NIHR | National Institute for Health Research

EVIDENCE SYNTHESIS PROGRAMME

Annual Report

01 April 2020 - 31 March 2021

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Abbreviations

ACD	Appraisal Consultation Document
CDF	Cancer Drug Fund
CHEW	Centre for Health Economics at Warwick
DAR	Diagnostic Assessment Reviews
DSU	Decision Support Unit
ERG	Evidence Review Group
ESP TAR	Evidence Synthesis Programme Technology Assessment Research
FAD	Final Appraisal Determination
FTA	Fast Track Appraisal
HTA	Health Technology Assessment
InterTASC	Independent Technology Appraisal Support Collaboration
MB ChB	Bachelor of Medicine, Bachelor of Surgery
MTAs	Multiple Technology Appraisals
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NIHR ESP	National Institute for Health Research Evidence Synthesis Programme
PPIE	Patient and Public Involvement and Engagement
STA	Single Technology Appraisal
TAR	Technology Assessment Research
TE	Technical Engagement
CHEW	Centre for Health Economics at Warwick
WCTU	Warwick Clinical Trials Unit
WEST	Warwick Evidence Senior Team
WMS	Warwick Medical School

1 Summary of Contract Activity

This year has been like no other for all concerned. The uncertainty of the pandemic has required a change in our working patterns. It has led to a recognition of the need for inventive ways to harness opportunities, whilst adjusting to the new realities and challenges which we faced including the sudden closure of the University, virtual NICE committee meetings and the call to work from home. Whilst this has unsurprisingly impacted our team, it has not impacted our ability to deliver our work on time and target, due to our structured project management, robust organisational development, and team dedication. Our operational infrastructure has withstood the challenges faced since March 2020 and enabled us to complete all the allocated projects on time. The approach NICE took during the pandemic meant that since mid-March 2020:

- We saw pausing and rescheduling of technology appraisals and appraisals committee meetings
- NICE prioritised topics to best support the health and care system; and
- NICE put greater focus on supporting a new series of rapid COVID-19 related guidelines, and other therapeutically critical guidance (e.g., cancer appraisals).

Autumn 2020 saw the restarting of regular NICE committees with therapeutically critical appraisals and paused appraisals continuing in parallel, increasing pressure on the NICE teams, committee members and TAR teams. In Spring 2021, we witnessed a slow return to normal with continuing disruption, and the need for NICE to continue and review plans.

Supplementary to the TAs conducted for NICE, we have collectively published **39 peer reviewed** journal papers. Our team have attended a range of **virtual training courses and conferences** and have contributed to virtual and in-person teaching activities within Warwick Medical School (WMS). This includes a new undergraduate BSc Health and Medical Sciences, the Masters in Public Health and the postgraduate MB ChB course, as well as courses and lectures delivered within and external to the University. We were also delighted to support the following staff towards **academic promotions** during the past year:

- Dr Amy Grove – from Assistant Professor to Associate Professor and from Co-Director to Director of Warwick Evidence.
- Professor Sian Taylor-Phillips from Associate Professor to Professor.
- Professor Ola Uthman from Associate Professor to Professor.
- Ms Hannah Fraser from Research Assistant to Research Project Manager in Warwick Screening.

1.1 Additional Activities, Developments and Improvements

As a successful group of academic methodologists and health services researchers, members of the team have been engaged in a multitude of other research, teaching and impact activities. We have provided some examples below:

- Warwick has been appointed to **chair of InterTASC** (Dec 2020 – Dec 2022).
- Members of Warwick Evidence (Grove, Clarke, Taylor-Phillips, Freeman, Zanganeh, Osokogu, Court, Brown) produced **two systematic reviews in response to COVID-19.**
- Members of the team are collaborating with colleagues from Warwick Clinical Trials Unit (WCTU)[1] and WMS on **research surrounding COVID-19**.
- Professor Aileen Clarke, Professor Sian Taylor-Phillips, Dr Dan Todkill, Dr Chris Stinton, Dr Felix Achana, Dr Amy Grove, Dr Paul Sutcliffe, Mr Peter Auguste, Dr Mandana Zanganeh, Dr Hema Mistry and Dr Lena Alkhudairy all supervise students at either **Masters** or **PhD level**.
- Dr Felix Achana, Dr Paul Sutcliffe, and Dr Amy Grove have two **PhD topics associated with the work of Warwick Evidence**:
    - Enabling patient access to new drugs within the NHS: a mixed methods study to assess the impact of research conducted by Technology Assessment Review teams in the UK
    - Scoping the potential for organ donation following cardiac arrest in the UK.
- Staff in Warwick Evidence and Warwick Screening continue to lead and support systematic reviews for the National Screening Committee/Public Health England. These include:
    - Newborn screening for Tyrosinaemia type 1: extension work
    - Hereditary Haemochromatosis in Adults
    - Artificial Intelligence in Screening
    - Systematic review of screening for Group B streptococcus in pregnancy
    - Informed Choice Standards in Screening
- Warwick Evidence staff have two research collaborations with WCTU via the **NIHR HTA Evidence Synthesis researcher led programme:**

