

BIOMEDICAL RESEARCH UNIT ANNUAL REPORT 2015/16 Financial Year

Note: The accompanying *NIHR Biomedical Research Units – Guidance on Completion of Annual Reports for 2015/16 Financial Year* contains essential guidance on the information you need to provide when completing this proforma. **Please complete the form using a font size no smaller than 10 point (Arial).**

1. UNIT DETAILS

Name of the NIHR Biomedical Research Unit:

The NIHR Biomedical Research Unit in Nutrition, Diet and Lifestyle at the University Hospitals Bristol NHS Foundation Trust and the University of Bristol

Contact details of the individual to whom any queries on this Annual Report will be referred, and to whom feedback on the annual report will be sent:

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2. DECLARATIONS AND SIGNATURES

Contact details of the NHS Organisation administering the NIHR Biomedical Research Unit award:

Name: University Hospitals Bristol NHS Foundation Trust

Address: Trust Headquarters, Marlborough Street, Bristol BS1 3NU

Name of the Chief Executive of the NHS organisation:

Robert Woolley

I hereby confirm, as Chief Executive of the NHS organisation administering the NIHR Biomedical Research Unit award, that this Annual Report and the Financial Report have been completed in accordance with the guidance issued by the Department of Health and provides an accurate representation of the activities of the NIHR Biomedical Research Unit:

Signature
(Chief Executive)

Date:

3. OVERVIEW OF ACTIVITIES (no more than two pages)

Progress against objectives

The Bristol Nutrition BRU has been open for four years. We have made significant progress with our short term objectives and have also made progress with our medium and long term objectives which we have outlined in the sections below. We now have over 70 approved projects across all our five research themes, and recruited over 1500 participants to these studies. The details of these are listed in the Finance and Activity Report previously submitted and on our website, <http://www.bristolnutritionbru.org.uk>.

Leadership, governance and management arrangements

The management structure and reporting framework the Bristol Nutrition BRU are firmly established. Our executive group comprises the director (Professor Andy Ness), the deputy director (Professor Julian Hamilton-Shield), two other theme leads (Professor Richard Martin and Professor Ashley Cooper), and the unit manager (Dr Vanessa Marshall). The Executive Group has agreed terms of reference and meets every two weeks. We have also introduced the role of deputy theme lead. The deputy theme leads are: Dr Charlotte Atkinson (Peri-operative theme), Dr Angie Page (Sedentary/Diabetes theme) and Dr Athene Lane (Prostate cancer theme). They attend larger quarterly meetings of the executive. Research themes and cross cutting activities (including PPI, engagement, training, statistics, systematic reviewing, qualitative methods) provide formal reports to the unit's executive group. These are then collated into a quarterly update report that is tabled at meetings of the NHS trust's research group and at equivalent research groups in the two university faculties within which the unit operates.

Strategic developments

Our strategy is reviewed and refreshed each year with our strategy group. The strategy group comprises three external senior academics (Professor Janet Cade, University of Leeds; Professor Kay-Tee Khaw, University of Cambridge; Professor Ivan Perry, University of Cork) and two patient representatives drawn from our BRU patient and public involvement groups in colorectal surgery and prostate cancer, (Rik Lander and David Casley). They last met on the 20th May 2016. They were positive about our achievements and extension of our themes (described below as one of our three highlights). In particular they felt that our engagement with industry for academics working in clinical nutrition and lifestyle research was to be commended.

BRUs top three achievements during the 2015/16 financial year

1. *Providing a focus for clinical nutrition and lifestyle research in Bristol*

In our full proposal we stated that "The Unit will provide a focus for nutrition and lifestyle research in clinical populations in Bristol..." and that "[The Unit] will create an integrated programme of nutrition research." We believe that the Bristol Nutrition BRU has provided this focus and integration. We have built strong links with the MRC Integrative Epidemiology Unit (for example see the description of our feasibility study on folate supplementation and long-term epigenetic changes), the Nutrition Behaviour Unit (for example we worked together on the recently published systematic review reporting on low energy sweeteners and obesity), Exercise Nutrition and Health Sciences (ENHS) (with nearly all ENHS staff running at least one clinically relevant project in partnership with the BRU) and with our clinical colleagues in paediatrics, gastroenterology, endocrinology and surgery. We have provided methodological support in statistics, systematic reviewing and qualitative methods and administrative support in database management and trial co-ordination that has allowed investigators to run a wide range of feasibility studies in clinical nutrition and lifestyle. We have developed and shared our expertise in specific areas such as the measurement and modification of speed of eating, sedentary behaviour and active travel. We are providing a comprehensive training programme that includes a successful seminar series and sabbatical programme. Further we have facilitated the development of research dieticians and now support dieticians in junior, intermediate and senior research roles. We have also developed links with other NIHR infrastructure. We work with the Southampton BRC and the Leicester/Loughborough BRU and are supporting Cancer and nutrition NIHR infrastructure collaboration. We are working up an active travel project with CLAHRC West.

2. *Extension of our themes*

One of the specific aims included in our full proposal was to "Identify further interventions for clinical populations translated from observational studies and transferred from trials in primary care and the general population" We have supported this aim partly by running projects in our core theme (described below) that did not fit logically in any of our four themes. Also with the support of our strategy group we have extended the scope of our four main research themes. We have attracted further funding to support this expansion in

activity so that this expansion has not detracted from our planned work (we highlighted grant funding as one of our top three achievements in our annual report last year). In our children's theme we have built strong industry collaborations (we are now testing a number of nutrition focused devices that could improve the care of children with disease), extended our work to other important conditions potentially influenced by nutrition and lifestyle (such as asthma and cystic fibrosis related diabetes) and worked in partnership with Great Ormond Street BRC and the NINR rare diseases translational research collaboration. Our sedentary theme has extended to include work on active travel and work on dietary behaviour with the University of Bristol Nutrition Behaviour Unit. Our prostate cancer theme helped support a successful bid for a Cancer Research UK programme that has strengthened and broadened our pipeline of research questions in cancer. The BRU has hosted the NIHR funded clinical cohort – head and neck 5000 (<http://www.headandneck5000.org.uk/>) and the BRU has recently started some systematic reviews on lifestyle change in oral dysplasia. Our peri-operative theme has been widened to include peri-treatment nutritional interventions in part guided by findings from feasibility studies to date and from our PPI groups.

3. Research outputs and dissemination

Our studies are now producing important findings that are being written up for publication. We have now published 73 papers (10 in 2013, 18 in 2014, 27 in 2015 and 18 in first 6mths 2016) with many more manuscripts in preparation. We have published several policy relevant reviews and the two Cochrane reviews have linked podcasts. We have also managed to change the publication policy in a major journal so that it now complies with NIHR open access requirements (see our added value case study for more details). In addition to publications we have also presented our work at a number of national and international conferences and we have a number of presentations accepted for the next six months. We also disseminate our findings through our comprehensive programme of engagement activities that we highlighted as one of our top three achievements in last year's annual report.

