Acknowledgements

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Foreword

It is predicted that cancer will increasingly be the most frequent cause of death and a major cost to the delivery of health care over the next 30 to 40 years. Good nutritional state is integral to the prevention of cancer, as well as to the treatment of the disease and end of life care. The general public look to doctors and other health professionals for clear guidance on how they can help themselves. Doctors in turn look to researchers for the evidence that will enable clear answers to the difficult questions they are asked. There are superb researchers studying many aspects of cancer and its treatment, but they seldom worry themselves about nutritional considerations. There are outstanding researchers exploring aspects of food, nutrition and physical activity, but cancer does not feature as a main concern on their agenda. We would like these two groups of researchers to draw on each other’s skill and experience to enable insight and add value to their respective efforts. The availability of this greater knowledge and understanding can then be the basis of better advice and support to those who deliver, and receive, services.

In early 2014, Professor Alan Jackson and his team at the NIHR Southampton BRC, together with the World Cancer Research Fund (WCRF UK), supported by NOCRI, recognised the need to bring coherence to existing activities in the area of cancer and nutrition and provide a coordinated framework for future research into these areas.

This summary report provides an overview of the initiative from its conception (Spring 2014) to the completion of the first phase (March 2015) and outlines the main areas of consideration: a patient experience survey, a clinicians’ survey, a mapping of cancer and nutrition research activities in the UK and stakeholder engagement. The report also provides recommendations for the next phase of work. An extended version of the report is freely available on the collaboration’s website www.cancerandnutrition.nihr.ac.uk

Nutrition and cancer: working definitions

The collaboration uses the following definitions of cancer and nutrition:

**Nutrition**

Nutrition is the set of integrated processes by which cells, tissues, organs and the whole body acquire the energy and nutrients for normal structure and function, which is achieved at body level through dietary supply, and the capacity of the body to transform the substrates and cofactors necessary for metabolism. All of these domains (diet, metabolic capacity, body composition and level of demand for energy and nutrients) are influenced by levels of physical activity and can vary according to different physiological and pathological or disease states.

**Cancer**

All types, sites and stages of cancer are included in our definition. Stages of cancer include prevention, diagnosis, treatment, survivorship and palliative and end of life care.

These definitions were written and agreed by the Task and Finish Group at the start of the mapping activity to ensure the mapping was as comprehensive as possible.

Key activities

The following activities were planned and delivered in phase 1:

1. A patient experience survey for cancer patients to understand their experiences of nutritional care during the cancer process and perceived gaps in this care.
2. A clinicians’ survey to collect information about routine practices of nutritional care and support for cancer patients as well as clinicians’ perceptions of the major gaps in terms of evidence, research and care.
3. A mapping of the cancer and nutrition research awards in the NCRI database from 2009 to 2013 to characterise the extent of cancer and nutrition research in the UK.
4. Stakeholder engagement activities to build a community of practice made up of patients, researchers and clinicians.

The results from these activities were triangulated in order to help identify gaps in research, evidence and clinical practice in relation to nutrition and cancer and to develop priorities for future work.

Patient Experience Survey

In recognition of the importance of translational research and the need to deliver quality nutritional care to cancer patients, we conducted a patient experience survey with the aim of understanding perceived gaps in nutritional care and support. The survey was open, online and available for eight weeks (January – February 2015). It sought to answer the following questions:

- Are patients being given consistent, evidence-based advice?
- What other nutritional support, advice and care would patients like to receive?
- What are the major gaps in service provision at diagnosis, during treatment and after treatment?

Summary of results

A total of 96 responses were received; 71.9% were female and most participants were aged between 60-69 years (33%) and 50-59 years (29%) (Figure 2).

Patients were asked what nutritional problems they faced as a result of their cancer. The most commonly reported problems were changes in taste and smell (70%), appetite loss (69%), followed by nausea and vomiting (56%), being unsure what to eat (56%) and inability to be physically active (56%) (Figure 3). Of these, the most commonly reported nutritional problems were all those related to the side effects of chemotherapy.
Patients were asked about the quality and consistency of nutritional advice at different stages of cancer. Of the 22 patients who answered, most said that the advice was easy to follow, and it was consistent (more so at treatment and after treatment than at diagnosis). Figure 5 shows how well patients believed their nutritional needs were met according to the treatment phase.

