to the first publication as
18 well.
19

20 21 **Comparison with other studies**

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

31 It takes ~32 months for half of the clinical trials funded by the US NIH to publish; only 46% were
32 published within 30 months of trial completion, with an overall publication rate of 68%. In comparison,
33 the median time to publication of HTA Programme-funded trials is 24 months, 67.5% publish by 30
34 months, and 93.7% publish overall. The HTA figures also compare very favourably with results from
35 industry sponsored trials; trials conducted by GlaxoSmithKline in Spain between 2001 and 2006 had a
36 publication rate of 61% and a median time to publication of 28.4 months. However, it was not clear
37 whether this was the median of the published trials or of the funded ones.¹⁰ The median time to
38 publication of more recent NIH clinical trials (those with a ClinicalTrials.gov identifier, published during
39 2009 and indexed in MEDLINE) is 21 months,¹¹ but the study did not comment on how long it took for
40 50% of the trials to publish. Lastly, Sixty-eight per cent of NIH-funded studies publish overall and 62.6%
41 of HTA-funded primary research publishes externally. This highlights the importance of the HTA
42 journal series as it provides a means of publication for those projects that would not otherwise reach
43 the public domain.
44

45
46 HTA-funded evidence syntheses are also produced in a timely manner, with a median time to
47 publication of 25.5 months and 65.0% of studies being published by 30 months (93.3% publishing
48 overall). In comparison, Cochrane reviews have a median time to publication is 29 months, with only
49 80.9% publishing in full after eight years of follow-up.
50

51 52 **Implications**

53 The median time to publication in the monograph and an external journal could only be compared for
54 primary research (as over half of the evidence syntheses do not have a recorded external publication);
55 here the monograph is produced nine months earlier. Publication rate, for both types of research, was
56 considerably higher in the monograph than for other peer reviewed biomedical journals. The shorter
57 time to publication and high publication rate in the monograph is laudable; ensuring information from
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3 research is easily accessible and widely available is important because it facilitates its use, increases
4 its impact and consequently its value to society. Unpublished data may also invalidate conclusions
5 from meta-analyses, and systematic reviews. These are not just a valuable source of information for
6 health care professionals and researchers, but definitive conclusions about an intervention also
7 prevent putting more patients at risk in further unneeded trials or depriving them of the correct
8 treatment. Having the HTA journal is clearly important for dissemination of research to the public in a
9 timely fashion and ensures that data are not lost as a result of publication bias. US federal
10 requirements¹² call for “results of an Applicable Clinical Trial of a drug, biologic, or device that is
11 approved, licensed, or cleared by FDA must be submitted by the Responsible Party no later than 12
12 months after the Completion Date”. There is an important distinction between the user’s (HTA
13 Programme, clinicians and patients, NICE, etc.) perspective and the researcher’s perspective of the
14 process. Once they have submitted the draft final report, aside from editing the researcher may
15 assume their task is finished, but the users are more concerned with when the research is in the
16 public domain.
17

18 **Conclusion and recommendations**

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20 Research funded by the HTA Programme publishes in a timely fashion; where a comparison was
21 possible, time to publication was nine months shorter for the monograph than an external journal and
22 publication rate was considerably higher in this than for other peer-reviewed journals. HTA trials
23 publish more promptly than those funded by the NIH and industry and HTA evidence syntheses are
24 produced sooner than Cochrane reviews. This current study highlighted the importance of HTA
25 research being funded via a contract (researchers are contractually obliged to publish their findings in
26 full) as well as the value of the HTA journal series and its rigorous editorial procedure.
27

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29 Recommendations include encouraging other funding organisations to make it a condition for their
30 investigators to publish final project results in full, within a set time, and to support this practice,
31 regardless of whether findings are significant or not. In the UK, the Health Research Authority (HRA)
32 is responsible for protecting and promoting the interests of patients and the public in health research.
33 It plays a key leadership role in promoting transparency and has made a number of commitments to
34 ensure the publication and dissemination of health research results.¹³
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37 Future work should investigate the time to publication for other funders and ways in which delays can
38 be reduced without compromising quality. Regardless of the funder, all trials should be registered and
39 the methods and results reported in full and in a timely fashion.
40

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44 their publication date in the monograph; Stephen Lemon for his advice about data extraction from the
45 NIHR research programmes database and Jo Merritt for sharing her data concerning authors not
46 reporting projects that publish in an external journal. We would also like to acknowledge the Metadata
47 team for providing their database and trial details used in the study.
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50 **COMPETING INTERESTS**

51
52
53 FC has worked for the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) since
54 February 2012; AY is an employee of NETSCC which hosts the Research on Research Programme,
55 from where this work originated; JG worked for NETSCC from January 2006 to April 2013; M A-K is
56 currently an editor for the Health Technology Assessment journal and a full-time employee of
57 NETSCC; RM is employed as the Head of NETSCC and has worked for NETSCC (and its
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3 predecessor organisation) in senior roles on and off since 1996. He was an editor of the Health
4 Technology Assessment journal (1997-2005) and a founder editor for other journals in the new NIHR
5 Journals Library (2011-12).
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7

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9
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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