4. PROGRESS MADE IN EACH RESEARCH THEME (no more than one page per theme)

Core Theme

Progress against specific objectives detailed in the original application

Objective 1 - Training in nutritional research methods for clinicians and non-clinical scientists to strengthen research in nutrition in clinical populations- See training section.

Objective 2: Identify further interventions for clinical populations translated from observational studies and transferred from trials in primary care and the general population: Our core theme is carrying out experimental research projects not included in any of the specific themes to help identify further interventions for clinical populations. We report on progress with new and ongoing projects since our last report:

- Aberdeen Folic Acid Supplementation Trial: Follow up of offspring – We are working with the MRC Integrative Epidemiology Unit (IEU) to assess the feasibility of following up the offspring born to mothers in this trial (conducted between 1966 and 1967) and measuring their epigenetic profile on DNA extracted from saliva samples. A draft manuscript is being prepared.
- Effects of nicotine challenge on eating topography – we are planning to examine the effect of nicotine on eating in collaboration with the MRC Integrative Epidemiology Unit and the Nutrition Behaviour Unit in the School of Experimental Psychology – we are designing the protocol.
- The Association between Adiposity and the Presentation and Clinical Course of Crohn's disease - this is an MD project. A systematic review is underway and fieldwork is complete.
- Pilot Study using Wellpoint healthcheck Kiosk in the Education Centre at United Hospitals Bristol for staff and visitors - a NOCRI introduced collaboration with industry carried out in conjunction with Leicester/Loughborough BRU. The study is completed and an abstract has been presented as a poster presentation at the annual scientific meeting of Society and Faculty of Occupational Medicine, June 2016. A short report is being prepared to be submitted to a relevant academic journal.
- Evaluation of urinary chloride dipsticks for the rapid estimation of hydration status in patients- a BRU supported study which won Gus Hamilton, the lead research clinician, an Innovations Challenge Award. A paper describing the comparison of dipsticks and laboratory tests is under consideration by the Nutrition Journal. In the development of a feasibility study we met with four individuals with intestinal failure (IF) to discuss issues around hydration when using home parenteral nutrition (HPN). Feedback has been incorporated into a draft for a feasibility study (with a nested observational study) to look at Cl (and Na) concentrations among individuals with IF on HPN. The aim is to look at variation within and between days, and to assess acceptability of study processes. Data will be used to inform a trial of self-management with dipsticks vs. usual care.
- Pulsed glucocorticoid replacement therapy for patients with adrenocortical insufficiency secondary to Addison's disease and congenital adrenal hyperplasia (Pulses Study): qualitative work to support this trial. Sixteen participants have been recruited to the trial.
- Developing a framework for efficiently document BRU research data. The project is nearly completed. A novel package, 'D2', is being finalized for submission to the Comprehensive R Archive Network (CRAN), a widely used repository for deploying such a statistical package. The 'D2' software generates Print-Ready (PDF) as well as website documentation (HTML) for a wide range of studies. A journal paper describing the developed framework and its potential applications in preparation.
- Diavit and VEGF splicing in diabetic neuropathy: designing feasibility study to assess acceptability and impact on intermediate biomarkers of a dietary supplement in diabetics with renal failure.

Objective 3: Multidisciplinary research capacity for each of the areas: Our core team provides co-ordinated methodological support across all themes. Our core team offers mentorship and practical support in data management, systematic reviewing, statistics and qualitative methodology. Our core team is also supporting patient and public involvement and public engagement. It continues to be effective and is described in the relevant sections below.

Progress with leadership of the theme: There have been no changes to leadership.

Details of the progress of research area strategy, including any changes (e.g., discontinuation of originally planned work, or new areas of research): We have continued our work as planned. We opened two projects and completed three projects.

Examples of effective translation, or significant progress along the translational pathway: We have completed two policy relevant reviews 1) On Omega-3 fatty acids and depression in adults: a Cochrane review and 2) Systematic review of animal and human studies of low energy sweeteners on appetite and obesity

Examples of the creation and development of intellectual assets

Intellectual assets in the form of publications (including Cochrane reviews and podcasts) and conference presentations have resulted from work in this research area (see Publications section of Finance and Activity report).

Perioperative Theme

Progress against specific objectives detailed in the original application.

- Cochrane reviews on gum chewing (sham feeding) after abdominal surgery, early post-operative feeding after colorectal surgery, and immunonutrition in people undergoing surgery for head and neck cancer and postoperative recovery have been/will be completed.
- Two qualitative interview studies have been completed to address our objectives. One explored experiences of perioperative nutrition in people undergoing colorectal surgery, and one explored the experiences, practices and contexts of healthcare providers towards the enhanced recovery after surgery (ERAS) programme. Three manuscripts (one published, two submitted) have resulted from these studies.
- We looked into the potential to use length of hospital stay (LOS) data from Hospital Episode Statistics (HES) as a proxy for ERAS implementation across hospitals. Given that several factors (which may or may not be related to ERAS) can affect LOS, the ability to make inferences about ERAS implementation from data on LOS is being carefully considered. We are scoping the literature for studies that have looked at determinants of LOS.
- We have established links with colleagues in clinical oncology to develop studies of diet-drug (chemotherapy) interactions and with local stoma nurses for trialling diets in stoma patients (a group identified as particularly vulnerable in the qualitative studies). We have expanded our studies into the role of parenteral nutrition in managing inoperable bowel obstruction in women with ovarian cancer.

Progress with leadership of the theme

The research area continues to be led by Dr Charlotte Atkinson (deputy theme lead), under the guidance of Professor Andy Ness.

Details of the progress of the theme's strategy

- Existing trial data (from an NIHR RfPB funded trial of chewing gum after colorectal surgery) were used by a PhD student to look at predictors of early feeding, and early feeding as a predictor of outcome. Several factors were associated with delayed time to consumption and/or tolerance (eating at least half of three consecutive meals without vomiting) of food, including use of pre-operative bowel preparation, nausea and/or vomiting, anti-emetics, surgical approach, and opiate use. Delayed time to consumption and tolerance of food were weakly associated with increased LOS. A manuscript from this work will be prepared for submission within the next review period.
- Work in the chewing gum trial was expanded by obtaining CT scans from Bristol study participants to measure fat free mass, subcutaneous and visceral fat. We will determine relationships between body composition, and also sarcopenia, and surgical complications.
- We worked with Clinical Trials and Evaluation Unit (CTEU) colleagues to design an RCT to look at perioperative immunonutrition in people undergoing surgery for head and neck cancer. We identified that further developmental work is needed (e.g., evaluation of use of immunonutrition, feasibility of administering perioperative immunonutrition in this population).
- We continued to collaborate with colleagues at the CTEU and the NIHR Cardiac BRU in Bristol on prehabilitation studies, with the ultimate goal of developing a multi-component prehabilitation intervention for people undergoing major surgery for cancer. A systematic review protocol paper has been published, and data extraction for the review is almost complete (>100 papers have been extracted to date). A survey of preoperative services has been conducted, and a cohort study is being established to describe a contemporary cancer surgery population and comorbidities.
- Also in regards to prehabilitation, we began developing a long-term food-based intervention (frozen meals delivered to participants' homes) in frail elderly waiting to undergo joint replacement. Work to date includes gaining the views of an established PPI group and trialling the meals.
- Additional discussions regarding progression of the theme have resulted in the following areas of work to be developed both within and beyond the next review period: sarcopenia and chemotherapy dose; fasting and chemotherapy dose/side effects; low iodine diet and radio-iodine ablation.