The majority of patients (n=64) said they would like additional nutritional support at all stages of treatment. Patients commonly reported feeling confused and vulnerable when suffering from cancer (‘I only found out what to eat by trial and error’) and would like more support to reduce these feelings. There was some contradiction with other patients who reported feeling like they had information overload, which made them feel “ultimately clueless”.

Key findings

1. Many patients reported unsatisfactory experiences of nutritional care in relation to cancer
2. Particular gaps identified by patients include how to deal with side-effects of chemotherapy, weight changes and specific foods and diets that patients should or should not consume.
3. There is a need for better evidence to allow more reliable and consistent nutritional and dietetic information for cancer patients

Clinicians’ survey

We also conducted a survey of UK clinicians working in cancer and/or nutrition to understand their perceptions of the major gaps in terms of evidence, research and care in relation to nutrition and cancer. Specifically, the survey sought to answer the following questions:

- What kind of nutritional support, care and advice do clinicians give to cancer patients?
- Is nutritional status routinely assessed in cancer patients and if so how?
- What are the top three priorities for cancer and nutrition research in the UK?
- What are the main barriers to conducting nutritional research?

The survey was available online for a period of three weeks during February 2015.

Summary of results

A total of 77 participants completed the survey (Figure 6). Seventy per cent of respondents reported that they actively assess or manage the nutritional status of their cancer patients (Figure 7). Of those who do not do so, their reasons included not being able to do so because they do not feel adequately trained (n=23), that they do not have access to relevant infrastructure (n=7) and that it is not a necessary part of their work (‘not of primary importance to their patients’) (n=10).
The most common methods that clinicians reported using to assess patients’ nutritional status was simply by measuring weight, body composition (DXA) and waist circumference. Dietitians also use MUST (Malnutrition Universal Screening Tool) when concerned about a patient’s weight. Other assessments mentioned included grip strength, muscle function, the Oxford equation and malabsorption indicators (e.g. stool colour). Two dietitians said they were restricted by time and therefore not able to conduct detailed anthropometric and nutritional assessment of patients. This was particularly an issue for patients who have finished their treatment as dietitians could “only provide very limited services to patients to promote survivorship after treatment”.

It was also mentioned that there are no robust national training programmes on nutrition and cancer for specialists or for dietitians post registration; competence is based on clinical experience and improvement through self-study, for example journal clubs. This suggests that there are specific training needs within the fields of cancer and nutrition to be able to provide better nutritional support and care. Clinicians were asked what barriers exist in undertaking nutrition and cancer research. The most common barrier was the perceived difficulties in securing funding, frequently attributed to an under appreciation of the problem; one dietitian said there is an “almost complete failure of the oncology community to take nutrition and lifestyle seriously”. Getting funders, clinicians and the research community to recognise the importance of nutrition can be “extremely difficult”. Money is reportedly frequently given to small pilot studies that duplicate each other, rather than putting funding into large scale trials that produce high quality epidemiological data on lifestyle factors and outcomes. Another barrier to research is poor national infrastructure in which to undertake research: “there is lack of structure and co-operation between different organisations. Whether it’s NHS or charities such as Cancer Research, more needs to be done to bring organisations together to help improve nutrition and cancer for patients”. More personnel with time dedicated to research are needed, for example specific oncological dietitians. Clinical dietitians would like support from peers and colleagues to undertake research as well as additional time around their “already heavy workloads” to do so: “proper collection of patient data and patient education/follow-up with regards to nutritional issues is a laborious process if bias is to be avoided”.