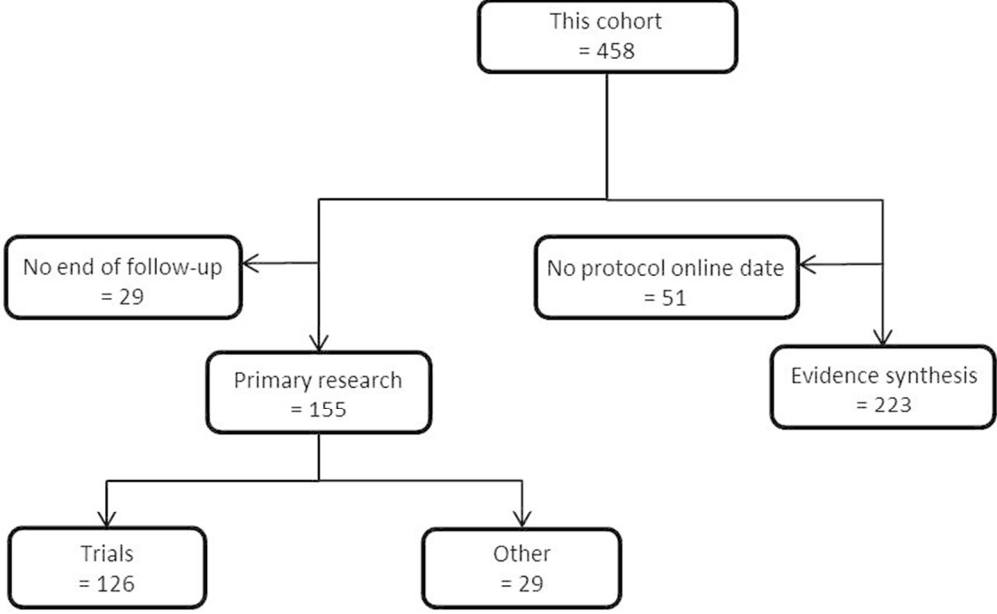
Table 2: Publication characteristics of HTA Programme-funded evidence synthesis (studies with a protocol online date).

	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

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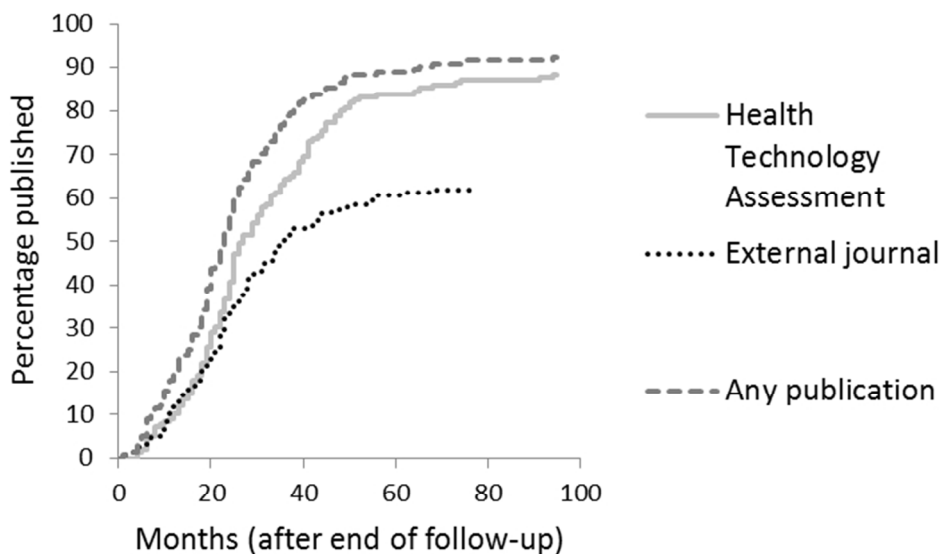
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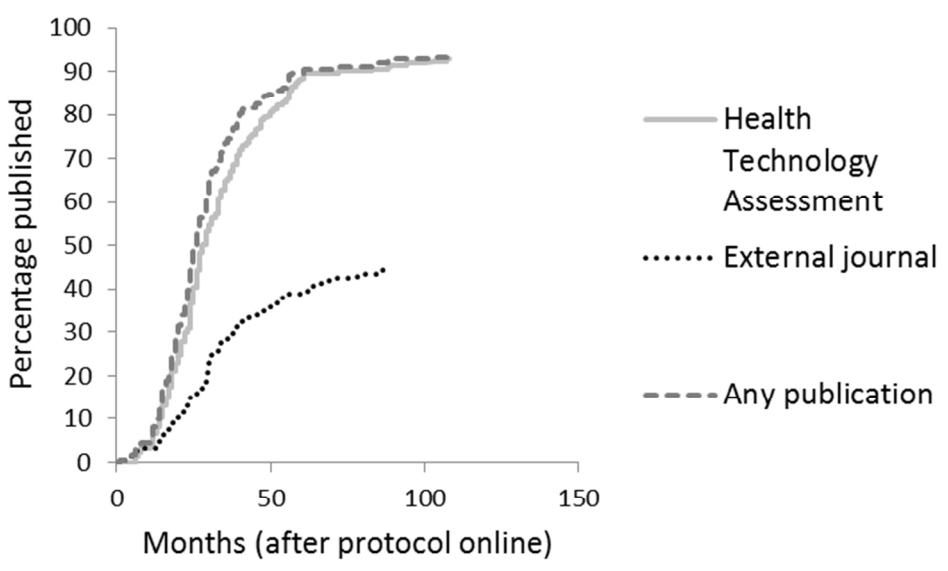
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Contributors

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.

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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

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

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

14 **Strengths and limitations of this study**

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

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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).

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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.~~

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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.

~~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 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 ~~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).

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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 HTA monograph versus other peer reviewed biomedical journals and time to the first publication anywhere.

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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* journal versus other peer reviewed biomedical journals and to the first publication anywhere.

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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 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* 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.