Examples of effective translation, or significant progress along the translational pathway, as a result of NIHR BRU funding.

Findings from studies conducted in this research area have pin-pointed areas of work in which further feasibility studies are needed. By addressing these gaps in knowledge and providing sufficient supporting information, we will be able to apply for funding to definitively evaluate interventions in clinical trials.

Examples of the creation and development of intellectual assets through the work of the research theme.

Intellectual assets in the form of publications (Cochrane reviews, a protocol paper, and original research) and conference presentations have resulted from work in this research area (see Publications section).

Prostate Cancer Theme

We have now finished recruitment to the Prostate Cancer: Evidence of Exercise and Nutrition (PrEvENT) Trial and the feasibility results are in write-up for publication. A total of 108 participants have been recruited into the cohort with 83 expected to be randomised and allocated to the nested trial. The trial has demonstrated good retention rates of participants with only a small number of drop-outs at 3 and 6 month follow-ups (8% and 2% respectively). The ProDiet feasibility study in dietary green tea and lycopene interventions for men at increased risk of prostate cancer has also concluded with results expected for publication later this year. Of the 469 men invited, 154 responded (32.8%), 133 were randomised (86.4%) and 130 completed 6 month follow-up (97.7%). The trial concluded that men at elevated risk of prostate cancer adhered to dietary interventions for 6 months, suggesting that dietary interventions would be feasible and acceptable in this population group. There was suggestive (but inconclusive) evidence that lycopene supplementation may raise IGFBP-2 levels, and green tea supplements may lower IGFBP-3 levels, in men at risk of PCa. The trial also found evidence for a trend in increased levels of acetate and decreased levels of valine in men who were randomised to lycopene supplements compared with the lycopene placebo arm. While in the dietary advice arm, there was a trend for decreased levels of valine and diacylglycerol compared with the lycopene placebo arm. These findings suggest that lycopene supplementation may alter the serum metabolome of men with increased risk of developing PCa and warrants further investigation in larger trials.

- **Impact of interventions on biomarkers** – We continue to collect blood and surgical tissue samples from participants as they progress through the PrEvENT Trial. To date 236 plasma and 103 prostate tissue samples have been collected. DNA has been extracted from 206 tissues (103 benign and 103 cancer tissues). Circulating concentrations of IGF-II from serum will be determined using an ‘in-house’ radioimmunoassay once all samples have been collected. Immunohistochemistry antibody optimisation for tissue sections is also ongoing with optimisation complete for some key markers such as metabolic status. Within the ProtecT trial, analysis of covariance has shown that healthy changes in fruit and vegetable, and protein intake, body mass index, and physical activity following a prostate cancer diagnosis were associated with favourable changes in post-diagnosis serum IGF-I and IGFBP-3.
- **Systematic Reviews of the impact of nutritional/physical activity interventions in prostate cancer** – This work has now been completed and the review has been published (see publications section of the Finance and Activity Report). Data were presented at The International Society of Behavioural Nutrition and Physical Activity (ISBNPA) Conference, 2016, Cape Town, South Africa.
- **Qualitative Research to explore acceptability of interventions** – Qualitative Analysis of PrEvENT is now complete and is currently in the process of being written up for publication in peer reviewed journals. This analysis has found that the interventions delivered as part of PrEvENT were deemed acceptable by participants, as were the data collection methods utilised. It has also highlighted some considerations to be taken into account for further behavioural change interventions in this population.

Progress with leadership of the research area, including any changes or challenges faced

The theme continues to be led by Professor Richard Martin and Dr Athene Lane from the School of Social and Community Medicine.

Details of the progress of the research area’s strategy, including any changes

We continue to explore the expansion of our work in other cancer sites and are currently conducting systematic reviews into lifestyle interventions in people with oral dysplasia.

Major grant awards received as a consequence of NIHR BRU funding;

- Eileen Sutton (Senior Research Associate in Qualitative Methods) is co-applicant on the NIHR STAMINA (Sustained exercise Training for Men with prostate cancer on Androgen deprivation) Programme Development Grant led from the University of Sheffield. She has been helping to supervise a qualitative researcher whose work will inform the submission of a Programme Grant application in October 2016.
- We have applied to the CRUK Catalyst Award call for £5million (Lead PI Richard Martin) to create a pipeline to translation from the analysis of high dimensional data via evidence synthesis into cancer risk prediction rules and interventions focused on tailored risk communication.
- Sarah Lewis, Richard Martin, Julian Higgins, Carolina Bonilla, Tom Gaunt. Re: Exploitation of molecular and mechanistic data to identify modifiable factors which cause prostate cancer incidence and progression and elucidate their mechanism of action. WCRF UK. 31st March 2016 for 3 years. Grant reference number: 2015/1421 £213, 085

Examples of effective translation, or significant progress along the translational research pathway, as a result of NIHR BRU funding for the research area.

The PrEvENT Trial is ongoing; therefore, there is limited progress along the translational pathway at this time. However data analysis is now underway with results expected for publication over the following year.

Type 2 Diabetes/Sedentary Theme

Progress with the strategy to achieve the specific objectives of this theme is described below.

Systematic reviews: We have conducted two systematic reviews. 1. A published review of the evidence for the association between objectively measured sedentary time and metabolic outcomes, shows that the strongest association between time spent sedentary and metabolic outcomes is with insulin sensitivity 2. A review into eating architecture, obesity, T2D and cardiovascular disease is ongoing, with screening of ~21,000 search hits is completed and full-text retrieval (n=262) and eligibility checking is ongoing.

Efficacy of modifying sedentary time on change in metabolic outcomes.

We have conducted a small (n=18) randomised crossover trial to investigate the effect of interrupting sedentary time by standing and walking on the blood glucose level of office workers measured with a continuous blood glucose monitor. We found that breaking up prolonged sitting every 20 minutes with two minutes of standing or two minutes of light-intensity walking lowered postprandial interstitial glucose incremental area under the curve by 21.6% (p = 0.443) and 52.3% (p = 0.009) respectively. Preprandial interstitial glucose iAUC by 44.0% (p = 0.510) and 60.3% (p = 0.349) respectively. (manuscript in review).

Qualitative investigation of sedentary behaviour.