[1] Warwick Clinical Trial Unit (WCTU) is an award-winning clinical trials unit based at Warwick Medical School. The Unit was established in 2005 and in 2007, received full registration status from the UK Clinical Research Collaboration. It is an interdisciplinary Unit with collaboration between clinical trialists, statisticians, economists, clinical experts and project managers. The Unit specialises in trials investigating complex health states and interventions and has expertise in both designing and conducting trials.

- Dr Hema Mistry, Dr Felix Achana, Dr Amy Grove and Mrs Anna Brown “What is the comparative clinical and cost-effectiveness of pharmacological treatments for adults with chronic migraine”.
- Dr Amy Grove, Dr Yen-Fu Chen, Prof Ola Uthman and Mrs Rachel Court “Perioperative Oxygen Therapy: An overview of systematic reviews and meta-analyses”.

1.2 Patient and Public Involvement and Engagement (PPIE)

Over the last year as part of the retendering process, Warwick Evidence has been in discussions with Professor Sophie Staniszewska and Dr Magdalena Skrybant about how we might explore PPIE involvement in work undertaken for NICE. Warwick Evidence welcomes the engagement of patient and public contributors but have come up against several barriers as to how we might move this forward. As a first step, we consider PPIE would contribute to or long reports (e.g., MTAs and DARs). The welcomed increase in DARs/MTAs has enabled us to invite contributors and we are pleased that the current MTA (Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes [update of DG2]) has an active PPIE contributor.

1.3 Additional Work Request

During 2020-2021 we have requested the additional units listed in Table 1 for work undertaken outside of the contract unit allocation.

Table 1. Additional Unit Allocation

Project number and title	TA type	Type of Additional Work	Brief description of work undertaken	Extra units
130960 Encorafenib in combination with cetuximab and / or binimetinib for BRAF-mutant metastatic colorectal cancer [ID1598]	STA	Analysis of new clinical data and critique of new model (simple) during and after the stage of technical engagement	- Critique of company's response to TE, which included new clinical data and new model (simple) - Critique of company's response to ACD, which included new clinical data and new model (simple) - Upon NICE's request (following the company's revision of patient access scheme), additional cost-effectiveness analyses conducted prior to the 2nd Appraisal Committee meeting	0.4
132231 Lisocabtagene maraleucel for Treating large B-cell lymphoma after at least 2 therapies [ID1444]	STA	ERG was working on the STA until two days before the report due date and the work was suspended	- Attendance at meetings with NICE and the company - Clarification questions formulated - Further questions formulated to address the limited responses received from the company - Clinical and cost effectiveness sections were written using information available - Responses from the company and a new data-cut of the pivotal trial anticipated, with neither arriving by the deadline in mid-February	1
128899 Urothelial cancer – pembrolizumab (previously treated advanced or metastatic) NICE appeal. (CDF Review TA519) [ID1536]	CDF	Appeal meeting advice and attendance	- Previous reports, company submissions, ACDs and FADs revisited. A comprehensive report was completed and advice provided to NICE for the appeal meeting. Three preparation meetings and a training meeting were attended	0.1
128899 Urothelial cancer – pembrolizumab (previously treated advanced or metastatic) (CDF Review TA519) [ID1536]	CDF	Following on from appeal, in addition to attending meetings, ERG took on further analyses and additional Appraisal Committee meeting preparation	- Review of new submission and evidence - Attendance at additional meetings and addressing correspondence - Further analyses	0.4
130526 Brolucizumab for wet age-related macular degeneration [ID1254]	STA	Analysis of new clinical data, and	- Following factual accuracy check (FAC), the company submitted additional comments on ERG's model assumptions, data from a new	0.3