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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* journal 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

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

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

19 Implications

20 The median time to publication in the monograph ~~series~~ and an external journal could only be
21 compared for primary research (as over half of the evidence syntheses do not have a recorded
22 external publication); here ~~a the~~ monograph is produced nine months earlier. Publication rate, for both
23 types of research, was considerably higher in the monograph ~~series~~ than for other peer reviewed
24 biomedical journals. The shorter time to publication and high publication rate in *Health Technology*
25 ~~Assessment the monograph~~ is laudable; ensuring information from research is easily accessible and
26 widely available is important because it facilitates its use, increases its impact and consequently its
27 value to society. Unpublished data may also invalidate conclusions from meta-analyses, and
28 systematic reviews. These are not just a valuable source of information for health care professionals
29 and researchers, but definitive conclusions about an intervention also prevent putting more patients at
30 risk in further unneeded trials or depriving them of the correct treatment. Having ~~the Health~~
31 ~~Technology Assessment HTA journal~~ is clearly important for dissemination of research to the public in
32 a timely fashion and ensures that data are not lost as a result of publication bias. US federal
33 requirements¹² call for "results of an Applicable Clinical Trial of a drug, biologic, or device that is
34 approved, licensed, or cleared by FDA must be submitted by the Responsible Party no later than 12
35 months after the Completion Date". There is an important distinction between the user's (HTA
36 Programme, clinicians and patients, NICE, etc.) perspective and the researcher's perspective of the
37 process. Once they have submitted the draft final report, aside from editing the researcher may
38 assume their task is finished, but the users are more concerned with when the research is in the
39 public domain.

40 Conclusion and recommendations

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

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

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

11 12 **ACKNOWLEDGEMENTS**

13
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15 their publication date in the monograph [series](#); Stephen Lemon for his advice about data extraction
16 from the NIHR research programmes database and Jo Merritt for sharing her data concerning authors
17 not reporting projects that publish in an external journal. We would also like to acknowledge the
18 Metadata team for providing their database and trial details used in the study.

19 20 **COMPETING INTERESTS**

21
22 FC has worked for the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) since
23 February 2012; AY is an employee of NETSCC which hosts the Research on Research Programme,
24 from where this work originated; JG worked for NETSCC from January 2006 to April 2013; M A-K is
25 currently an editor for the Health Technology Assessment journal and a full-time employee of
26 NETSCC; RM is employed as the Head of NETSCC and has worked for NETSCC (and its
27 predecessor organisation) in senior roles on and off since 1996. He was an editor of the Health
28 Technology Assessment journal (1997-2005) and a founder editor for other journals in the new NIHR
29 Journals Library (2011-12).

30 31 **FUNDING**

32
33 This research was supported by the NIHR Evaluation, Trials and Studies Coordinating Centre through
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35 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%)

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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%)

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

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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

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

8 For primary research, the time to publication was determined by calculating the number of months
9 from when the study concluded (i.e. end of follow-up, using the same methodology as Ross *et al.*⁸) to
10 when the monograph was first published online and to when the first external publication was
11 available online. For evidence syntheses, we followed the protocol of Tricco *et al.*⁹ Time to publication
12 was measured as the number of months from when the protocol was first made available online to the
13 online publication date of the monograph and to the online availability of the study in an external
14 journal.
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17 Three researchers (FC, M A-K and JG) conducted data extraction for the primary research dataset
18 and any disagreement was resolved in discussion. Two researchers (FC and JG) extracted the data
19 for the evidence synthesis projects. Again, any disagreement was settled in discussion.
20

21 **Data analysis**

22 Kaplan-Meier survival curves were produced for primary research and evidence synthesis projects,
23 the percentage of HTA-funded studies published in the monograph series was compared to other
24 peer reviewed journals. We calculated the median (time for 50.0% of funded studies to publish) time
25 to publication in *Health Technology Assessment*, elsewhere and for the first output for primary
26 research, trials, and evidence syntheses.
27

28 Ross *et al.*⁸ have emphasised the need for timely publication and have stated a cut-off of 30.0 months
29 for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at
30 30.0 months and the total percentage published, both in the monograph series and elsewhere.
31

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

38 We identified 458 projects for inclusion in our analyses (figure 1).
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40 Figure 1: Flow diagram of projects in this study.
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48 **Primary research**

49 The primary research subset contains 184 projects; however, 29 of these did not state an end of
50 recruitment date, or it was not possible to determine length of follow-up. Consequently, it was not
51 possible to calculate the last point of data collection for 15.8% of HTA Programme-funded primary
52 research, even though many of these studies do have a publication.
53

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

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3 This project relied heavily on data from the NIHR research programmes database and the *Health*
4 *Technology Assessment* journal website to determine if a study has published elsewhere, which in
5 turn depends on self-declarations from the principle investigators (PIs), as per contractual obligations.
6 Preliminary work in an internal NETSCC report found that PIs were under-reporting their external
7 publications by 15.8% and so the overall external publication rate is likely to be higher and we are
8 overestimating the median time to publication in an external journal. In addition, the under-reporting
9 may also be affecting the “Any publication” Kaplan-Meier curve and so influencing the median time to
10 the first publication as well.
11

12 **Comparison with other studies**

13 Ross et al.⁸ highlighted the need for the publication process to be prioritised in order to shorten the
14 time taken for research findings to be available to the public. Their work found that the median time to
15 publication of clinical trials funded by the US NIH and registered with ClinicalTrials.gov (and
16 completed by 31st December 2008) was 23.0 months. However, this is only the median of the trials
17 that published, not the whole cohort (i.e. the trials that were funded) and so it is underestimating the
18 time to publication. Funders and researchers should aspire to publish all of their research, so the time
19 taken for 50.0% of all funded studies to publish is the appropriate median time to publication.
20 Arguably, the 30.0 month publication rate may be the truly important measure of timeliness to
21 publication.
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24 It takes ~32.0 months for half of the clinical trials funded by the US NIH to publish; only 46.0% were
25 published within 30.0 months of trial completion, with an overall publication rate of 68.0%. In
26 comparison, the median time to publication of HTA Programme-funded trials is 24.0 months, 67.5%
27 publish by 30.0 months, and 93.7% publish overall. The *Health Technology Assessment* figures also
28 compare very favourably with results from industry sponsored trials; trials conducted by
29 GlaxoSmithKline in Spain between 2001 and 2006 had a publication rate of 61.0% and a median time
30 to publication of 28.4 months. However, it was not clear whether this was the median of the published
31 trials or of the funded ones.¹⁰ The median time to publication of more recent NIH clinical trials (those
32 with a ClinicalTrials.gov identifier, published during 2009 and indexed in MEDLINE) is 21.0 months,¹¹
33 but the study did not comment on how long it took for 50.0% of the funded trials to publish. Lastly,
34 68.0% of NIH-funded studies publish overall and 62.6% of HTA-funded primary research publishes
35 externally. This highlights the importance of the monograph series as it provides a means of
36 publication for those projects that would not otherwise reach the public domain.
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39 HTA-funded evidence syntheses are also produced in a timely manner, with a median time to
40 publication of 25.5 months and 65.0% of studies being published by 30.0 months (93.3% publishing
41 overall). In comparison, Cochrane reviews have a median time to publication of ~29.0 months, with
42 only 80.9% publishing in full after eight years of follow-up.
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45 **Implications**