Clinicians identified a need for better data and more high-quality research. Epidemiological data are “flawed in cancer patients due to confounding and poor data on treatment and histology and much more work is needed”. Interventional studies are hard to conduct given the large numbers of participants needed, and adequate blinding, controlling for bias and randomisation are also problematic. There are also ethical issues in undertaking randomised controlled trials: populations may be too unwell to cope with the demands of participating in a trial, for example the time needed to attend extra appointments. The time it takes to submit ethical and research applications may also prevent clinicians from undertaking research whose clinical commitments occupy their time.

**Key findings**

1. Incorporation of nutrition in cancer care is challenging.
2. More large-scale interventional trials are needed, but they are difficult to conduct for practical (funding and infrastructure) and ethical reasons.
3. Better evidence is needed to produce meaningful advice for patients and recommendations for clinical care.
4. Nutritional assessment is not carried out in a systematic way.
5. There is insufficient training for dietitians and other clinicians wishing to specialise in nutrition and cancer.

**Mapping**

**Rationale for mapping activity**

The mapping exercise looked at data from the National Cancer Research Institute (NCRI) from 2009 to 2013 to characterise the extent of cancer and nutrition research in the UK. Although this database excludes several smaller but important funders (e.g. WCRF), it was chosen because of its wide coverage, inclusion of all study types and systematically coded information on cancer research areas and cancer sites. Subject to adequate resourcing, the mapping could be extended to five to ten years in the future.

**Methodology**

In total, 14,439 award entries were in the original NCRI database. After removing duplicate awards (awards that were active for more than one year and thus had multiple entries), 6,579 unique awards remained and were imported into a custom made Access database (Figure 8). Searching the Access database using predefined nutrition keywords identified 1,408 awards, of which 158 (11%) were included for analysis. Codes were then given to each included award to define the study type, study design and nutrition element studied. Full details of the methodology used in the mapping are available in the full report.
Summary of results

The most frequently studied nutrition themes, according to the number of awards, were lifestyle exposures and nutrition, included in 44% and 37% of awards respectively. A breakdown of the nutrition themes into sub-themes (there were no sub-themes within metabolic conditions) is shown in Figure 9. A full list of the nutritional themes and sub-themes used with examples is available in the full report.

A significant proportion (80%) of the included awards was human studies, with only a few awards being made to animal and in vitro studies (see Figure 10). The stringent exclusion criteria applied during the mapping may have excluded some animal and in vitro studies. There was a large spread of different study types within ‘nutrition’ studies. Most of the human observational research was on understanding the link between lifestyle exposures and cancers (69%). In vitro studies were predominantly used to study metabolism (45%) with very few human studies in this area.

*After the mapping started, the group decided to include lifestyle as a keyword and remove smoking: smoking is considered an environmental carcinogen rather than a nutritional factor.

* Awards may investigate more than one nutrition theme.
For 10 cancer sites with the highest cancer and nutrition spend, an analysis of cancer and nutrition spend as a proportion of the total cancer research spent in the NCRI database was performed (see Figure 11). The greatest nutrition-related cancer research spend was on non-site-specific cancers (£14.3m, 2.6% of total research spend on non-site-specific cancers), and colon and rectal cancer (£10.8m, 9.3% of total research spend on colon and rectal cancer). The proportion spent on nutrition in relation to testicular cancer was greater (16%). However, as we were unable to estimate the proportion of spend attributable to nutrition in individual awards and there were only three awards for testicular cancer research, it is possible that this observation is skewed by the large size of these awards.

There was more money spent on aetiology (CSO2) and prevention (CSO3) than other categories. Investment in early detection, diagnosis and prognosis (CSO4) and cancer control, survivorship and outcomes (CSO6) research was reduced during the five-year period, whereas biology (CSO1) and treatment (CSO5) research increased (Figure 12).