		critique of new model (simple) e.g. same model with new parameters	expert survey, additional scenario analyses and an updated price for one of the comparators (manufactured by the same company) during technical engagement, which required ERG's critique and a re-run of ERG's analyses. The FTA was subsequently suspended due to the pandemic but the ERG undertook tasks below before the Appraisal Committee meeting finally took place on 10 November 2020: - Checked/ unmarked some AIC marking and new information on emerging adverse events after receipt of an update from the company, and responded to further queries on modelling from NICE technical team in May 2020 - Re-ran ERG analyses due to a change in price for another comparator, updated ERG report to reconcile changes made after FAC and answered further queries from NICE technical team in June 2020; - Responded to an additional FAC from the company for the updated ERG report and revised the report in July 2020; and - Re-ran ERG analyses again to update confidential PAS appendix in October at NICE's request due to a change in preferred confidential price to be used.	
131645 Olaparib for previously treated, hormone-relapsed metastatic prostate cancer [ID1640]	STA		Further work undertaken included: - analysis of knowledge management data and quality of life, data, etc, and analysis and incorporation into economic model. - several rounds of clarification and appraisal of new target group - RPSFTM adjustment: with and without re-censoring - full further assessment of clinical and cost effectiveness given company resubmission in TE response - Further rounds of clarification due to incomplete data - Additional requests from NICE for extra PMB and information due to new technical team	1

2 Impact

Below we list publications from the TAR work and work completed by staff funded or part funded by Warwick Evidence during the financial year 01 April 2020 to 31 March 2021. Warwick Evidence staff are highlighted in **bold**. No conference presentations were delivered in the 2020-2021 year.

2020

1. Ayorinde A, Mannion R, Song F, Skrybant F, **Chen Y-F.** Publication and related bias in quantitative health services and delivery research: a multimethod study. Health Services & Delivery Research; 2020;8:33.
2. Aguiar M**, Andronis L,** Pallan M, Högler W, Frew E. The economic case for prevention of population vitamin D deficiency: a modelling study using data from England and Wales. European journal of clinical nutrition. 2020;74(5):825-33.
3. Aguiar M, **Andronis L**, Pallan M, Högler W, Frew E. Micronutrient deficiencies and health-related quality of life: the case of children with vitamin D deficiency. Public health nutrition. 2020;23(7):1165-72.
4. Ahmed SAKS, Ajisola M, Azeem K, Bakibinga P, **Chen Y-F,** Choudhury NN, et al. Impact of the societal response to COVID-19 on access to healthcare for non-COVID-19 health issues in slum communities of Bangladesh, Kenya, Nigeria and Pakistan: results of pre-COVID and COVID-19 lockdown stakeholder engagements. BMJ Glob Health. 2020;5(8).
5. Alhodaib HI, Antza C, Chandan JS, Hanif W, Sankaranarayanan S, **Sutcliffe P.** Mobile Clinical Decision Support System for the Management of Diabetic Patients With Kidney Complications in UK Primary Care Settings: Mixed Methods Feasibility Study. JMIR Diabetes. 2020;5(4):e19650.
6. **Armoiry X**, Späth H-M, Henaine A-M, Dussart C, Counsell C, **Connock M.** Ocrelizumab not recommended in France for patients with primary progressive multiple sclerosis while recommended in England: a review comparing the assessment by HAS and NICE. Expert Opinion on Biological Therapy. 2020:1-7.
7. **Auguste P, Colquitt J, Connock M, Loveman E, Court R,** Ciccarelli O, Counsell C, **Armoiry X.** Ocrelizumab for Treating Patients with Primary Progressive Multiple Sclerosis: An Evidence Review Group Perspective of a NICE Single Technology Appraisal. PharmacoEconomics. 2020;38(6):527-36.
8. Ayorinde AA, Williams I, Mannion R, Song F, Skrybant M, Lilford RJ, **Chen YF**. Publication and related biases in health services research: a systematic review of empirical evidence. BMC Medical Research Methodology. 2020;20(1):137.
9. Ayorinde AA, Williams I, Mannion R, Song F, Skrybant M, Lilford RJ, **Chen YF**. Assessment of publication bias and outcome reporting bias in systematic reviews of health services and delivery research: A meta-epidemiological study. PloS one. 2020;15(1):e0227580.
10. Blazeby J, **Andronis L** . Bluebelle pilot randomised controlled trial of three wound dressing strategies to reduce surgical site infection in primary surgical wounds. BMJ Open. 2020;10(1):e030615.
11. Cooper JA, Ryan R, Parsons N, **Stinton C,** Marshall T, **Taylor-Phillips S.** The use of electronic healthcare records for colorectal cancer screening referral decisions and risk prediction model development. BMC Gastroenterology. 2020;20(1):78.
12. Couper K, **Taylor-Phillips S, Grove A, Freeman K, Osokogu O, Court R, Mehrabian A**, Morley PT, Nolan JP, Soar J, Perkins GD. COVID-19 in cardiac arrest and infection risk to rescuers: A systematic review. Resuscitation. 2020;151:59-66.
13. Couper K, **Taylor-Phillips S**, **Grove A, Freeman K., Osokogu O, Court R, Mehrabian A**, Morley P, Nolan JP, Soar J, Berg K, Olasveengen T, Wychoff M, Greif, R, Singletary N, Castren M, de Caen A, Wang T, Escalante R, Merchant R, Hazinski M, Kloeck D, Heriot G, Neumar R, Perkins GD on