46 The median time to publication in the monograph series and an external journal could only be
47 compared for primary research (as over half of the evidence syntheses do not have a recorded
48 external publication); here a monograph is produced nine months earlier. Publication rate, for both
49 types of research, was considerably higher in the monograph series than for other peer reviewed
50 biomedical journals. The shorter time to publication and high publication rate in *Health Technology*
51 *Assessment* is laudable; ensuring information from research is easily accessible and widely available
52 is important because it facilitates its use, increases its impact and consequently its value to society.
53 Unpublished data may also invalidate conclusions from meta-analyses, and systematic reviews.
54 These are not just a valuable source of information for health care professionals and researchers, but
55 definitive conclusions about an intervention also prevent putting more patients at risk in further
56 unneeded trials or depriving them of the correct treatment. Having *Health Technology Assessment* is
57 clearly important for dissemination of research to the public in a timely fashion and ensures that data
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3 are not lost as a result of publication bias. US federal requirements¹² call for “results of an Applicable
4 Clinical Trial of a drug, biologic, or device that is approved, licensed, or cleared by FDA must be
5 submitted by the Responsible Party no later than 12 months after the Completion Date”. There is an
6 important distinction between the user’s (HTA Programme, clinicians and patients, NICE, etc.)
7 perspective and the researcher’s perspective of the process. Once they have submitted the draft final
8 report, aside from editing the researcher may assume their task is finished, but the users are more
9 concerned with when the research is in the public domain.
10

11 **Conclusion and recommendations**

12 Research funded by the HTA Programme publishes in a timely fashion; where a comparison was
13 possible, time to publication was nine months shorter for a monograph than an external journal article
14 and publication rate was considerably higher in *Health Technology Assessment* than for other peer-
15 reviewed journals. HTA-funded trials publish more promptly than those funded by the NIH and
16 industry and HTA-funded evidence syntheses are produced sooner than Cochrane reviews. This
17 current study highlighted the importance of HTA Programme research being funded via a contract
18 (researchers are contractually obliged to publish their findings in full) as well as the value of *Health*
19 *Technology Assessment* and its rigorous editorial procedure.
20

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22 Recommendations include encouraging other funding organisations to make it a condition for their
23 investigators to publish final project results in full, within a set time, and to support this practice,
24 regardless of whether findings are significant or not. In the UK, the Health Research Authority (HRA)
25 is responsible for protecting and promoting the interests of patients and the public in health research.
26 It plays a key leadership role in promoting transparency and has made a number of commitments to
27 ensure the publication and dissemination of health research results.¹³
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29
30 Future work should investigate the time to publication for other funders and ways in which delays can
31 be reduced without compromising quality. Regardless of the funder, all trials should be registered and
32 the methods and results reported in full and in a timely fashion.
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34 **ACKNOWLEDGEMENTS**

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37 The authors would like to thank Sheila Turner for providing the reference numbers of the projects and
38 their publication date in the monograph series; Stephen Lemon for his advice about data extraction
39 from the NIHR research programmes database and Jo Merritt for sharing her data concerning authors
40 not reporting projects that publish in an external journal. We would also like to acknowledge the
41 Metadata team for providing their database and trial details used in the study.
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43

44 **COMPETING INTERESTS**

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

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4 This research was supported by the NIHR Evaluation, Trials and Studies Coordinating Centre through
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6 and do not necessarily reflect those of the Department of Health or of NETSCC.
7

8 **Contributors**

9 The study was designed by RM, M A-K, FC and AY. FC, AY, JG and M A-K performed data extraction,
10 FC and AY conducted the data analyses. FC drafted the manuscript, guided by M A-K, RM and AY.
11 All authors have read and approved the final manuscript.
12

13 **Data sharing statement**

14 There are no additional data available.
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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%)