We have conducted an in depth analysis of transcripts from the Early ACTID RCT to explore the barriers and facilitators of physical activity behaviour change in that study. This work gives insights into the factors influencing motivation of people with type 2 diabetes to both take part in a research study and for initial and continued lifestyle behaviour change. Two manuscripts are in preparation.

Sedentary Time And Metabolic health in People with type 2 diabetes (STAMP-2)

We have conducted an observational study (STAMP-2) in 177 patients (55.7±8.9 yrs, 49.7% male, BMI 34.4±7.3) newly diagnosed (n=139) or at high risk (n=38) of type 2 diabetes to investigate three main issues:

1. Accuracy of objective measurement of sedentary time

We have compared associations measured with both a waist worn accelerometer (often misclassifies) and an activPAL inclinometer (gold standard). We have found that the waist worn accelerometer overestimated sedentary time by approximately 25%, and that the relationship between the two instruments was not consistent, with a smaller difference at higher levels of sedentary time.

2. Spatial mobility of people with type 2 diabetes

Time spent outdoors and association with higher physical activity has not been described in adults. We measured time spent and physical activity outdoors in Bristol participants (n=91) by integrating accelerometer and global positioning system (GPS) data. Participants spent 26.9% (148 minutes) of measured time outdoors and recorded a total of 29 minutes of MVPA, of which 19 minutes (65.5%) was outside. Being outdoors is associated with higher physical activity, but overall amounts of MVPA are small.

3. Co-existing behaviours

We have collected four-day food diaries that will allow us to explore the interaction between sedentary time/behaviour and eating pattern/diet and metabolic outcomes. All 162 diaries have been coded and a database constructed to allow comparison. Analyses are ongoing.

Feasibility of intervention to target sedentary time.

We have developed a feasibility study to explore the use of electric bikes (e-bikes) in people with T2D. We have recruited 20 patients (60.0±7.8 yrs, 60.0% male, BMI 30.8±5.9) who have received cycle training through a third sector partner (Life Cycle) and who have been issued with an e-bike for personal use for 5 months to October 2016.

Progress with leadership of the theme

Ashley Cooper continues to lead the theme, with Angie Page as deputy lead. Dr Rob Andrews, Clinical Theme Lead, has moved to Exeter University but continues to work with the theme.

Examples of effective translation, or significant progress along the translational pathway, as a result of NIHR BRU funding:

A translational route by which cycling may be used to improve the health of people with T2D is being explored with colleagues in Sustrans Newcastle. The Stockton CCG has part funded, in collaboration with Bristol BRU, a pilot scheme for GP referral of patients with T2D to Sustrans for 6 weeks of active travel coaching/facilitation, using self-monitoring of physical activity to support behaviour change. The Bristol BRU is providing the overarching evaluation of physical activity and spatial mobility. This intervention is ongoing to March 2017.

Examples of the creation and development of intellectual assets through the work of the research theme:

We have evaluated a brief dietary assessment tool, the UK Diabetes and Diet Questionnaire (UKDDQ), for test-retest reliability and in comparison with 4-day food diaries in the STAMP-2 cohort. Overall relative and absolute test-retest reliability was excellent (r=0.90; ICC = 0.90 (95% CI =0.85 to 0.93)) and overall relative and absolute agreement in comparison with food diaries was good (r=0.61; ICC = 0.54 (95% CI =0.27 to 0.70)). A manuscript is being revised for Public Health Nutrition and the tool is undergoing further assessment for its sensitivity to change in the Tier 3 weight management service in Taunton.

Childhood Theme

Details of the progress of the theme's strategy

(1) The theme's strategy remains the study of lifestyle and nutritional interventions to improve the health of children with chronic disease. Whilst we have extended our work to include asthma, one of the most common chronic diseases in childhood, we have only done so as this condition appears amenable to significant lifestyle interventions mainly in terms of exercise. In our core work, we have made significant progress in understanding the influences of eating behaviours on calorie consumption in terms of genomics and neural/hormonal responses. We have also worked with colleagues in community child health exploring the influence of Chronic Fatigue Syndrome and child abuse/neglect on childhood obesity. We now have an active study on the influence of a low glycaemic index diet on glucose control in cystic fibrosis related diabetes. No dietary study has ever been undertaken in this condition before. Dietary manipulation to improve glycaemic control in young people with cystic fibrosis related diabetes (Clinical Academic Training Programme Internship Award to Birch L). We have a series of collaborations with UK SMEs on devices that can improve safety in children presenting and living with Type 1 diabetes. We have completed important national studies of the associations and outcomes of children developing type 2 diabetes and acute pancreatitis (the latter the first such study in the world). We have tested the feasibility and refined the collection methodology (with Genotek for microbiomic work), establishing the only birth cohort of children with Down's syndrome to study the influence of early feeding practices and the development of autoimmunity and its relationship to genomics and the microbiome. Within the NHS Trust and University, we have established links allowing us to study the influences of exercise on childhood diabetes and asthma.

(2) We have developed a close collaboration with the Nutrition Behaviour Unit (NBU) in Experimental Psychology allowing us to study parental opinions regarding optimal meal sizes for children at risk of obesity and how 'memory of meals' influences later eating habits. We have developed close links with staff in the MRC IEU allowing us to begin to understand the influence of obesity variant genotypes on eating behaviour.

(3) We have successfully applied for NIHR grants in two diseases related to chronic disease in childhood and plan further industry collaborative applications with at least two other studies nearing completion (both in type 1 diabetes)

a. EME (Treatment of Barth syndrome by CARDIOlipin MANipulation (CARDIOMAN): A randomised placebo-controlled pilot trial conducted by the nationally commissioned Barth Syndrome Service). £440,000 awarded. This is a randomised trial with qualitative and clinical input from BRU.

b. i4i Award. Feasibility study of breath ammonia device to manage children with the nutritionally treated diseases of the urea cycle (AmBeR). Industry collaboration with Breath UK. Hamilton-Shield PI with Breath Dx (UK SME) as partner: £750,000

(4) We have actively collaborated with the Loughborough/Leicester BRU Nutrition and Lifestyle at the request of NOCRI on an evaluation of a Health Kiosk for Cardiovascular Health Screening. We actively collaborate with Great Ormond Street Biomedical Research Centre on childhood obesity (Viner) and Urea Cycle Defects/device development (Abulhou). We have planned a collaborative study with the potential BRC in Exeter on further behavioural modifiers in children with obesity using 'Training response inhibition'.

Progress with leadership of the theme: The research area continues to be led by Professor Julian Hamilton Shield. Dr Kate Hawton joined the team in September 2015 for a six month, Elizabeth Blackwell/Wellcome, clinical primer using functional MRI scans to explore the neural/hormonal responses to eating slowly. She remains an affiliate of the team as does Dr Fiona Lithander a nutrition scientist (metabolic physiology) and dietitian.

Examples of effective translation, or significant progress along the translational pathway, as a result of NIHR BRU funding.

