Do high protein diets increase cancer risk?

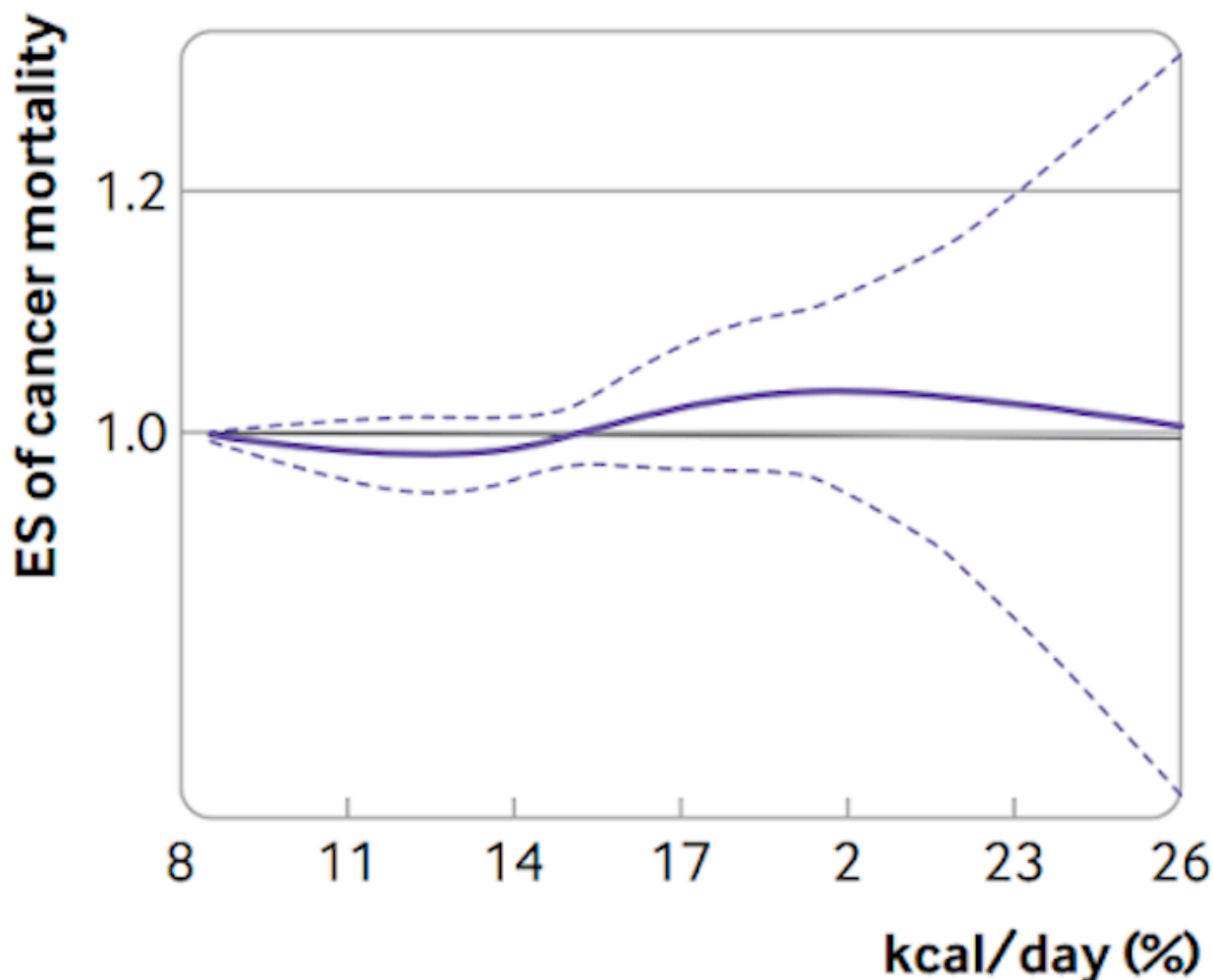Peter Attia   June 12, 2024

Figure 1: Dose-response association of intakes of total protein (based on percentage of kcal/day) with risk of mortality from cancer in adults (>18 years of age)aged 19 or older. Black line indicates the linear model; solid purple line indicates a non-linear model with dashed lines representing 95% confidence intervals. ES=effect size. From Naghshi et al., 2020.[10]

Sufficient protein consumption is critical for health and longevity. Too little protein in the diet leads to low muscle mass, which in turn is strongly associated with increased mortality risk. We have frequently pointed out why the Recommended Dietary Allowance (RDA) of 0.8 grams of protein per kilogram (kg) of body weight per day is too low, and my team generally recommends a daily intake of at least twice that amount – around 1.6 to 2 grams of protein per kg of bodyweight. Many active individuals and those seeking to build muscle aim for even higher levels of protein intake,[1] raising the question: is there such a thing as *too much*?

