Warwick Evidence annual report for period 2021/2022

1. Summary of Contract Activity

Brief summary of activity outlining any problems encountered in filling contract capacity. Please do not include the full list of projects undertaken as we already have them on record.

Following the disruption of 2020-21, Warwick Evidence, the National Institute for Health and Care Research Evidence Synthesis Programme (NIHR ESP) and the National Institute for Health and Care Excellence (NICE) have been in a period of recovery and catch up. We have seen the restart and introduction of Health Technology Assessment (HTA) topics which were paused during the pandemic. This move away from therapeutically-critical guidance (e.g., cancer appraisals) increased the workload of all involved, and required more flexibility from Warwick Evidence than ever before.

As a group, we are contracted to deliver **15 TAR units** each year (1 unit = 1 short report, 2.67 units = 1 long report). During TAR year 2021-22 we completed **74% of our contracted activity**, representing work on 13 individual appraisals. NIHR ESP have a target to allocate us at least 80% of contracted capacity. As a senior team, we are pleased with our achievements considering the significant disruption to the timelines of some of the projects.

Include here a full account of additional work requests allocated to the period under review using the following table:

Additional work requests

Four of the 13 projects worked on in 2021/22 (31%) required work that was over and above the standard contracted activity. Previously, a request such as this for additional units happened occasionally. Now we are seeing it as part of standard practice. This reflects the increasing complexity of the HTA work and companies seeking to undergo appraisal earlier in the process than before and updating their submission mid-appraisal, i.e., when their data is are immature, or marketing authorisation has not yet been awarded.

For example, when appraising *Ixazomib citrate with lenalidomide and dexamethasone, post prior therapy for relapsed, refractory multiple myeloma* the company decided that they had made a mistake in their analysis which required a four-month pause and entire new submission. This topic was consequently allocated one whole unit rather than 0.5 and we are still anticipating it returning a third time.

During 2021-22 we requested an additional 3.09 units. These are detailed in Error! Not a valid bookmark self-reference.

Table 1: Additional capacity requests 2021-22

Project number and title	**Type of project** (e.g. STA)	**Type of Additional Work** (please see guidance below)	**Brief description of work undertaken**	**Extra units approved** (e.g. 0.1)
133048 – Inclisiran for primary, high cardiovascular risk hypercholesterolemia (ID1647)	STA	Analysis of new data New critique of model Simple PAS	Additional evidence submitted following technical engagement Additional evidence submitted following technical engagement closure/call 4 additional meetings with NICE technical teams Check subgroup analyses Update PAS	0.32
133547 - Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes [ID3957]	MTA	Other	Restart agreed - critique undertaken up to pause in Sept 2021	1.7
131645 - Olaparib for previously treated, hormone-relapsed metastatic prostate cancer (ID1640)	STA	2nd AC attendance Analysis of new data Other	AC2, 2x additional analysis of information / data provided by company after AC1, additional FAC check, NICE additional requests for PMB meeting prior to AC2.	0.43
Ixazomib citrate with lenalidomide and dexamethasone, post prior therapy for relapsed, refractory multiple myeloma (CDF review of TA505) (ID1635)	CDF	Other	Full additional critique - following company errors, substantial rewrite was required. Complete re-work of original appraisal undertaken.	0.5

Project number and title	**Type of project** (e.g. STA)	**Type of Additional Work** (please see guidance below)	**Brief description of work undertaken**	**Extra units approved** (e.g. 0.1)
Lisocabtagene maraleucel for treating large B-cell lymphoma after at least 2 therapies (ID1444) Part 2	STA	Analysis of new data Simple PAS	Additional analysis over the buffer resource at Technical Engagement New PAS provided just before AC1	0.14

'Type of additional work' guidance, please use one of the following:

- 2nd AC attendance
- 3rd AC attendance
- 4th AC attendance
- 5th AC attendance plus
- Analysis of new clinical data
- Critique new model (simple) *e.g. same model with new parameters*
- Critique new model (complex) *e.g. attempting to re-build the model using a different approach*
- Simple PAS *e.g. straight forward discount*
- Complex PAS *e.g. one that requires monitoring of patients*
- Appeal
- Other – provide details in the 'Brief description of work undertaken' column

Please include details of the additional work under the 'Brief description of work undertaken' column.

2. Impact

Impact is defined as the demonstrable contribution that research makes to society and the economy, of benefit to individuals, organisations, and nations. Taking this definition into account, provide a list of 3 outputs completed during the report period that YOU consider the most impactful and briefly describe why (100 words max.)

Project number, title and why
129546 – Screening of endometrial cancer for Lynch syndrome **Stinton C, Fraser H, Al-Khudairy L, Court R, Jordan M**, Grammatopoulos D**, Taylor-Phillips S**. Testing for lynch syndrome in people with endometrial cancer using immunohistochemistry and microsatellite instability-based testing strategies - A systematic review of test accuracy. Gynecol Oncol. 2021;160(1):148-60.