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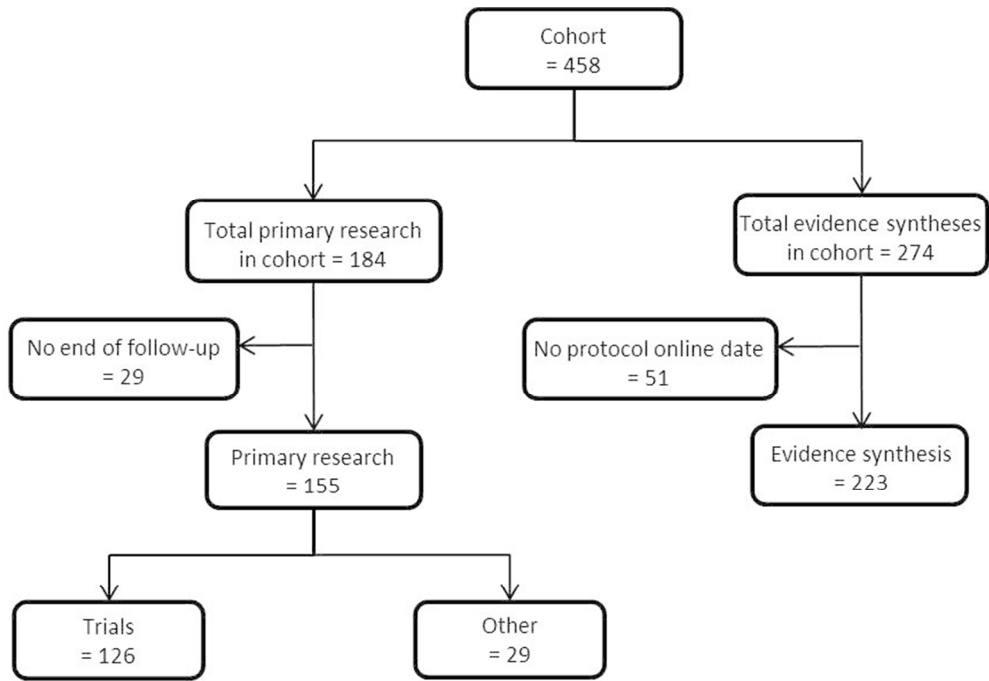


Figure 1: Flow diagram of projects in this study.
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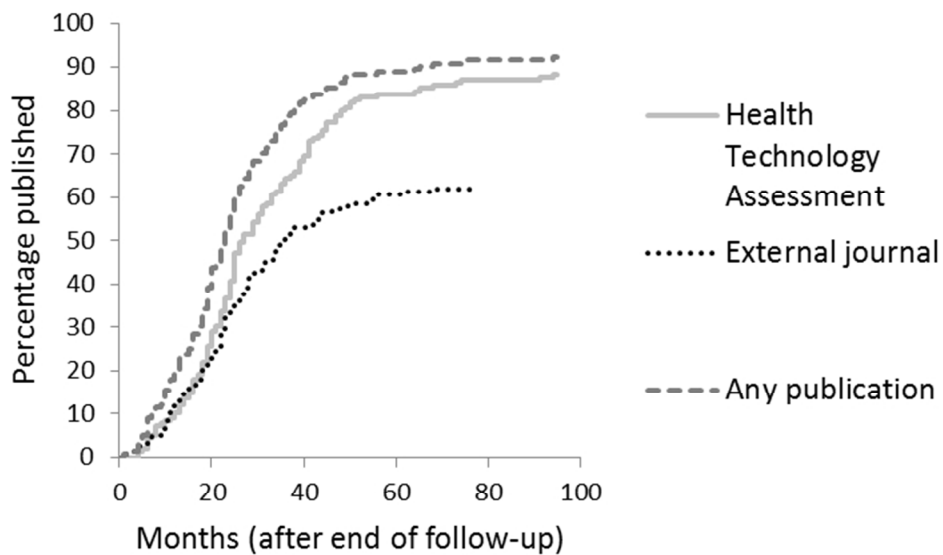


Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the Health Technology Assessment versus other peer reviewed biomedical journals and time to the first publication anywhere.
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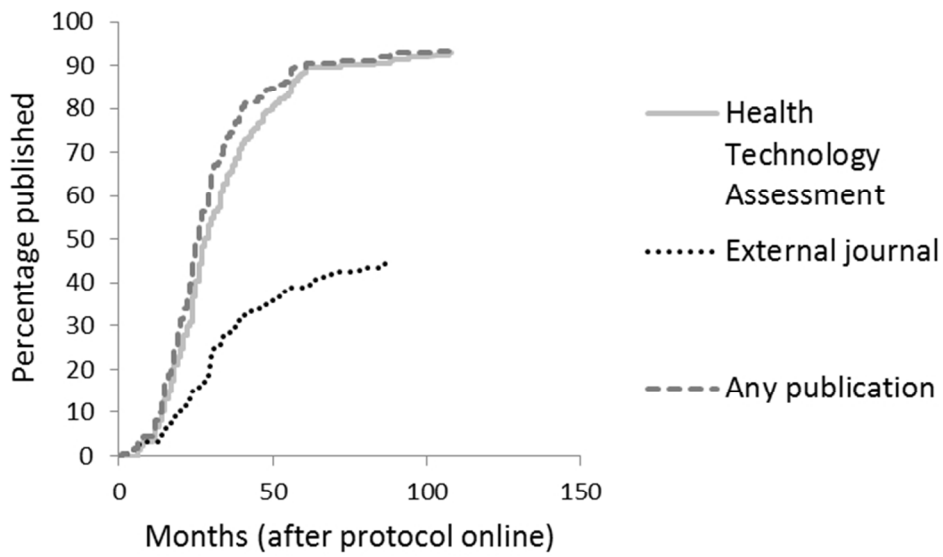


Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in Health Technology Assessment versus other peer reviewed biomedical journals and time to the first publication anywhere.
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Time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

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3 online. The *Health Technology Assessment* monograph (or draft final report or external publication if
4 the project did not have a published monograph) was hand-searched for the end of recruitment date
5 and length of follow-up in order to calculate the study conclusion date for the primary research
6 projects. We also hand searched the *Health Technology Assessment* journal website for the online
7 publication date of the first report for all projects in an external journal. We took a pragmatic approach
8 and excluded protocols, background papers and systematic reviews that may have been conducted
9 before the research began. We included the first report that used clinical data from the project, and
10 excluded cost-effectiveness analyses (unless the project report specifically stated that it was an
11 economic evaluation).
12