Key findings

1. A small proportion of cancer research awards included an explicit nutrition component (11%).
2. A large proportion (80%) of included awards were human studies, more than a third of which looked at the relationships between non-site specific cancers and lifestyle exposures without specifically characterising a nutrition theme. These human study awards were predominately for:
   - Supporting large cohort studies to collect dietary data and specimens, or conduct statistical data analysis
   - Understanding the effects of nutrients or nutritional status on cancer risk by using observational or interventional data
3. There were only a small number of relevant animal and in vitro study awards, which may be due to the stringent exclusion criteria applied. However, animal studies explicitly exploring at the link between cancer and nutrition were included, e.g. a mouse prostate cancer model to test oral supplements
4. The most frequent specific cancer sites studied in relation to nutrition were colon and rectal cancer, breast cancer, lung and oesophageal cancer. These cancer sites have most potential preventability through diet and physical activity.
Stakeholder Engagement

As a collaborative initiative, involving and engaging key stakeholders is integral to our work and has been a focus from the collaboration’s inception. We have sought to be as inclusive as possible, keeping interested parties informed at each stage.

We have given presentations at a number of meetings and conference (e.g. NCR conference 2014, the UK Therapeutic Cancer Prevention Network [UKTCPN] meeting, October 2014) and engaged a range of other organisations to give publicity to our work (e.g. CRUK and WCRF UK).

Building a community of practice

A primary aim of our work is to build (and maintain) a community of practice of researchers and clinicians working in nutrition and cancer and to foster better collaborative working in these important areas. The following methods have been employed to achieve this:

1. Named individuals identified as points of contact at major organisations; contacts are asked to disseminate news and updates within their networks to increase publicity further;
2. A dedicated website to provide information about the initiative to interested parties;
3. an online discussion forum (via website) for interested parties to share ideas; it is the hope that this will grow considerably as the collaboration develops;
4. A mailing list to share results of the mapping and additional updates; an invitation to join the mailing list is on the home page and invites all researchers, clinicians and patients to sign up;
5. Presentations at stakeholder events to raise awareness and provide updates (e.g. NCRI conference);
6. Support from NCR communications teams to broadcast news and produce promotional materials.

Public and patient involvement

Ultimately, patients are the intended beneficiaries of improved research in nutrition and cancer, and should have an opportunity to voice their concerns and suggestions.

We were invited to take part in the Consumer Liaison Group’s Dragons’ Den session at the 2014 NCRI conference; the Dragons’ Den is a relatively informal opportunity to run focus groups with patients and consumers who have experience of cancer research (and a potential personal interest in the proposed topic). We used this opportunity to understand the best way to engage patients in the initiative.

The results of this session formed a major part of our PPI strategy; in particular the decision to conduct a patient experience survey. We also subsequently invited a PPI representative to sit on the Steering Committee (from December 2014) to ensure that patients’ opinions were represented in all decisions the collaboration makes.

“...I think this is one of the most exciting new initiatives to happen for some time...this is a long overdue piece of work so brave to Southampton for taking it on. How can I add my voice to this important work?”

Cancer patient, November 2014

Triangulation of results

Triangulating the findings from the mapping exercise, patient experience and clinicians’ surveys, the Task and Finish Group made the following observations:

1. A relatively small proportion of cancer research funding was spent on nutrition. This may reflect difficulties in securing funding for nutrition research (as suggested by the clinicians’ survey).
2. Few animal studies exploring the mechanisms linking nutrition to cancer risk or progression have been conducted during the last five years.
3. Patients who participated in the Dragons’ Den session at the NCRI 2014 conference and those who completed the patient experience survey reported that the quantity and quality of nutritional care currently provided is unsatisfactory. In particular, patients felt there was a lack of support and advice given to overcome the side effects of chemotherapy.
4. Clinicians observed that there is no agreed approach to nutritional assessment of cancer patients, and it is therefore not carried out in a systematic way. Clinicians also felt that there is insufficient support and formal guidance on how assessment should be conducted.
5. The mapping exercise highlighted the relatively small number of nutritional intervention studies taking place in the UK. The clinicians’ survey supports this finding as clinicians reported difficulties in accessing funding and in receiving ethical approval for large-scale clinical trials as well as a lack of infrastructural support to conduct research. They highlighted the need for good quality evidence which could be translated into improving clinical practice. Similar comments were given by attendees at the NCRI workshop who explicitly stated the need for more large scale intervention studies in the UK.
6. Nutrition is recognised as an important factor in cancer risk and progression but it is under investigated for a variety of reasons. Consequently clinicians do not have robust evidence to support nutritional care. A common approach to measuring nutritional status is lacking.