129546 – Screening of endometrial cancer for Lynch syndrome continued

Lynch syndrome is an inherited genetic condition that is associated with an increased risk of cancer, including endometrial cancer. Various new testing has become available for detecting Lynch syndrome, which could inform clinical decisions for women diagnosed with endometrial cancer and their relatives. However the testing was not routinely offered. Our work was the first systematic review to comprehensively evaluate relevant studies, and was the main piece of evidence that directly informed NICE's Diagnostic guidance (DG42), which recommended offering the test to all people who are diagnosed with endometrial cancer and has led to direct change in UK clinical practice.

16/108/09 - Pembrolizumab after platinum chemotherapy for urothelial cancer (ID1019)

17/156/04 - Venetoclax in combination with rituximab for treating relapsed or refractory chronic lymphocytic leukaemia (ID1097)

17/56/03 - Pertuzumab for the adjuvant treatment of HER2-positive breast cancer (ID1192)

127889 Dacomitinib for untreated EGFR-positive non-small-cell lung cancer (ID1346)

Gallacher D, Stallard N, Kimani P**.** Extrapolating parametric survival models in Health Technology Assessment: A Simulation Study Medical Decision Making 41 (1), 37-50.

and

Gallacher D, Kimani P**,** Stallard N**.** Extrapolating Parametric Survival Models in Health Technology Assessment Using Model Averaging: A Simulation Study Medical Decision Making 41 (4), 476-484.

These papers address the important gap in the evidence by demonstrating the utility of current methods for estimating treatment benefit from follow-up of clinical trials. Extrapolating time-to-event data using parametric survival models is common practice when assessing health technologies, yet no work existed to demonstrate whether this is a reliable method of predicting treatment benefit. These papers simulated follow-up from four trials that were pivotal in contributing evidence to a NICE technology appraisal, and found bias associated with selecting the wrong parametric model and demonstrated potential benefit of model averaging when data are immature.

3. Intellectual Property (IP)

Please list TAR projects that produced IP and what the IP is e.g. model.

SurvExtrap is a tool that estimates the parameters of common parametric survival models which interpolate key survival time co-ordinates specified by the user, which could come from external trials, real world data or expert clinical opinion. SurvExtrap provides a solution to the problem when regular parametric models do not result in plausible extrapolations, or fully explore scenarios of uncertainty over future efficacy.

It was inspired by ID1019: Pembrolizumab after platinum chemotherapy for urothelial cancer, where the extrapolations of overall survival disagreed with the long term estimates provided by CRUK. SurvExtrap provides a simple way of obtaining a parametric model that is consistent with both short term trial data and external data.

4. Organisational Structure

Provide an updated list of team members detailing roles, and specialties. Include team members that only work occasionally. Outline any changes to staff, use of subcontractors for TAR contract activity, and anything else considered relevant here.

Name	Role(s)	Core or Ad Hoc	Full Time Equivalent (FTE)
Dr Amy Grove	Director, Lead, Clinical Effectiveness	Core	0.4
Dr Lena Al-Khudairy	Associate Prof, Lead, Clinical Effectiveness	Core	0.7
Dr Dan Todkill	Clinical Academic oversight, Quality Assurance	Core	0.2
Prof Sian Taylor-Phillips	Diagnostics Academic advisor	Core	0.1
Prof Jason Madan	Health Economics Academic advisor	Core	0.1
Dr Chris Stinton	SRF, Lead, Clinical Effectiveness / Diagnostics	Core	0.8
Dr Yen-Fu Chen	Assoc Prof, Lead, Clinical Effectiveness	Core	1.0
Dr Felix Achana leaving April 2022	Assoc Prof Health Economist, Lead	Core	0.6
Dr Ewen Cummins	Health Economist	Subcontract	0.75
Mr Peter Auguste	RF, Health Economist	Core	1.0
Dr Mandy Maredza	SRF, Health Economist	Core	1.0
Ms Mary Jordan	RF, Health Economist	Core	1.0
Dr Karoline Freeman	SRF, Clinical Effectiveness/Diagnostics. Currently out on *22-23 NIHR methods Fellowship*	Core	-
Dr Asra Asgharzadeh	RF, Clinical Effectiveness	Core	1.0
Dr Hesam Ghiasvand	RF, Health Economist	Core	1.0