- (1) **NIHR i4i Award.** Feasibility study of breath ammonia device to manage children with the nutritionally treated diseases of the urea cycle (AmBeR). Industry collaboration with Breath UK. Hamilton-Shield PI with Breath Dx (UK SME) as partner: £750,000 –Starting in Late Summer 2016
- (2) **Cutaneous Hypoglycaemia detection device:** We have undertaken preliminary work on a previous manufactured device and have used that data with our industry partners (Cambridge Temperature Concepts. UK), to develop a specific device to detect nocturnal hypoglycaemia in children with type 1 diabetes. We are preparing to apply for a further i4i award using our current data to establish the devices clinical utility within the next 9 months.

Examples of the creation and development of intellectual assets through the work of the research theme

Intellectual assets in the form of publications conference presentations have resulted from work in this research area (see Publications section of Finance and Activity report).

5. PATIENT AND PUBLIC INVOLVEMENT AND ENGAGEMENT (no more than one page)

Patient and public involvement:

The Bristol Nutrition BRU's PPI strategy has been reviewed and updated (approved by the Executive in April 2016). Our work aims to meet the Unit's strategic aims by encouraging PPI in the design and assessment of feasibility/acceptability of research studies and seeking advice on the direction of our future work. Two new members have been recruited to both the Prostate Cancer and Perioperative Health PPI groups which now each have six members. A joint meeting was held in June 2015 where group members were given the opportunity to make suggestions on the future research directions of the BRU. The PPI lead, Dr Eileen Sutton, has worked with Dr Claire England to recruit and set up a new Diabetes Action Research Group (DRAG) comprising four members. Induction/training is provided for all group members. The new and established groups have supported the Unit's researchers by attending regular meetings and providing feedback on proposed and ongoing BRU research projects including suggesting changes to improve the readability of lay research summaries and explanations of continuous glucose monitoring equipment (*Stand up for your health2*). A PPI consultation was held at the Bristol Create Centre for interested participants from the *Stamp2* study who provided feedback on feasibility/acceptability to aid the design of the *PEDAL* study. Our group members have also provided advice to external researchers working in the NIHR Bristol Cardiac BRU (Gabapentin Trial). BRU researchers continue to liaise with existing local PPI groups for research in the Childhood Theme (i4i/UWE David Evans) and receive ongoing support for the FADES study from the Down's Syndrome Association. We have liaised with an external PPI group (Patient Experience in Research Group: PEP-R group) for condition-specific advice (developing prehabilitation intervention). Our researchers have also facilitated meetings with patients of clinical academics working in the UHB NHS Foundation Trust to gauge feasibility and aid the design of future research (EEN/ANTI-TNF study - Crohn's Disease study and Quantab study - estimating fluid status using urine dipsticks). The PPI lead has been trialling an assessment of our PPI activities using the PiiAF with the aim of capturing the impact of PPI activities in the short and longer term. Group members receive regular feedback on the progress of our work and details of any amendments to studies as a result of their input. The PPI lead regularly attends NIHR PPI Leads meetings and liaises with local PPI contacts in the CLAHRC and the WEAHSN, submits a quarterly report on PPI activities for approval by the Executive and authors an annual report of our PPI work which is available via the Unit's website.

Public engagement:

The Bristol Nutrition Biomedical Research Unit is committed to public engagement. We have a Public Engagement Lead, Rachel Perry, and a Unit Engagement Policy to guide engagement activity within the unit. It was developed with support from the University of Bristol Centre for Public Engagement, discussed with BRU staff and agreed by the BRU Executive. Prof Hamilton Shield has regularly been asked to comment in the lay media (Panorama, News at Ten, Telegraph, Guardian, Daily Mail) on Nutrition related issues. We continue to work with the University and Trust to support their strategies and centrally organised engagement activities (we have run a stall at the Clinical Trials Day for the past three years). We have led the IDEAL Community Project to support the delivery of a new health-related module in their peer-mentoring scheme for people. Members of the BRU worked with the IDEAL Community Action Group to support the delivery of a new health-related module. IDEAL offers a peer-mentoring scheme for people affected by issues such as drugs and offending. Three initial workshops have been undertaken so far, designed to offer participants a taster course on Nutrition. Over the course of three weeks, talks were delivered on national nutritional guidelines and the hidden dangers of sugar. Particular emphasis was placed on developing the participants' critical awareness skills regarding claims made about health, food and diet in the popular press. This 'behind the headlines' focus lead participants to research a health food claim of their choice and present their findings to the group. We are currently working with the project co-ordinator, Nick Bentley, to evaluate the pilot work and look forward to further work with the group. We had planned to expand our Engagement work with school-aged children by collecting real-time data in a school setting around the theme of asthma. Unfortunately due to staff changes within the school and difficulties in gaining shared responsibility of the project, this work has been put on hold. However, Dr Elanor Hinton continues to actively engage with sixth form children from Redland Green School. Our Engagement policy is reviewed and updated annually. The engagement lead regularly updates the team with Engagers' Digest which enables them to find engagement activities that they are interested in. Engagement progress is written in a quarterly report and sent to the Executive team.

Please also describe how you make patients and the public aware of the research being undertaken within your Unit, and signpost them towards appropriate information about participating in research. PPI and Engagement Policies are both available on the Bristol Nutrition BRU website and all activities are regularly reported on the News section of the website.

6. TRAINING (no more than two page)

Our aim is to ensure equitable opportunities to enable the development of all clinical and non-clinical staff and students within the BRU. We have continued to offer a wide range of training opportunities, as described in our training policy (see <http://www.uhbristol.nhs.uk/research-innovation/our-research/bristol-nutrition-bru/training/>). Activities and opportunities in the training policy are grouped into five areas which are briefly described below, along with some highlights from the past year.

1. Students and placements

- *Studentships*: Four PhD students (three non-clinical and one clinical) have been, or are being, fully (n=3) or part (n=1) funded by the BRU. In the past year one student successfully defended her thesis, one submitted her thesis and is awaiting her viva, one is finalising her thesis, and one has research studies that are ongoing (and has just returned from maternity leave). The BRU also part-funded an MRes student who recently passed her viva, and currently part funds and hosts an MD student (and hosts one other MD student), and hosts an NIHR Research Methods Fellow. The BRU will host two Academic Foundation Placement students from August 2016.

- *Internships*: These are aimed at post-graduates looking to obtain experience in the areas of scientific research administration or clinical trial management. Building on the success of our previous intern [who is now doing a PhD at the University of Bristol (UoB)] we have appointed two 6 month internships to start in September 2016.

- *Dietetic research training*: The BRU's designated Dietetic liaison lead (Laura Birch) continues to work closely to support research training and development for clinical dietetic colleagues in the UHBristol NHS Trust. Ongoing activities include research workshops and the provision of individualised advice to local dietitians looking to set up research studies. One of these studies has recently been awarded NIHR funding as part of a Masters in Clinical Research and will be supported by the BRU. Laura attends dietetic departmental meetings to notify dietetic colleague of research events such as the BRU seminar series and any other relevant training opportunities.