behalf of the International Liaison Committee on Resuscitation. COVID-19 infection risk to rescuers from patients in cardiac arrest. Consensus on Science with Treatment Recommendations [Internet] Brussels, Belgium: International Liaison Committee on Resuscitation (ILCOR). 2020.
14. Edwards G, **Freeman K,** Llewelyn MJ, Hayward G. What diagnostic strategies can help differentiate cellulitis from other causes of red legs in primary care? Bmj. 2020;368:m54.
15. Estecha Querol S, **Al-Khudairy L**, Iqbal R, Johnson S, Gill P. Adolescent undernutrition in South Asia: a scoping review protocol. BMJ Open. 2020;10(1):e031955.
16. **Fraser H, Gallacher D, Achana F, Court R, Taylor-Phillips S, Nduka C, Stinton, C**, Willans, R, Gill, P, **Mistry H**, 2020. Rapid antigen detection and molecular tests for group A streptococcal infections for acute sore throat: systematic reviews and economic evaluation. Health technology assessment (Winchester, England). 2020;24(31):1-232.
17. **Freeman K,** Dinnes J, Chuchu N, Takwoingi Y, Bayliss SE, Matin RN, Jain A, WalterF, Williams H, Deeks J. Algorithm based smartphone apps to assess risk of skin cancer in adults: systematic review of diagnostic accuracy studies. BMJ. 2020;368:m127**.**
18. **Geppert J, Stinton C, Johnson S, Clarke A,** Grammatopoulos D, **Taylor-Phillips S**. Antenatal screening for fetal trisomies using microarray-based cell-free DNA testing: A systematic review and meta-analysis. Prenatal diagnosis. 2020;40(4):454-62.
19. **Grove A, Clarke A, Currie G,** Metcalfe A, Pope C, Seers K. Advancing clinical leadership to improve the implementation of evidence-based practice in surgery: a longitudinal mixed-method study protocol. Implement Sci. 2020;15(1):104**.**
20. Patel S, **Achana F,** Carnes D, Eldridge S, Ellard DR, Griffiths F, Haywood K, Wan Hee S, Mistry D, **Mistry H**, Nichols V, Petrou S, Pincus T, Potter R, Sandhu H, Stewart K, Taylor S, Underwood M, Matharu M. Usual care and a self-management support programme versus usual care and a relaxation programme for people living with chronic headache disorders: a randomised controlled trial protocol (CHESS). BMJ Open. 2020;10(4):e033520.
21. Pearce E, Jolly K, Jones LL, Matthewman G, **Zanganeh M,** Daley A. Exercise for premenstrual syndrome: a systematic review and meta-analysis of randomised controlled trials. BJGP open. 2020;4(3):bjgpopen20X101032.
22. Raftery J, Williams HC, **Clarke A,** Thornton J, Norrie J, Snooks H, Stein K. 'Not clinically effective but cost-effective' - paradoxical conclusions in randomised controlled trials with 'doubly null' results: a cross-sectional study. BMJ Open. 2020;10(1):e029596.
23. **Taylor-Phillips S**, Berhane S, Sitch AJ, **Freeman K,** Price MJ, Davenport C, Geppert J, Harris M, **Osokogu O**, Skrybant M, Deeks JJ. Information given by websites selling home self-sampling COVID-19 tests: an analysis of accuracy and completeness. BMJ Open. 2020;10(11):e042453.
24. **Uthman OA, Al-Khudairy L, Nduka CU, Court R, Mistry H,** Melendez-Torres GJ, **Taylor-Phillips S**, **Clarke A**. Determining optimal strategies for primary prevention of cardiovascular disease: systematic review, cost-effectiveness review and network meta-analysis protocol. Systematic Reviews. 2020;9(1):105
25. Williams I, Ayorinde AA, Mannion R, Skrybant M, Song F, Lilford RJ, **Chen Y-F**. Stakeholder views on publication bias in health services research. J Health Serv Res Policy. 2020;25(3):162-71.
26. Yeong JL, Loveman E, Colquitt JL, **Royle P,** Waugh N, Lois N. Visual cycle modulators versus placebo or observation for the prevention and treatment of geographic atrophy due to age-related macular degeneration. The Cochrane database of systematic reviews. 2020;12:Cd013154.
27. Yeong JL, Loveman E, Colquitt JL, **Royle P,** Waugh N, Lois N. Visual cycle modulators versus placebo or observation for the prevention and treatment of geographic atrophy due to age-related macular degeneration. The Cochrane database of systematic reviews. 2020;12:Cd013154.

