Cancer is a complex disease. As our understanding of the genetic makeup of cancer cells improves treatment can be refined to provide targeted therapies optimising the chances of eradicating or at least controlling tumour growth. Exciting new developments such as immunotherapy offer a new way of using the immune system to attack tumour cells. In the 1920s Warburg identified that cancer cells exhibit a preference for using glucose as an energy source and had an atypical method of processing glucose compared to ‘normal, healthy’ cells. However, Warburg went on to claim the changes in the cell mitochondria drive the conversion of the cell into a cancerous cell. This hypothesis has several problems – numerous non-tumour cells exhibit the Warburg effect (for example embryonic cells) and there are a great number of tumour cells (60-90% depending upon cancer type) that do not exhibit the Warburg effect. In a single tumour the cells will be hetrogenous and will not all exhibit the same level of Warburg effect or inability to metabolise ketone bodies and free fatty acids (Schroeder et al 2013). In addition the genetic make-up of cancer cells can also change with time.

There is little clinical evidence to support the use of the ketogenic diet in the control or eradication of tumour cells (Stemanakova et al 2018, Weber et al 2019). Most research is hampered by methodological limitations (case reports, small sample sizes, limited follow up) or has focused on outcomes such as the feasibility of following a ketogenic diet (for example Martin-McGill et al 2018, a Nebeling et al 1995, Reiger et al 2014, Zucchelli et al 2010). The interventions in different studies vary both in the level of ketogenesis desired, the length of time spent following the diet, level of ketosis achieved and the use of concomitant conventional treatments. (for example Reiger et al 2014, Schmidt et al 2011, Tan-Shalaby et al 2016) Tumour types studied and those with tumours which vary in their genetic make-up and behaviour are often combined making drawing conclusions difficult. (for example Fine et al 2012, Schmidt et al 2011, Zehra et al 2017) This makes it difficult to justify at present (Martin-McGill et al 2018, Oliveira et al 2017). Stemanakova et al 2018, Weber et al 2019).
Many patients are keen to explore self-help measures when faced with a cancer diagnosis. The opportunity to take control over their health, contributes to a perceived benefit and feel that they are ‘doing something’ which can be helpful for some patients. The concept of ‘battling’ a cancer is seen commonly in the media. However, there are dangers in this approach. Many report feeling that they had not tried hard enough if they ‘fail’ or ‘lose their battle’, they experience a sense of loss, disappointment and despair if they are unable to continue with a self-help strategy such as a diet. There may be a feeling of guilt for not embarking on a dietary intervention and for letting family and friends down. As health care professionals it is also important not to raise false hope and expectations, particularly when patients are hoping for disease control or eradication. We must ensure patients are not pressurised or coerced into following complex and restricting dietary interventions that are not supported by robust, high quality clinical evidence. This is especially important when safeguarding those with the quietest voice i.e. patients with cognitive changes and the sizeable paediatric brain tumour population.

Some question if there is any harm in following a ketogenic diet in the absence of clinical evidence. ‘Some’ question if there is any harm in following a ketogenic diet in the absence of clinical evidence. Pursuing a non-evidenced based dietary intervention may cause unintended consequences for health. By the same token that there isn’t clinical evidence highlighting the efficacy of the ketogenic diet in tumour management there is also no research unequivocally demonstrating that following a ketogenic diet is harmless or risk free. Could reducing those cells that can only metabolise glucose mean that those tumour cells adapted to utilising ketone bodies and fatty acids thrive and therefore change the nature of the tumour composition which may or may not be more difficult to control? Pre-clinical research has suggested in some tumour lines (certain types of myeloma, kidney and breast cancers) a ketogenic diet may promote tumour growth and survival. (Lisanti et al 2010, Liskiewicz et al 2016, Xia et al 2017). Recent laboratory-based research published by the Institute of Cancer Research (ICR) showed that there is a potential that a cellular environment high in ketone bodies may promote metastatic spread of breast cancer cells (Weverwijk et al 2019). In clinical practice, there may be disadvantages to following a very low carbohydrate diet including weight loss and gastrointestinal symptoms. In some circumstances this may lead to patients declining treatment or recommended medication (including IV analgesia). A published study highlighted that following complementary therapies may be associated with worse outcome (Schroeder et al 2019).

The health challenges related to following a ketogenic diet are well documented and not restricted to those who suffer from medication resistant epilepsy. Renal and liver dysfunction are recorded as well as gastrointestinal changes (Champ et al 2014). A high fat, relatively low fibre diet and diet restricted in fruit and some vegetable content is not in line with the advice from World Cancer Research Fund recommendations and the NHS guidance on healthy eating. It is important to remember that cancer may not be the only health challenge faced by those choosing to follow the ketogenic diet.

The economic cost of following a ketogenic diet should not be ignored. This is a cost not only to the individual choosing to follow the diet (a cost both in terms of finance and time) but also to the health service. An important factor in times of limited resources - should the NHS fund non-evidence based clinical interventions? What conclusions can we draw from a survey of well-motivated, compliant patients? It is gratifying to read that the patients who answered the survey responded positively to the aspect of self-help and control. What would be even more interesting would be to explore the experience of those who did not complete the survey - their reasons for non-completion, how they felt when they stopped following the diet or failed to start? Data gathered from a survey is interesting to read but is not sufficiently robust to warrant changing practice, particularly in the face of a lack of clinical evidence.

So when will we have more robust evidence to support or discount the use of ketogenic diets? Unfortunately this is still a long way off. Research into the tolerability, safety, impact on weight loss, body composition and metabolism of cancer cells continues. Currently there are 16 clinical trials listed on Clinical Trials website on the use of ketogenic diets in a number of cancer diagnoses including prostate, breast, endometrial, colorectal and melanoma. Brain tumours, primarily glioblastomas, continue to be the most common diagnosis in which ketogenic diets are being studied. Many studies use ketogenic diets alongside conventional chemotherapy and radiotherapy in non-randomised studies and therefore will be unable to comment on the efficacy of the diet. Over the next few years there may be clearer evidence as to any possible detrimental effects of this restrictive diet; however, it will be longer before any effects on tumour growth are known.

REFERENCES
See online: https://bit.ly/2U2ABaZ