13 **Time to publication**

14 For primary research, the time to publication was determined by calculating the number of months
15 from when the study concluded (i.e. end of follow-up, using the same methodology as Ross *et al.*⁸) to
16 when the monograph was first published online and to when the first external publication was
17 available online. For evidence syntheses, we followed the protocol of Tricco *et al.*⁹ Time to publication
18 was measured as the number of months from when the protocol was first made available online to the
19 online publication date of the monograph and to the online availability of the study in an external
20 journal.
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23 Three researchers (FC, M A-K and JG) conducted data extraction for the primary research dataset
24 and any disagreement was resolved in discussion. Two researchers (FC and JG) extracted the data
25 for the evidence synthesis projects. Again, any disagreement was settled in discussion. In the case of
26 primary research, the first output registered was often the protocol or a background paper;
27 consequently, two researchers (AY and FC) hand-searched the HTA journal website to determine the
28 publication date of the first report from a project and this date was confirmed in discussion.
29

30 **Data analysis**

31 Kaplan-Meier survival curves were produced for primary research and evidence synthesis projects,
32 the percentage of HTA-funded studies published in the monograph series was compared to other
33 peer reviewed journals. We calculated the median (time for 50.0% of funded studies to publish) time
34 to publication in *Health Technology Assessment*, elsewhere and for the first output for primary
35 research, trials, and evidence syntheses.
36

37
38 Ross *et al.*⁸ have emphasised the need for timely publication and have stated a cut-off of 30.0 months
39 for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at
40 30.0 months and the total percentage published, both in the monograph series and elsewhere.
41

42 Minitab was used to establish distribution of the data subsets (Anderson-Darling normality test) and
43 the interquartile ranges (IQR) were also determined. Any statistical difference between the median
44 times to publication was established using the Mann-Whitney U test.
45

46 **RESULTS**

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48 We identified 458 projects for inclusion in our analyses (figure 1).
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51 Figure 1: Flow diagram of projects in this study.
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54 INSERT FIGURE 1 HERE
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56 **Primary research**

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3 The primary research subset contains 184 projects; however, 29 of these did not state an end of
4 recruitment date, or it was not possible to determine length of follow-up. Consequently, it was not
5 possible to calculate the last point of data collection for 15.8% of HTA Programme-funded primary
6 research, even though many of these studies do have a publication.
7

8 Of the 155 primary research projects with a completion date, the median time to any publication (time
9 for 50% of the funded studies to publish) was 23.0 months (IQR 19.0 months), 26.5 months (IQR 20.5
10 months) for publication as a monograph in *Health Technology Assessment* and 35.5 months (IQR
11 19.0 months) for publication in any other external journal, but this difference was not statistically
12 significant ($P=0.149$).
13

14 Sixty-nine per cent of all primary research funded by the HTA Programme is published by 30.0
15 months, but only 56.1% of monographs are produced within this time. Limiting the analysis to trials,
16 directly comparable to the work of Ross *et al.*⁸, 67.5% publish within 30.0 months and have a median
17 time to publication of 24.0 months (IQR 15.3 months) (table 1). Overall publication rates are 92.9% for
18 any publication, 88.4% in the monograph and 62.6% in an external journal (table 1, figure 2).
19

20 INSERT TABLE 1 HERE
21

22 Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion
23 date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed
24 biomedical journals and time to the first publication anywhere.
25

26 INSERT FIGURE 2 HERE
27

28 Evidence synthesis

29 Of the 274 evidence syntheses, the database did not record a protocol online date for 51 (18.6%)
30 projects and so these could not be included in further analyses. Of the remaining projects, the median
31 time to any publication was 25.5 months (IQR 16.0 months) and the median time to publication of a
32 monograph is 28.0 months (IQR 19.0 months) but, unlike primary research, fewer than 50.0% of
33 evidence synthesis projects publish in other peer-reviewed journals (table 2, figure 3), so it was not
34 possible to test for statistical significance. Evidence syntheses publish in a timely fashion, with 65.0%
35 of studies publishing within 30.0 months and 93.3% publish overall.
36

37 INSERT TABLE 2 HERE
38

39 Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online
40 date). Publication rate in the *Health Technology Assessment* monograph versus other peer reviewed
41 biomedical journals and time to the first publication anywhere.
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43 INSERT FIGURE 3 HERE
44

45 DISCUSSION

46 Using the standard of Ross *et al.*,⁸ HTA-funded research publishes promptly; 69.0% of primary
47 research projects publish by 30.0 months, with a median time to publication of 23.0 months. Sixty-five
48 per cent of evidence synthesis projects publish by 30.0 months and the median time to publication
49 was 25.5 months.
50

51 Strengths and limitations

52 The main strength of this study is that it involves a large cohort, representing almost 20 years of
53 research funded on behalf of the NHS. This report complements previous work which has shown that
54 98.0% of HTA projects funded since 2002 will publish a monograph.⁷ This project used a subsample
55 of the dataset of Turner *et al.*⁷ with the intention to determine the time to publication of all of the
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3 primary research and evidence synthesis projects that do publish. However, a major limitation of this
4 project is the amount of data missing from the analyses. It was not possible to determine the end-of-
5 follow up for over 15.0% of primary research projects, and over 18.0% of the evidence synthesis
6 studies did not have a recorded protocol online date, so they were not included in the analyses. Since
7 data-recording was poorer in earlier years (unpublished data), we have disproportionately excluded
8 more of the older projects. Consequently, since older projects generally took longer to publish
9 (unpublished data), we may be underestimating how long HTA-funded studies take to publish overall.
10

11 This project relied heavily on data from the NIHR research programmes database and the *Health*
12 *Technology Assessment* journal website to determine if a study has published elsewhere, which in
13 turn depends on self-declarations from the principle investigators (PIs), as per contractual obligations.
14 Preliminary work in an internal NETSCC report found that PIs were under-reporting their external
15 publications by 15.8% and so the overall external publication rate is likely to be higher and we are
16 overestimating the median time to publication in an external journal. In addition, the under-reporting
17 may also be affecting the “Any publication” Kaplan-Meier curve and so influencing the median time to
18 the first publication as well.
19