Mechanistic data on the effects of protein on cellular signaling pathways have led to a hypothesis that excess protein intake promotes the development and progression of cancer, an idea that has been widely spread by advocates for protein restriction. However, the fact that a given hypothesis is mechanistically plausible does not necessarily mean that it is true, and in evaluating how protein intake impacts cancer risk, we must adopt a wider perspective. While randomized trials addressing this question are lacking, combining human epidemiological studies with a closer look at mechanistic studies paints a more nuanced picture of the relationship between protein and cancer.

Proposed mechanisms: how is protein thought to raise cancer risk?

As we've discussed in detail in our premium article on [protein and aging](#), protein influences several interrelated cell signaling pathways, and hypotheses regarding dietary protein and cancer have largely arisen from observed effects of this macronutrient on pathways involving mammalian target of rapamycin complex 1 (mTORC1) and insulin-like growth factor 1 (IGF-1) – the same pathways underlying hypotheses regarding protein and aging.

As a central regulator of cell growth, division, metabolism, and survival, mTORC1 (along with its core protein, mTOR) is highly sensitive to the availability of nutrients required for anabolic processes – particularly amino acids, the building blocks of protein.[2] Following ingestion of protein, circulating concentrations of amino acids increase and activate mTORC1, which in turn promotes cell growth and proliferation, two hallmarks of cancerous cells. Indeed, hyperactivation of mTOR is an extremely common feature of several cancers,[3] and various mTOR inhibitors have received FDA approval as effective cancer treatments[4]. Thus, because dietary protein is known to stimulate mTORC1 activity, high protein intake has been hypothesized to increase cancer risk.

Consumption of high-protein diets also correlates with elevated levels of IGF-1,[5] a peptide hormone which mediates growth processes by driving cell proliferation and inhibiting apoptosis (a form of regulated cell death by which the body rids itself of damaged and abnormal cells). Like uncontrolled cell proliferation, uncontrolled cell survival is also a feature of cancer, and high circulating levels of IGF-1 have been shown to correlate with increased risk of several types of cancers.[6]

Human data don't uphold these hypotheses

The proposed mechanisms linking high protein consumption with increased cancer risk are plausible, but when we look at the overarching connection between protein intake and cancer incidence or mortality, the data don't uphold the hypotheses we might draw from the series of mechanistic steps.

Unfortunately, robust randomized trials on high-protein diets and cancer risk have not been conducted – and likely never will be due to the extraordinary costs and logistical challenges that such a study would entail. Further, animal studies cannot easily address this question. Since rodents commonly used in such research do not spontaneously develop cancers at a sufficient rate, cancer induction typically requires genetic or other manipulations which may not

reflect human cancer development or may mask more subtle effects of diet.[7] Therefore, we must look primarily to large-scale human epidemiology studies, full of their own numerous limitations, which tend to discredit the hypothesis that high protein consumption increases risk of developing or dying from cancer.

Among the most recent studies on associations between protein and cancer is a 2020 systematic review and meta-analysis which pooled data from seven cohort studies on protein intake and cancer mortality. Investigators Qi and Shen reported no significant difference in risk between the highest and lowest categories of protein intake (as defined by the individual studies included), with a relative risk (RR) of 0.96 (95% CI: 0.89-1.04; P=0.117).[8] Indeed, data from only one of the individual studies included in the analysis had indicated a significant association, and this association *favored* higher protein consumption, as the highest quintile of protein intake (mean intake of ~22% calories from protein) correlated with a 37% *lower* risk of cancer mortality (RR=0.63; 95% CI: 0.43-0.93) relative to the lowest quintile of protein intake (mean intake of 11-12% calories from protein).[8,9]