2021

28. Anderson D, Sturt J, McDonald N, Sapkota D, Porter-Steele J, Rogers R, Temple A, Seib C, McGuire A, Tjondronegoro D, Walker R, **Al-Khudairy L,** White C. Women's Wellness with Type 2

Diabetes Program (WWDP): Qualitative findings from the UK and Australian feasibility study. Diabetes Research and Clinical Practice. 2021;172.
29. **Connock M, Auguste P, Armoiry X.** A comparison of published time invariant Markov models with Partitioned Survival models for cost effectiveness estimation; three case studies of treatments for glioblastoma multiforme. The European journal of health economics : HEPAC : health economics in prevention and care. 2021;22(1):89-100.
30. Cooper C, **Court R,** Kotas E, Schauberger U. A technical review of three clinical trials register resources indicates where improvements to the search interfaces are needed. Research synthesis methods. 2021;12(3):384-93.
31. **Freeman K,** Ryan R, Parsons N**, Taylor-Phillips S,** Willis BH**, Clarke A.** The incidence and prevalence of inflammatory bowel disease in UK primary care: a retrospective cohort study of the IQVIA Medical Research Database. BMC Gastroenterology. 2021;21(1):139.
32. **Freeman K, Taylor-Phillips S**, Willis BH, Ryan R, **Clarke A.** Test accuracy of faecal calprotectin for inflammatory bowel disease in UK primary care: a retrospective cohort study of the IMRD-UK data. BMJ Open. 2021;11(2):e044177.
33. **Gallacher D,** Kimani P, Stallard N. Extrapolating Parametric Survival Models in Health Technology Assessment: A Simulation Study. Med Decis Making. 2021;41(1):37-50
34. **Grove A, Osokogu O, Al-Khudairy L**, **Mehrabian A**, **Zanganeh M, Brown A**, **Court C, Taylor-Phillips S, Uthman O,** McCarthy N, Kumar S, **Clarke A**. Association between vitamin D supplementation or serum vitamin D level and susceptibility to SARS-CoV-2 infection or COVID-19 including clinical course, morbidity and mortality outcomes? A systematic review. BMJ Open. 2021;11(5):e043737.
35. Kumar MB, **Madan JJ, Auguste P,** Taegtmeyer M, Otiso L, Ochieng CB, et al. Cost-effectiveness of community health systems strengthening: quality improvement interventions at community level to realise maternal and child health gains in Kenya. BMJ Glob Health. 2021;6(3).
36. Lois N, Cook JA, Wang A, Aldington S, **Mistry H,** Maredza M, McAuley D, Aslam T, Bailey C, Chong V, Ganchi F, Scanlon P, Sivaprasad S, Steel D, Styles C, Azuara-Blanco A, Prior L, **Waugh N.** Evaluation of a New Model of Care for People with Complications of Diabetic Retinopathy: The EMERALD Study. Ophthalmology. 2021;128(4):561-73.
37. **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.
38. **Stinton C, Fraser H,** Geppert J, **Johnson R, Connock M,** Johnson S, et al. Newborn Screening for Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase and Mitochondrial Trifunctional Protein Deficiencies Using Acylcarnitines Measurement in Dried Blood Spots-A Systematic Review of Test Accuracy. Front Pediatr. 2021;9:606194.
39. **Zanganeh M, Jordan M, Mistry H.** A systematic review of economic evaluations for donor human milk versus standard feeding in infants. Matern Child Nutr. 2021;17(2):e13151.

3 Intellectual Property

None to report.

4 Organisational Structure

In addition to the 25 WE core staff and our subcontract with McMDC Ltd. (see Table 2) we continue to add to our list of experts and external consultants who play a supportive role in delivering our core work at short notice. They include Dr Emma Loveman and Dr Jill Colquitt from Effective

Evidence, Dr Christine Clar, Dr Wendy Knerr, Dr Jacoby Patterson, Dr Toyin Lamina, Dr Emanuela Castelnuovo from Ananke Consulting, Dr Martin Connock, Dr Angela Noufaily and Dr Alex Tsertsvadze. We are equally fortunate to have a group of Honorary Fellows and Clinical Fellows and other supporters, including Prof Norman Waugh, Prof Xavier Armoiry, Dr Ejaz Cheema and Mr Amin Mehrabian and Dr Ji-Eun Park, whose expertise in HTA and Pharmacy are an asset to the team.

We wished well Dr Hema Mistry, Associate Professor of Health Economics, who in mid-March 2021, left after eight years of work at WE to join the Clinical Trials Unit at Warwick Medical School. Additionally, Dr Pam Royle retired during the reporting period. Our vacancies during the reporting period are displayed in Table 3.