20 21 **Comparison with other studies**

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

32 It takes ~32.0 months for half of the clinical trials funded by the US NIH to publish; only 46.0% were
33 published within 30.0 months of trial completion, with an overall publication rate of 68.0%. In
34 comparison, the median time to publication of HTA Programme-funded trials is 24.0 months, 67.5%
35 publish by 30.0 months, and 93.7% publish overall. The *Health Technology Assessment* figures also
36 compare very favourably with results from industry sponsored trials; trials conducted by
37 GlaxoSmithKline in Spain between 2001 and 2006 had a publication rate of 61.0% and a median time
38 to publication of 28.4 months. However, it was not clear whether this was the median of the published
39 trials or of the funded ones.¹⁰ The median time to publication of more recent NIH clinical trials (those
40 with a ClinicalTrials.gov identifier, published during 2009 and indexed in MEDLINE) is 21.0 months,¹¹
41 but the study did not comment on how long it took for 50.0% of the funded trials to publish. Lastly,
42 68.0% of NIH-funded studies publish overall and 62.6% of HTA-funded primary research publishes
43 externally. This highlights the importance of the monograph series as it provides a means of
44 publication for those projects that would not otherwise reach the public domain.
45
46

47 HTA-funded evidence syntheses are also produced in a timely manner, with a median time to
48 publication of 25.5 months and 65.0% of studies being published by 30.0 months (93.3% publishing
49 overall). In comparison, Cochrane reviews have a median time to publication of ~29.0 months, with
50 only 80.9% publishing in full after eight years of follow-up.
51

52 53 **Implications**

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

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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).

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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.

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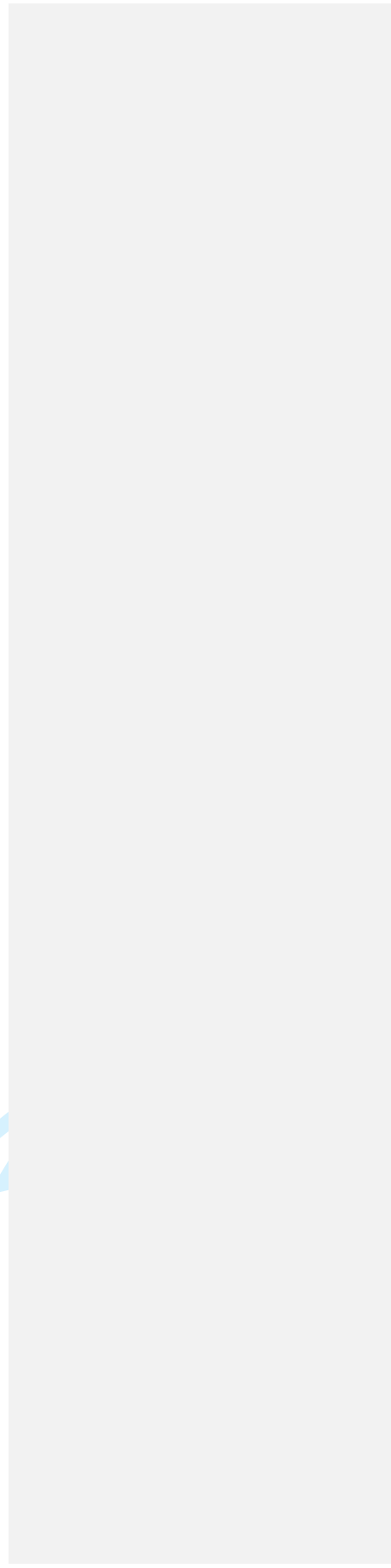
Data sharing statement

There are no additional data available.

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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.

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Strengths and limitations of this study

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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.

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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:

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

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

21 **Time to publication**

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

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

35 **Data analysis**

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

41 Ross *et al.*⁸ have emphasised the need for timely publication and have stated a cut-off of 30.0 months
42 for trials funded by the NIH. We also calculated the percentage of HTA-funded studies published at
43 30.0 months and the total percentage published, both in the monograph series and elsewhere.

44
45 Minitab was used to establish distribution of the data subsets (Anderson-Darling normality test) and
46 the interquartile ranges (IQR) were also determined. Any statistical difference between the median
47 times to publication was established using the Mann-Whitney U test.

48 **RESULTS**

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

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52 Figure 1: Flow diagram of projects in this study.

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11 Primary research

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

16 Of the 155 primary research projects with a completion date, the median time to any publication (time
17 for 50% of the funded studies to publish) was 23.0 months (IQR 19.0 months), 26.5 months (IQR 20.5
18 months) for publication as a monograph in *Health Technology Assessment* and 35.5 months (IQR
19 19.0 months) for publication in any other external journal, but this difference was not statistically
20 significant (P=0.149).

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

26
27 INSERT TABLE 1 HERE

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

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32 INSERT FIGURE 2 HERE

33 Evidence synthesis

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

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42 INSERT TABLE 2 HERE

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

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48 DISCUSSION

49 Using the standard of Ross *et al.*,⁸ HTA-funded research publishes promptly; 69.0% of primary
50 research projects publish by 30.0 months, with a median time to publication of 23.0 months. Sixty-five
51 per cent of evidence synthesis projects publish by 30.0 months and the median time to publication
52 was 25.5 months.
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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 requirements¹² 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.^{12,3}

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.

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ACKNOWLEDGEMENTS

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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).