Name	Role(s)	Core or Ad Hoc	Full Time Equivalent (FTE)
Ms Iman Ghosh	RA, Clinical Effectiveness	Core	1.0
Ms Anna Brown	Information Specialist	Core	0.6
Ms Rachel Court	Information Specialist	Core	0.7
Mr Mubarak Patel	RA, Statistician	Core	1.0
Mr Daniel Gallacher	Assistant Prof, Lead, Statistics	Core	1.0
Mrs Sarah Abrahamson	Research Centre Manager	Core	0.5
Mr Nick Sahunta	Project Officer	Core	0.92
Ms Kate Evans Leaving April 2022	Project Administrator / Clinical Effectiveness Reviewer	Core	0.4
Dr Saran Shantikumar	Quality Assurance	*Ad-Hoc*	-
Dr Jill Colquitt	Clinical Effectiveness Reviewer	*Ad-Hoc*	-
Dr Emma Loveman	Clinical Effectiveness Reviewer	*Ad-Hoc*	-
Dr Wendy Knerr	Clinical Effectiveness Reviewer	*Ad-Hoc*	-
Dr Alex Tsertsvadze	Clinical Effectiveness Reviewer	*Ad-Hoc*	-
Dr Christine Clar	Clinical Effectiveness Reviewer	*Ad-Hoc*	-
Dr Toyin Lamina	Clinical Effectiveness Reviewer	*Ad-Hoc*	-
Dr Jacoby Patterson	Clinical Effectiveness Reviewer	*Ad-Hoc*	-
Dr Angela Noufailly	Medical Statistician	*Ad-Hoc* WMS	-
Dr Martin Connock	Medical Statistician	*Ad-Hoc*	-
Dr Emanuela Castelnuovo	Health Economist	*Ad-Hoc*	-
RA = Research Associate, RF = Research Fellow, SRF = Senior Research Fellow			

Vacancies during reporting period

Detail all staff vacancies during reporting period.

Vacancy Duration	Role(s)	Core or Ad Hoc	Full Time Equivalent (FTE)
2 months	Project Manager	Core	0.92

5. NICE

Brief summary of engagement with NICE, outlining any issues, concerns with current and new processes, including communications with NICE technical teams and any other issues you might consider relevant to include here.

Warwick Evidence continues to work closely with NIHR ESP and NICE. We were pleased to receive positive feedback from both organisations in terms of our work output and flexibility in the work programme for the 2021-22 TAR year during the annual contract review meeting held 25th March 2022.

New NICE methods and process

NICE have undergone a huge programme of work to update the methods and process of their technology appraisals. The changes aim to streamline and improve the way HTA is performed. However, this again generates upheaval for the team as we learn another new way of working. The old 'new TA process', and the 'interim TA' process introduced between 2019-2021 will be removed. NICE now have a single guidance development manual, covering:

- diagnostic assessment
- highly specialised technologies
- medical technologies evaluation
- technology appraisal
- new topic selection manual.

Some of the changes made to how health technologies are evaluated include:

- More weight given to health benefits in the most severe conditions (known as a severity modifier)
- New approaches to the evidence considered in our assessments, for example, real world evidence
- More flexibility for NICE's independent committees in cases when generating evidence is difficult
- New criteria for treatments for very rare diseases in our Highly Specialised Technologies (HST) Programme
- Aligned the methods and processes across different types of evaluations (e.g., drugs and diagnostics).

As a team, we have had little involvement in the production of these updated methods and processes and are learning the changes as they are implemented. We consider that the methods and process guide does not provide the methodological detail required for TAR teams to perform appraisals. We anticipate an updated scope of work document from ESP TAR.

Diagnostic reviews

In 2021-22 we saw a slight increase in the number of Diagnostic Appraisal Reviews (DARs) (long reports) coming through the NICE process. We welcomed the opportunity to undertake more DARs as they generate academic output for the team. However, NICE has raised concerned with ESP TAR regarding the quality of DAR reports. Earlier in the year TAR Directors were called to a meeting with NIHR ESP to review the feedback from NICE and to facilitate the best way forward.

It was agreed that a subset of the nine TAR teams would be allocated DARs for the next few years – to match demand for DARs and to ensure quality of the reviews. We were pleased to be one of the teams who will be allocated DARs (1-2 per year). In developing the new contract application, and over the last year, we have focused on the capacity development of the team to allow us to perform two DARs in parallel. We recognise the national shortage in reviewers and economists who can undertake reviews of diagnostic technologies, therefore are working with Warwick Screening to build our in-house skills.

6. NIHR

Brief summary of engagement with NIHR, outlining any issues, concerns with current and new processes, including communications with the NIHR team and any other issues, you might consider relevant to include here.

InterTASC and Annual Contract Review

Warwick Evidence are current Chairs of InterTASC (InterTechnology Appraisal Support Collaboration) (Sept 2020-Sept 2022) which represents all the ESP TAR Technology Appraisal teams across the country and is one of the largest collaborations of HTA bodies internationally.

We are responsible for coordinating the twice yearly all TAR meeting, liaising with NICE and ESP TAR on behalf of all TAR teams and reporting to the Department of Health and Social Care (DHSC) at the Annual Contract Review (ACR) meeting.

At the most recent ACR (March 2022) Dr Kay Pattison OBE, Head of Research Contracting at the DHSC at the NIHR informed the TAR teams that ACR will not be part of the next contract. This meeting will be replaced with smaller one-to-one meetings between individual teams and the ESP TAR senior team. We welcome this change, as we believe more personalised feedback will support our development.