2. NHS and University Training

- *Generic / core training*: All BRU staff and students are encouraged to attend generic and core training courses offered by the Trust and UoB.

- *Good Clinical Practice (GCP)* and other mandatory training: All BRU staff and students have access to mandatory training such as GCP training courses and information security.

- *Short Courses*: These courses are run by the School of Social and Community Medicine at the UoB, and cover a range of health services research and epidemiological methods, as well as generic research skills. In the past year, five places on these courses have been funded by the BRU.

3. NIHR Training

- *NIHR training opportunities*: All BRU staff and students who are part or fully funded by the NIHR have the opportunity to take advantage of the courses and training meetings offered by the NIHR. One PhD student attended the NIHR summer school residential course at Ashridge in July 2015, and one attended the course in July 2016. Staff and students are notified of (and encouraged to participate in) NIHR-led webinars, and information on other training opportunities is cascaded to members of the Unit by the Training Lead.

4. BRU Internal Training and Staff Review

- *Reading Group*: The BRU has run a number of reading groups which all staff and students within the Unit are able to attend. Examples have included covering key basic methodological texts or specific articles / book chapters over several weeks to provide a platform for learning and discussion away from day to day tasks.

- *Present and Discuss*: The BRU holds regular Present and Discuss meetings. These provide an informal platform to talk about current or previous work, lessons learned from prior work, to practice a presentation, or to discuss developments in or changes to relevant processes and procedures (e.g., ethics, open access requirements, etc.). BRU staff, students, affiliates, and visiting fellows, in addition to other UoB and UHBristol staff and students, have presented at and attended these meetings.

- *Research Methods course*: All BRU staff and students have access to training on research methods, which consists of a series of e-lectures that have been developed by Dr Sam Leary (Senior Lecturer in Statistics, and member of the NIHR statistics group). Three associated 2-hour tutorials can be used in conjunction with the e-lectures to augment / reiterate information presented in the e-lectures.

- *Training Days*: Training workshops / seminars have been run with support and input from additional UoB and Trust groups and the NIHR, including the Research Design Service Southwest, Research and Innovation, and the UoB library services.

- *Team Building and Away Days*: The BRU from time to time runs Team Building Events (an example is working in teams to cook our own Christmas dinner at a local charity, The Square Food Foundation) and Away Days to further encourage cross-Unit interactions and to allow a more strategic discussion of topics related to the Unit. In the past year we have held a series of away days to facilitate strategic discussions for development of the Unit, including away days for BRU executive group members, BRU theme leads and affiliates, and BRU staff and students. We have arranged a 'Mindset Management Training' day in September 2016 for all interested staff and students.
- *Travel and Conferences*: BRU staff and students are encouraged to attend relevant national and international scientific meetings, and individualised training budgets fund or part fund these meetings.
- *Staff Review*: All staff are encouraged to meet regularly with their line manager / key colleague, and to undergo formal staff review once a year (at which training needs are discussed).
- *Co peer review*: Senior staff are encouraged to co peer review manuscripts with junior staff.

5. BRU Open Training

- *Seminar Programme*: The BRU continues to run a formal CPD accreditable seminar programme. Seminar speakers include both internal and external people and attract a varied audience. In addition to broadening knowledge base, they provide a valuable opportunity to develop collaborations.
- *Workshops*: Following the success of the pilot three-day 'Nutritional Epidemiology - An introduction to issues in analysis and interpretation of dietary data' course in 2015, the BRU ran this as a fee-paying course in 2016. The course had been updated based on feedback from the pilot, and covered areas such as nutrition research methods and the analysis of nutrition data. Attendees included staff and students from within the BRU, the Leicester/Loughborough BRU, and other national and international academic institutions. Feedback was excellent with a mean rating of 9/10 when combining all ratings (mean of individual sessions ranged from 8.0 to 9.8).
- *Sabbaticals and visiting fellows*: An agreement is in place between the BRU and the Institute for Advanced Studies (IAS) at the UoB regarding support for BRU Sabbaticals. These are run through the IAS, with one of a proposed two annual sabbaticals being funded by the IAS subject to them being competitive. In the past year the BRU has hosted Dr Sorrel Burden on a three month sabbatical from the University of Manchester, and Dr Brigid Lynch on a one week sabbatical from the Cancer Epidemiology Centre, Cancer Council Victoria.

Summary

As shown above, the training within the Bristol Nutrition BRU covers a broad range of areas and, as such, aims to develop staff in all clinical and non-clinical professions. We have a named Training Lead (Dr Charlotte Atkinson) along with a dedicated training budget, and we encourage all staff and students to take advantage of the opportunities available to them.

• Specific training plans for the BRU

In the next year, we will continue to facilitate access for BRU staff and students to a wide range of training opportunities both in house and elsewhere, as detailed above and within the training policy.

• Ongoing or planned collaborative training, secondment or networking with other parts of the infrastructure.

We have continued to share ideas with the training leads at BRU/Cs with an interest in nutrition and physical activity (Leicester/Loughborough and Southampton) through our Nutrition and Physical Activity Collaborative (see http://www.uhbristol.nhs.uk/media/2556091/npa_collaborative_bru_4.pdf for more information). Reciprocal training opportunities have been offered across these parts of the infrastructure, including the provision of free places on training courses that are usually run on a fee-per-person basis (e.g., the Nutritional Epidemiology course in Bristol and the MEASURE 2016 course in Leicester/Loughborough), and participation in relevant research meetings via live streaming (e.g., Leicester/Loughborough 'ACES' meetings during which staff and students can present and discuss their research).

• Overall amount of expenditure on training for this year

The total expenditure on training and conferences during 2015-2016 was £6,858 (NB - this does not include staff time costs).

7. LINKS WITH INDUSTRY (no more than two pages)

7.1 Please outline your NIHR BRU's progress against its strategy for engaging with industry, separately as appropriate in the following sectors: with i) pharma, ii) biotech, iii) medtech/devices, iv) *in vitro* diagnostics, v) CRO's, vi) non-life sciences companies. For each sector please describe any significant successes or any challenges faced during financial year 2015/16. Please also outline any strategic plans for increasing engagement with industry that are not outlined in your application.

Since the last annual report, significant progress has been made in our Industry portfolio. Our progress was commended by our Strategic Advisory Board for industrial partnerships in the field of nutrition.

We continue to work very closely with Breath Dx: see section 7.5 for further details.

Cambridge Temperature Concepts (UK): Development and testing of a cutaneous device to recognise hypoglycaemia in children with diabetes whilst asleep has almost completed its evaluation as a reliable indicator of hypoglycaemia. We now plan to submit an i4i or equivalent grant application to conduct a proof of concept study in children at home.

Maltron: BIOSCAN 920 – II: Evaluation of bio-impedance device for evaluation fluid shifts (extra cellular/intracellular fluid) in diabetic ketoacidosis in children with type 1 diabetes to ensure safer resuscitation. This study has recently started recruiting and has so far recruited 3 of the 20 patients required for the feasibility study. New presentations of Type 1 diabetes in DKA is seasonal and we expect more from September 2016. It is already showing interesting data on compartmental fluid shifts on rehydration.