Recommendations

Research and clinical practice

A primary objective of the collaboration is to facilitate the generation of evidence to improve cancer prevention and the nutritional care of people with cancer. To help achieve this, the following recommendations have been identified by the Task and Finish group:

1. There is a large evidence base on the associations between diet and behaviours and cancer incidence, but less on effective preventive interventions. Evidence for interventions on diet and behaviours to improve cancer outcomes is also limited and does not provide a firm base for the nutritional management of cancer in general, or specific cancers.

We recommend: There should be focused research on the efficacy and effectiveness of nutritional interventions on cancer prevention and in the management of diagnosed cancer. This could utilise existing studies e.g. through ‘piggy backing’ a nutritional component on to existing therapeutic trials.

2. Published research on cancer incidence in relation to food, nutrition and physical activity is systematically collected, analysed and synthesised by the Continuous Update Project of the World Cancer Research Fund. However, such evidence in relation to cancer treatment, recurrence and survivorship is not collected systematically, and therefore the nutritional management of patients already diagnosed with cancer is not well informed.

We recommend: A system to collate and synthesise this evidence should be established to enable and encourage systematic analysis of the effects of nutritional interventions on cancer outcomes. It would also help identify areas where future trials are most needed and also most likely to generate significant benefit.

3. Most laboratory experimental studies are directed at understanding tumour biology as a basis for identifying targets for pharmacological or immunological therapeutic interventions.
Little attention is paid to the transition from normal to cancer cell, which would help informpreventive approaches, or specifically address nutritional aspects of cancer management.

We recommend: Studies specifically addressing the nutritional biological mechanisms underpinning cancer development, progression and management, and variations between people and patients.

4. In contrast to randomised controlled trials (RCTs), observational data do not allow robust conclusions on efficacy or effectiveness. However, RCTs are resource intensive and can test only one or few hypotheses. Therefore careful analysis of good quality observational data is needed to generate hypotheses that are most likely to yield benefit. Currently there is no agreed or conventional set of measures of nutritional state that are performed routinely on all patients in a standardised and quality assured manner in order to generate such data. Opportunities to interrogate routine clinical data as a basis for developing hypotheses to test are limited.

We recommend: Sets of nutritional assessment measures (appropriate from routine to more complex clinical situations) should be developed and agreed for routine use. These nutritional toolboxes should comprise aspects of history (appetite, diet, physical activity), anthropometry (body composition), physiology, physical function or fitness and metabolic fitness, and biochemistry (nutrient status).

5. To generate reliable data across multiple settings using these toolboxes requires a trained workforce operating to defined and quality assured standards.

We recommend: Training programmes for health professionals should be developed to ensure that nutritional measures are collected routinely on all patients appropriate to their clinical needs. Such clinical information should be accessible (in anonymised form) to permit its use in identifying appropriate targets for therapeutic intervention trials.

Collaborative working with patients, professional groups and the research community

1. The purpose of the collaboration is to facilitate the improvement of translational research so that patients will benefit from better nutritional care. There is a need to explore how best to use patients’ experience and to ensure they are fully involved in all aspects of the research and service improvement agenda. Patients agree that this initiative meets a long-standing need and several have offered their time and active support to our work.

We recommend: Novel approaches to patient engagement should be developed, for example using crowd-sourcing platforms to help patients to help identify priorities for research.

2. There is wide variation between people in the progression of cancer and in its response to treatment. The possibility that nutritional factors might underpin this has not been extensively studied. Many existing research proposals could benefit from a robust nutritional component.

We recommend: Researchers testing therapeutic interventions in cancer should work with specialist nutrition professionals to include a nutritional component in the research proposal.

A platform which links researchers with complementary skills and expertise would facilitate the development of stronger research proposals. Groups with a particular interest in specific cancer sites and/or dietary, nutrition and physical activity should engage in structured discussions with the Research Councils to harmonise research where appropriate.