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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%)

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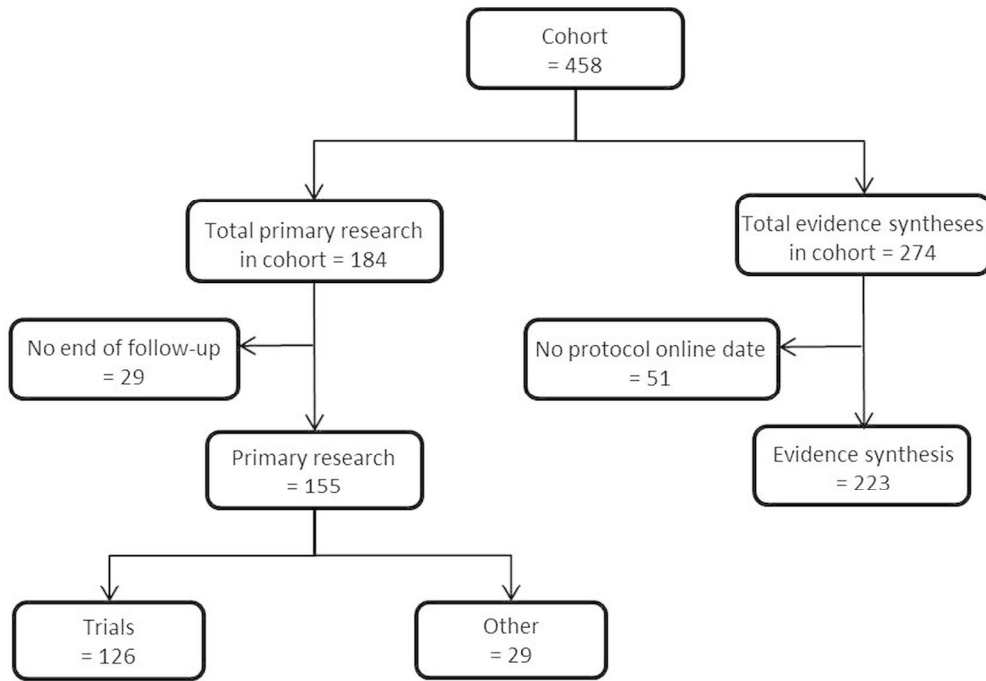


Figure 1: Flow diagram of projects in this study.
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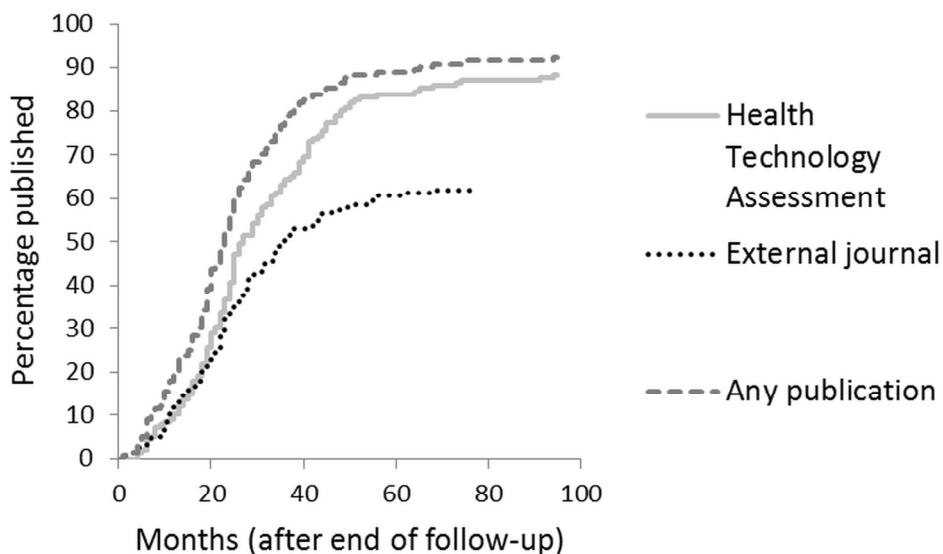


Figure 2: Cumulative percentage of HTA-funded primary research (studies with a study completion date). Publication rate in the Health Technology Assessment monograph series versus other peer reviewed biomedical journals and time to the first publication anywhere.
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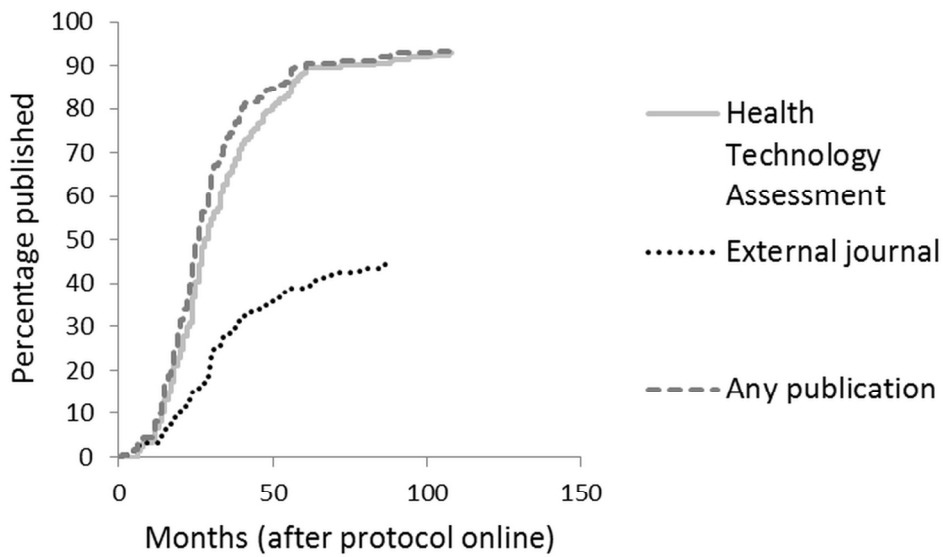


Figure 3: Cumulative percentage of HTA-funded evidence syntheses (studies with a protocol online date). Publication rate in the Health Technology Assessment monograph series versus other peer reviewed biomedical journals and time to the first publication anywhere. 150x90mm (300 x 300 DPI)

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