Pilot study to evaluate the performance of the DNA Genotek Stool Collection Kit compared to a standard stool self-collection kit for microbiome analysis. Completed. We have demonstrated that the Genotek sampling kit retains the true microbiome as if taken and analysed fresh, unlike samples taken in normal containers, thus allowing us to use this kit in our national cohort study with the parents simply posting the sample using Royal Mail. The paper is currently being prepared for a suitable microbiology/microbiome publication.

The findings of the completed Wellpoint Kiosk study has now been written up as an abstract and presented at the Annual Scientific Meeting of the Society of Occupational Health 2016 (27-30 June 2016, Stratford-upon-Avon). A full paper is in preparation.

We have signed a Confidential Disclosure Agreement (CDA) with HACH Lange UK to examine whether we could potentially use a product they currently make for non-medical purposes as a health technology to evaluate very simply, dehydration without the need for venepuncture in those with gastro-intestinal disorders and in the elderly population living in care.

One of our Research Associates, Dr Elanor Hinton has arranged a six-month secondment with Nutricia in order to continue to foster this industry/researcher link. We also intend to undertake a joint project of Nutritional Information Provision for patients in collaboration with this company.

Since the BRU co-authored publication of a systematic review in the International Journal of Obesity, the BRU are in active discussions with David Mela from Unilever. He is interested in seeing if Unilever could fund a further review on low energy sweeteners in relation to dysglycaemia and diabetes. The original review was regarding low-energy sweetener consumption and body weight, commissioned by International Life Sciences Institute (ILSI)

We have completed a NOCRI Expression of Interest for an opportunity to partner with Electric Bike Research Executive (EBRE), a pan UK-Scandinavian not for profit organisation. EBRE would like to explore the clinical value of the patient use of electrically-assisted-pedal-cycles within a wider treatment procedure for a variety of health conditions such as rehabilitation from orthopaedic surgery / sports injuries and health problems associated with obesity / poor diet and lifestyle.

Our strategic plan to increase engagement with industry includes utilising our links with secondary care (in particular Bristol Children's Hospital) to identify groups of patients with particular needs for improved disease monitoring to be used in proof of concept device testing and to feedback patient experience to device manufacturers. We also have access to patient groups from the Bristol Urological Institute, the Bristol Dental Hospital, and the Bristol Royal Infirmary. In addition, we have links to Bristol Robotics Laboratory and SPHERE- a Sensor Platform for Healthcare in a Residential Environment (University of Bristol EPSRC funded).

7.2 Please indicate the total number of UK Small and Medium Enterprises (SMEs) you have worked with during financial year 2014/15 and provide brief details of key examples. Please list ALL UK SMEs that you have worked with during 2014/15 in the Finance & Activity Report (BRU Finance & Activity Report 2014-15.xls).

We have worked with a total of six UK Small and Medium Enterprises, with brief details described above and noted on the Finance and Activity Report.

7.3 Please provide details of; i) any new strategic partnerships between your Unit and industry during financial year 2014/15 ii) the progress of ongoing strategic partnerships between your Unit and industry during financial year 2014/15. Please list all new strategic partnerships between your Unit and industry during 2014/15 in the Finance & Activity Report (BRU Finance & Activity Report 2014-15.xls).

We have no formal strategic partnerships to report but a series of project based collaborations as described above. We are hoping to form a strategic partnership with Nutricia and the development of a joint PhD opportunity. A further secondment is planned from October 2016- March 2017.

7.4 Please provide brief details of key examples of studies active in financial year 2014/15, as follows:

- **Contract commercial trials**
- **Industry collaborative research studies**
- **Other academic commercial research**

We do not have any Contract Commercial Trials at present. In the financial year 2015, the four Industry Collaborative studies are:

(1) Evaluation and validation of a breath ammonia measurement technology for the improved management of patients with urea cycle defects (Breath Dx UK)

(2) Evaluation of bio-impedance device for evaluation fluid shifts (extra cellular/intracellular fluid) in diabetic ketoacidosis in children with type 1 diabetes to ensure safer resuscitation. (Maltron)

(3) Study of user decision making subsequent to using health kiosk within United Bristol Hospitals NHS Foundation Trust: analysis of study data currently underway (Wellpoint)

(4) Pilot study to evaluate the performance of the DNA Genotek Stool Collection Kit compared to a standard stool self-collection kit for microbiome analysis (Genotek).

We are planning an i4i bid to develop and test a cutaneous device to recognised hypoglycaemia in children with diabetes whilst asleep with Cambridge Temperature Concepts. The final aim would be to produce a device that alerts parents to episodes of hypoglycaemia.

7.5 Please provide the number and key examples (including name of funder/grant scheme) of any partnerships or studies with industry which have led to further industry, public or charity research funding, including as part of consortia.

Professor Julian Hamilton-Shield's proposal "Evaluation and validation of a breath ammonia measurement technology for the improved management of patients with urea cycle defects" has been awarded together with Breath Dx, a UK SME, an Invention for Innovation (i4i) funding award as part of the NIHR Long-term Conditions in Children and Young People Themed Call.£750,000. Study starting late summer/early autumn 2016.

7.6 Please provide the number of Agreements signed with industry during financial year 2015/16 and provide brief details of key examples, as follows:

- **Non-Disclosure Agreements**
- **Model Trial Agreements including mICRA and mCTAs**

Number of agreements signed with industry:	
Non-Disclosure Agreements	1
Model Trial Agreements including mICRA and mCTAs	0

8. LINKS WITH OTHER NIHR INFRASTRUCTURE (no more than one page)

The Bristol Nutrition BRU has built up a network of UK Collaborations, including Aberdeen, Birmingham Bournemouth, Cambridge, Leicester, Leeds, Manchester, Plymouth, Southampton and Taunton.

We continue to host an NIHR Rare Disease Translational Research Collaboration research fellow - Ethan Sen – who is working on nephrotic syndrome. His supervisor Professor Moin Saleem is now a BRU affiliate. Bristol is also a collaborator in another NIHR Rare Disease consortium proposal in Type 2 diabetes in children. Rachel Perry, Dr Charlotte Atkinson and Professor Andy Ness are working with Dr Maria Pufulete in the Bristol Cardiac BRU regarding a joint BRU project in pre-surgical care. Dr Sam Leary is a member of the NIHR Statistics Group. She attended the Feasibility and Pilot Studies Workshop in April 2015 hosted by the group, and fed back the relevant information to the BRU staff in a "Present and Discuss" session. She has now become the Membership Secretary for the group, and will attend the next Steering Group meeting to discuss plans for taking this role forward. She has also volunteered to host an NIHR Statistics Group event such as a workshop in Bristol in the future. Dr Sam Leary, with Dr Jessica Harris set up a joint statistics group in 2013 with the NIHR Bristol NIHR Biomedical Research Unit for Cardiovascular Disease which has expanded to include CLAHRC West and the two Bristol Clinical Trials Units. The group meets quarterly.