3. The absence of a robust evidence base means that health professionals are not always able to provide relevant, constructive and consistent advice to patients. Health professional groups are responsible for ensuring the use of standardised approaches to nutritional assessment and producing a trained workforce.

We recommend: The relevant core professional groups including the Medical Royal Colleges, the British Dietetic Association and the Association for Nutrition should agree on core clinical nutritional information to be collected routinely (nutritional toolboxes) and supply the training needed to support its collection.

Immediate priorities

The scoping exercise has clearly identified unmet patient and public need, and a lack of evidence to help professionals meet this need. To improve the current situation, priorities for the next phase are to:

1. Agree a minimum toolbox of nutrition assessments for use in routine practice, and expanded options for more specialist application, which will be made available to clinicians, the NIHR infrastructure and the wider research community.

2. Develop a quality assured framework of training and capacity (clinical and laboratory) within which to conduct these measures. Develop competency based training for clinical staff to defined standards to ensure consistency of practice and acceptable standards of care.

3. Monitor the use of the toolbox and evaluate user experiences.

4. Identify the key research opportunities and priorities across the NIHR infrastructure, and explore opportunities for prosecuting an appropriate research agenda for the short, medium and long term.

5. Develop (and maintain) a community of practice to facilitate and promote better collaborative working.

Lessons learned

During the next phase, the collaboration should be responsible for a number of items and tasks, to:

1. Help facilitate on-going collaborative working in an effort to improve translational research.

2. Maintain awareness of existing and new work in nutrition and cancer in the UK.

3. Maintain a relationship with the NCR in order to share knowledge and learning with the wider cancer community through the network of NCR partners.

4. Continue a dialogue between stakeholders, for example through our online discussion forum, mailing list and website.

5. Sustain momentum to ensure that efforts to date are not wasted.

Next steps

1. The work for the next phase has been broken down into the following five work streams (WS):

   - WS1. Information provision and communication with cancer patients and the public.
   - WS2. Creating a skilled community of practice.
   - WS3. Identifying major research priorities.
   - WS5. Opportunities for engagement with the commercial sector.

   Detailed plans for each work stream will be developed and stakeholders will be invited to take responsibility for certain aspects.

2. The collaboration should seek to invite the wider NIHR research community and other stakeholders to use their research systems and funding to contribute to the WS.

3. Funding from NIHR Southampton BRC to support staff dedicated to working full time on this initiative has been instrumental in its success.

We recommend: To continue to build on this work, the collaboration should include securing funding to support dedicated personnel in future work plans. NOCRI support this decision (see letter of intent from the Managing Director of NOCRI in the full report).
Conclusions

The NIHR Cancer and Nutrition infrastructure collaboration has a challenging ambition to share knowledge and expertise across the fields of nutrition and cancer. However, the key goal of this collaboration is to improve the nutritional management of cancer patients, and the prevention of cancer through nutrition.

The identification of research gaps and the development and prosecution of a focused research agenda will generate new evidence of direct and lasting importance, to the benefit of patients and the professions alike. The next phase of this collaboration should be to start the generation of robust evidence through good quality observational studies (on specially constructed cohorts as well as routine patient data), through systematic reviews of existing evidence and through the identification of appropriate interventions to test in clinical trials. This work will offer important opportunities for strengthened links with academics, patients and industry and encourage the development of novel approaches to translational research.

Partner organisations of the Cancer and Nutrition NIHR infrastructure collaboration

- Cancer Research UK
- Experimental Cancer Medicine Centres
- NIHR Bristol Nutrition Biomedical Research Unit
- NIHR Imperial Biomedical Research Centre
- NIHR Leicester-Loughborough Diet, Lifestyle and Physical Activity Biomedical Research Unit
- NIHR Office for Clinical Research Infrastructure
- NIHR Royal Marsden Biomedical Research Centre
- NIHR Southampton Biomedical Research Centre
- World Cancer Research Fund UK