Table 2. Warwick Evidence Staff

Name	Role(s)	Core or Ad Hoc	Full Time Equivalent (FTE)
Dr Amy Grove	Director, Lead, Clinical Effectiveness	Core	0.4
Dr Paul Sutcliffe	Lead, Clinical Effectiveness	Core	0.5
Prof Aileen Clarke	Clinical academic oversight, Quality Assurance	Core	0.2
Dr Dan Todkill	Clinical academic oversight, Quality Assurance	Core	0.1
Prof Sian Taylor-Phillips	Diagnostics Academic advisor	Core	0.1
Prof Jason Madan**	Health Economics Academic advisor	Core	0.1
Dr Hema Mistry** – left 15.3.21	Assoc Prof Health Economist, Lead	Core	0.7
Dr Lena Al-Khudairy	Senior Research Fellow, Lead, Clinical Effectiveness	Core	0.7
Dr Chris Stinton	Senior Research Fellow, Lead, Clinical Effectiveness	Core	0.8
Dr Yen-Fu Chen	Assoc Prof, Lead, Clinical Effectiveness	Core	0.5
Dr Lazaros Andronis – Left 1.6.20**	Assoc Prof, Lead, Health Economist	Core	0.5
Dr Felix Achana** – started 5.1.21	Assoc Prof, Lead, Health Economist	Core	0.6
McMDC- Dr Ewen Cummins	Health Economist	Subcontract	1.0
Dr Mandana Zanganeh**	Research Fellow, Health Economist	Core	1.0
Mr Peter Auguste**	Research Fellow, Health Economist	Core	1.0
Ms Mary Jordan** FTE increase 1.2.21	Research Fellow, Health Economist	Core	1.0
Dr Karoline Freeman started 5.1.21	Senior Research Fellow, Lead, Clinical Effectiveness Reviewer	Core	0.5
Dr Osemeke Osokogu	Research Fellow, Clinical Effectiveness Reviewer	Core	1.0
Ms Hannah Fraser left 22.3.21	Research Associate, Clinical Effectiveness Reviewer	Core	0.9
Ms Anna Brown	Information Specialist	Core	0.6
Ms Rachel Court	Information Specialist	Core	0.7
Mr Mubarak Patel	Research Associate, Statistician	Core	1.0
Mr Daniel Gallacher	Research Fellow, Statistician	Core	1.0
Mrs Sarah Abrahamson	Research Centre Manager	Core	0.5
Mrs Mitra Murray started 2.11.20	Project Manager	Core	0.92
Ms Kate Evans returned 2.1.21	Project Administrator	Core	0.4
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 Tsertvadze	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*	

*Ad-Hoc as contractor

** Member of Centre for Health Economics at Warwick (CHEW)

Table 3. Vacancies during the reporting period

Vacancy Duration	Role(s)	Core or Ad Hoc	Full Time Equivalent (FTE)
March 2020 - Jan 2021	Project Administrator	Core (maternity leave)	0.4
September 2020 - November 2020	Project Manager	Core	0.92
June 2020 – Jan 2021	Assoc Prof Health Economics	Core	0.5
March 2021- June 2021**	Research Associate, Clinical Effectiveness Reviewer	Core	0.9
March 2021 – September 2021**	Assoc Prof Health Economics	Core	0.7

** replacement identified and appointed, with start date after the end of this reporting period

5 Engagement with NICE

Warwick Evidence continues to work closely with ESP TAR, the NIHR and NICE. We enjoy a productive relationship with colleagues across all the organisations. As projects evolve, our team members are in frequent contact with the NICE technical team and project managers.

5.1 Areas of Concern, Improvement and Development

As alluded to, 2020-21 has been a particular challenge for all. Due to COVID-19, appraisals which were considered 'non-therapeutically critical' were delayed or paused. Prior to the pandemic, NICE introduced an 'interim' Technical Engagement (TE) process, which was later updated to a 'new' TE process. These changes introduced new process steps into the appraisal process, which enable companies to submit additional data at various points of the appraisal prior to the Appraisal Committee meeting. The pausing and restarting of projects coupled with the introduction of the 'interim' and 'new' TE processes caused challenges for our team. Specifically, the parallel working across ongoing appraisals and the restarting of paused projects and the team's increased workload as new/additional data must be appraised in very short time frames. This extra burden coincided for many of the team with the additional burden of carer responsibilities during lockdown and school/childcare closure periods.

We do our utmost to meet the requests from NICE, however at times some negotiation around deadlines is required; during the pandemic this has been all the more necessary. The consensus across TAR teams and NICE at the InterTASC/Annual TAR Contract Review meeting was to continue to negotiate work and deadlines with NICE; request more reasonable timelines; and where necessary ask ESP TAR for additional units to compensate for additional work.