Directors, Managers and Training leads from Bristol Nutrition BRU, Leicester-Loughborough Nutrition BRU and the Southampton BRC hold regular meetings supported by and attended by NOCRI. We rotate the location between the three groups to share plans, progress and policies. The benefits of this collaboration are:

- **Exchanges of ideas and capacity building:** This gives managers, training and PPI leads the opportunity to exchange ideas giving added value and synergy to the three groups. In addition, the Bristol Nutrition BRU, the Leicester- Loughborough Nutrition BRU and the Southampton BRC Directors and Managers engage in a monthly teleconference. The 3 groups have produced a joint document "Nutrition and Physical Activity Collaborative 2012-2016, acknowledged by NOCRI and now shared on our individual websites.
http://www.uhbristol.nhs.uk/media/2556091/npa_collaborative_bru_4_.pdf
- **Standard Operating Procedures:** NIHR Southampton BRC Standard Operating Procedures are now available on their website and after peer review it is planned that these documents will be shared on Bristol and Leicester-Loughborough websites as a valuable resource for each institution's research. Further joint SOPs on dietary assessment and body composition are planned.
- **Training:** Bristol BRU ran a three day course on the analysis of dietary data (Nutritional Epidemiology Course) in 2015 and offered free places to the Leicester/Loughborough BRU and Southampton BRC. This was repeated in May 2016. Leicester Loughborough offered Bristol and Southampton colleagues free places on their MEASURE course which in 2016 Luke Robles and Eleanor Shingler from Bristol Nutrition BRU attended.
- **Research Meetings:** We have now held two joint "virtual research meetings" utilising technology- these are sessions for trainees to present via video link with senior members of staff from the reciprocal unit acting as discussants. This is a successful venture we intend to continue.
- **Joint Research:** A collaborative piece of work, Evaluation of the Wellpoint Healthcheck kiosks was the result of NOCRI introduced collaboration with industry, carried out in conjunction with Leicester/Loughborough BRU. A jointly authored abstract "The role of Wellpoint Health Kiosks: a service evaluation study" was accepted as a Poster presentation at the Society and Faculty of Occupational Medicine Annual Scientific Meeting on July 27th 2016.
- **Grant Awards:** Professor Sian Robinson, Southampton BRC and Professor Andy Ness are both Co-applicants on an MRC Grant award (Partnership and Innovation in Dietary Assessment for Improvement Technology, PI Janet Cade).

Please also outline any strategic plans for increasing engagement with these NIHR Infrastructure schemes:

We will continue to meeting with our local BRU and BRC and with the nutrition BRU and BRC to further develop collaboration. We will also aim to work closely with CLAHRC West, hosted by University Hospitals Bristol NHS Foundation Trust which offers opportunities to strengthen our link to ongoing and new applied research. We have specifically identified the area of information provision and active travel as areas of collaboration. We are also supporting Cancer and nutrition NIHR infrastructure collaboration (Professor Richard Martin is on the planning group).

9. IMPACT IN HEALTHCARE PROVISION (no more than one page)

Please list any significant new work showing how your Unit is translating its work into practice for the benefit of patients within your Trust and influencing its translation further afield; you may also summarise significant developments in examples reported previously.

As highlighted previously two policy relevant reviews have been published in this reporting period:

- Omega-3 fatty acids and depression in adults: a Cochrane review – in this review we focussed on people with clinical depression.
- Systematic review of animal and human studies of low energy sweeteners on appetite and obesity

Two Cochrane Podcasts have also been published:

<http://www.cochrane.org/podcasts/10.1002/14651858.CD006506.pub3>

http://www.cochrane.org/CD004692/DEPRESSN_omega-3-fatty-acids-depression-adults

Please also describe examples of work which has significant potential to improve patient outcomes or experiences in the future, setting out how the Unit plans to ensure that these potential benefits are realised.

- Our pilot study to evaluate the performance of the DNA Genotek Stool Collection Kit compared to a standard stool self-collection kit for microbiome analysis has demonstrated that the Genotek sampling kit retains the true microbiome as if taken and analysed fresh, unlike samples taken in normal containers, thus allowing us to use this kit in our national cohort study with the parents simply posting the sample using Royal Mail. This was commended by our Strategic Advisory Group as an important piece of work to disseminate to alter and improve research practice.
- Professor Julian Hamilton-Shield's "Evaluation and validation of a breath ammonia measurement technology for the improved management of patients with urea cycle defects" i4i funding award, by allowing more frequent and accurate measuring of ammonia could reduce intensive care admissions and haemofiltration and improve long term cognitive outcomes in children with these conditions.
- In our preliminary, observational study Evaluating a bio-impedance device for evaluation fluid shifts in diabetic ketoacidosis in children with type 1 diabetes, we are investigating whether changes identified by bio-impedance in ICF and ECF directly correlate with changes in hydration status and osmolality during conventional clinical management of. This has the potential to lead to safer resuscitation and prevent cerebral oedema (a rare but very serious complication of DKA).
- We are planning an i4i bid to develop and test a cutaneous device to recognise hypoglycaemia in children with diabetes whilst asleep with Cambridge Temperature Concepts. The aim is to produce a device that alerts parents to episodes of hypoglycaemia.
- We have signed a Confidential Disclosure Agreement (CDA) with HACH Lange UK to examine whether we could use a product they currently make for non-medical purposes as a health technology to simply and quickly assess dehydration in those with gastro-intestinal disorders receiving long term parenteral nutrition and in the elderly population living in care.
- We are exploring a translational route by which cycling may improve the health of people with T2D with colleagues in Sustrans Newcastle. The Stockton CCG has part funded, in collaboration with Bristol BRU, a pilot scheme for GP referral of patients with T2D to Sustrans for 6 weeks of active travel coaching/facilitation, using self-monitoring of physical activity to support behaviour change. The Bristol BRU is providing the overarching evaluation of physical activity and spatial mobility. This intervention is ongoing to March 2017.

In addition to these specific examples of future planned directions, two of the four substantive themes have secured funding to take forward research to larger patient outcome focussed trials. Some of our qualitative work across themes (particularly from the peri-operative and sedentary themes) may lead to implementation studies (potentially in partnership with CLARHC West).

10. OTHER COMMENTS (no more than one page)

Please use this space to provide us with any other information you would like to highlight, or comments you would like to make.

This form, together with the BRU Financial & Activity Report and an Added Value pro forma (using the structured template provided) must be submitted, by email, no later than **1pm on Friday 29 July 2016** to Dr. Katie Cook (Katie.cook@nih.ac.uk).

A signed copy of this report should be sent no later than **Friday 5 August 2016** to:

Dr Katie Cook
NIHR Central Commissioning Facility
Grange House
15 Church Street
Twickenham, TW1 3NL