5.2 Key Issues for Consideration

We are pleased to confirm that we were able to complete all work allocated to us against the updated timelines set by NICE. However, given the pandemic and its impact on all including NICE, we recognise that there will be ongoing capacity issues for Warwick Evidence while we all continue to work from home and balance other commitments. Key issues currently faced by the group and elaborated on later in this report include:

- changes to the NICE process (we had projects in all of the 'old', 'new' and 'interim' TE process in our allocation). This includes NICE allowing the companies to submit significant amounts of additional data at TE on a large proportion of the STAs, resulting in the requirement to undertake major analysis in just 8-10 days.
- changes/pauses in project timelines (over and above what we have seen in previous years).
- extending project end dates after the submission of additional evidence from the company.

5.3 Increasing Workloads Within Units

We are seeing an increase in the workload within each project. An example of this comes from an ongoing appraisal (Lisocabtagene maraleucel for treating large B-cell lymphoma after at least 2 therapies [ID1444]) whereby the company confirmed before the appraisal began that a second data cut of the pivotal trial evidence would not be available in time for its submission. This additional analysis would be submitted during TE which only allows 8-10 days for ERG to critique. This was followed by a pause and submission of a third data cut. Consequently, the amount of work involved in appraising the three evidence submissions resulted in an additional whole unit allocation. Subsequently, an additional model was provided post TE, resulting in four submissions which need to be appraised by the ERG. The expectation from NICE that companies can submit additional data and new models so late into the TA process is becoming increasingly problematic for the team. It limits our capacity to fully appraise the additional data in shorter time frames than the standard appraisal process (8 weeks).

As discussed at the InterTASC Autumn 2020 meeting and Annual TAR Contract Review meeting, the 'interim' and 'new' TE process is increasing rather than decreasing our workload. It can be very difficult to schedule the additional analysis requested by NICE or produced by the company required for TE (8-10 days) or in the lead up to the committee meeting. Usually, the individual teams have moved onto a new appraisal which means we have to ask staff working on new projects to work on an older TA/TE in parallel. We continue to have frequent correspondence with NICE during each TA,

but we note the frequent and multiple requests for clarification/additional pieces of work outside of the TE window.

The team have experienced issues with short-notice requests from NICE and this is an ongoing challenge. Often requests for additional work or advice are sent late in a working day, with a response expected soon after (sometimes less than 24 hours). These requests have on occasion included complex tasks and analysis which may need senior staff attention and work over weekends. We understand that the TE process will be formally reviewed again in late 2021 and Warwick Evidence would welcome involvement in this process and in the review of the NICE process guide.

Another ongoing challenge to the team is the provision of company submissions and models in varying formats, which at times fall outside the NICE standard accepted format, or come with extremely long/complicated instructions and appendices. For example, models are submitted which are not in a recognised NICE package. On occasions when this has happened, WE request external advice from the NICE Decision Support Unit (DSU) or external consultants in order to complete the projects. This has been raised as an issue with InterTASC and NICE but is yet to be resolved through discussion.

5.4 New TA Process

We welcome the introduction of the new ERG report template for STAs. We have found the new 'executive summary' issues reporting system to be useful in focusing on our key arguments ahead of TE. There appears to be a lack of clarity as to whether this report format should be used in other appraisal reports (e.g., CDF reviews). However, we are disappointed that the TE conference call is no longer attended by the Chair of the NICE Appraisal Committee and/or the clinician advisors. This gave the ERG an opportunity to review key issues the Chair might have ahead of the committee meeting and gave the team time to prepare key information that might be requested. We welcome the notification in mid-February that NICE will now take back ownership of redacting the reports ahead of dissemination or publication. This additional step in the process was given to the TAR teams on a trial basis but without additional capacity to perform the activity. It was not a valuable activity to allocate TAR team days to this procedure in the critical few days before report submission.

As a team, we are not comfortable with the NICE decision to limit ERG NICE Appraisal Committee meeting attendance to two people. The evidence for the effectiveness of this decision has not been shared with the teams. A blanket two-person limit reduces our ability to provide full technical

expertise to the committee and forces the teams to choose between who should attend: either the clinical effectiveness, cost-effectiveness or medical statistician role. NICE suggest we have the 'third' role attend the meeting as an observer who cannot contribute – however, this does not work in practice and it encourages the ERG to run a parallel internal virtual meeting whilst trying to focus on the committee meeting.

5.5 Academic Output

We have seen a slight increase in the number long reports coming through the NICE process and we welcome the opportunity to undertake more DARs/MTAs as they generate academic output for the team. Nevertheless, given the NICE focus on short reports, there can be limited opportunities for the production of academic output for staff members and junior academics. We continue to actively promote the involvement of our team in other research projects that can result in publication of papers in recognition of the fact that academic career progression is dependent on high quality output.

Ongoing external research helps to ensure staff remain abreast of developments in terms of methodological and clinical research, whilst contributing towards their continuing professional development. However, securing external grant funding brings with it organisational and managerial challenges for the senior team, as well as capacity issues for the work programme. To overcome this, we introduced the Warwick Evidence Business Committee process to ensure grant application is done in a planned and strategic way. The Committee meets once a month and evaluates not only the quality of the research proposals, but also the potential impact of the team members' time commitments against our ability to deliver the TAR work. We maintain a group of external consultants to support us when scheduling challenges arise. This model has worked well over the year.

6 NIHR

Warwick Evidence continues to work closely and enjoy a productive relationship with the NIHR, and we are in contact with the NIHR and ESP TAR as and when needed. We have no issues to report on.

7 Training and Capacity funding expenditure (£25,000/year)

Our training budget continues to support a broad range of courses and training events within the team including: Survival Analysis, Health Economics and Network Meta-analysis. Applications for funding are evaluated by the Warwick Evidence Senior Team on the suitability of the training to the

applicant's job description, career professional development, and on the overall benefits for the team. Staff attending courses are required to provide an overall rating of the course or conference. They are also required to provide a brief presentation at the Warwick Evidence team meeting. The details of the training courses attended by WE staff during the reporting year are provided in Table 4.

Table 4. Warwick Evidence Training Activity 2020-21

Name	Course Title	Date	Venue	Costs
Lena Al-Khudairy	Aurora Leadership course	**dates tbc – postponed due to COVID-19	Birmingham / Online	£1050
Lena Al-Khudairy	Leadership Development	Sept 20 – Mar 21	Online	£510
Sarah Abrahamson	Aurora Leadership course	**dates tbc – postponed due to COVID-19	Birmingham / Online	£1050
Sarah Abrahamson	WHF conference: "The future of NICE in health and social care"	Jan 2021	Online	£228
Felix Achana	Economic Evaluation for Oncology	Sept 2020	Online	£100
Xavier Armoiry	HTAi	Jun 2021	Online	£1000
Peter Auguste	Economic Evaluation Modelling Using R	**tbc		£0**
Peter Auguste	HTAi	Jun 2021	Online	£1000
Peter Auguste	Economic Evaluation for Oncology	Sept 2020	Online	£100
Anna Brown	Identifying Unpublished Trial Data: Trial Registers, Clinical Study Reports and Other Information Sources	Nov 2020	Online	£90
Anna Brown	Citation Analysis – Discovering New Uses within Systematic Reviews	Nov 2020	Online	£90
Yen-Fu Chen	Health Services Research UK Conference	Jul 2020 **	Manchester**	£650**
Aileen Clarke	Survival Analysis for Decision Making	Jan 2021	Online	£360*
Aileen Clarke	Leadership Development	Sept 2020 – Mar 21	Online	£630
Rachel Court	Searching the Evidence for Mixed Methods Reviews		Online	£90
Karoline Freeman	Fundamental Mathematics & Statistics for Health Data, University of Manchester	Autumn 2021	Manchester / Online	£1200
Karoline Freeman	Data Linkage, Bristol University	Autumn 2021	Bristol / Online	£440
Daniel Gallacher	Recent advances in statistical analysis of survival data	May 2020**	Bordeaux **	**

Name	Course Title	Date	Venue	Costs
Julia Geppert	Systematic Reviews and Meta-Analysis using STATA	Feb 2021	Online	£297
Amy Grove	WHF conference: "The future of NICE in health and social care"	Jan 2021	Online	£228
Amy Grove	Survival Analysis for Decision Making	Jan 2021	Online	£360
Amy Grove	Leadership Development	Sept 2020 – Mar 2021	Online	£160
Mary Jordan	Economic Evaluation for Oncology	Sept 2020	Online	£100
Osemeke Osokogu	Network Meta-analysis	June 2020 **		**
Mubarak Patel	Bayesian Meta-Analysis – virtual classroom	Oct 2020	Online	£652
Mubarak Patel	NICE / DSU / ABPI Virtual Masterclass: Optimising NICE submissions in Oncology	Nov 2020	Online	£0*
Chris Stinton	Survival Analysis for Decision Making	Jan 2020	Online	£360
Paul Sutcliffe	Course for Chief Investigators working on Clinical Trials	April 2020	Online	£0
Dan Todkill	Network Meta-analysis	June 2020 **		**

*costs not charged to Warwick Evidence

** training course cancelled due to COVID-19