This analysis was limited to studies in which cohorts were generally healthy at baseline (i.e., no significant comorbidities), raising the possibility of a selection bias that might hide an association between cancer and protein intake. However, another 2020 meta-analysis – which examined studies that included both healthy and unhealthy cohorts – corroborated the results of Qi and Shen. In their analysis of data from 12 prospective cohort studies comprising 292,629 participants, authors Naghshi et al. reported that those in the highest categories of protein intake exhibited statistically equivalent risk of cancer-related death to those in the lowest categories (pooled effect size: 0.98; 95% CI: 0.92-1.05, P=0.63).[10] Further, in a dose-response analysis across all levels of protein intake, the investigators reported no association between each 3% increment in energy from total protein intake and risk of cancer mortality (pooled effect size: 0.98, 95% CI: 0.94-1.03, P=0.39), as shown in **Figure 1** below.
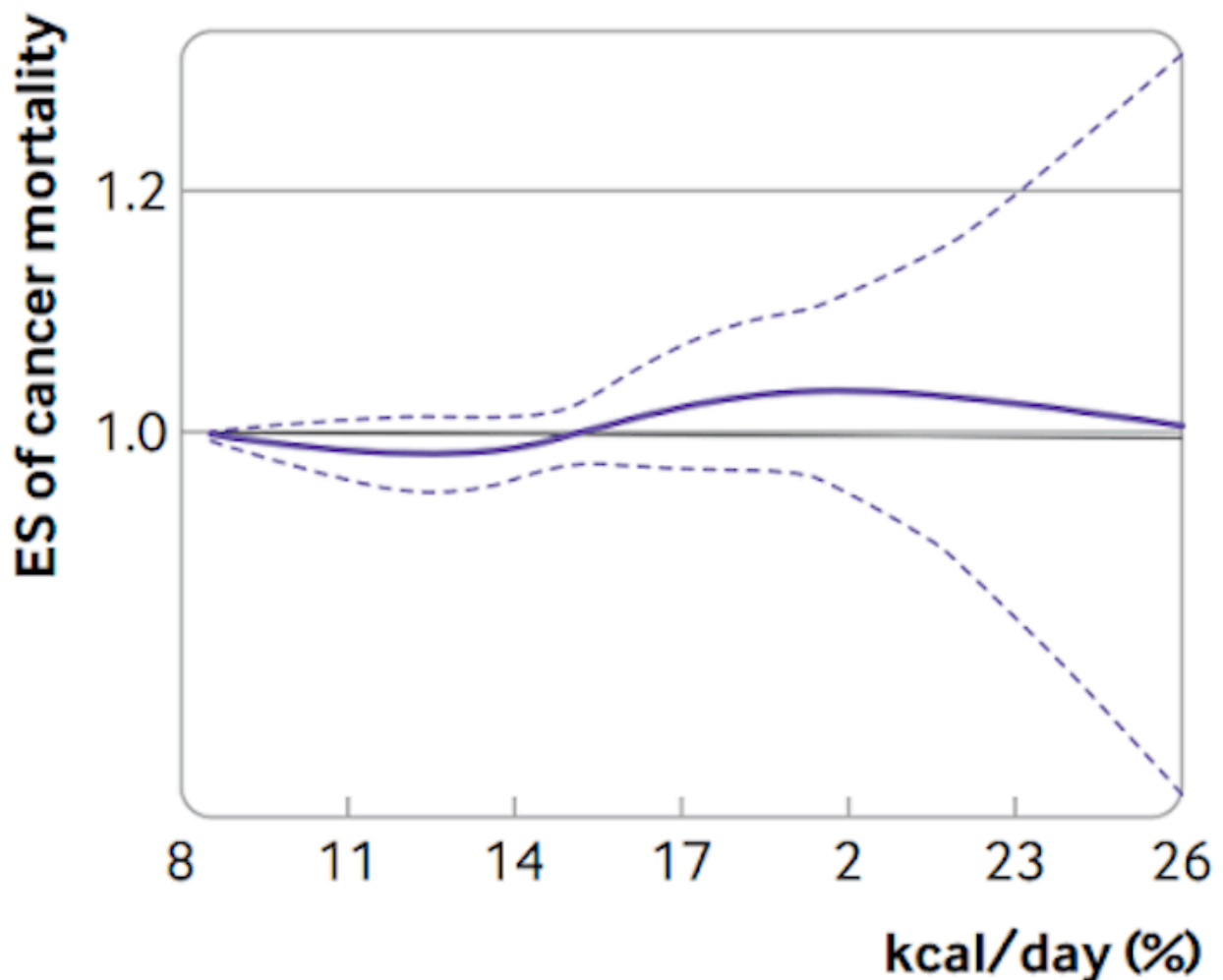
Figure 1: Dose-response association of intakes of total protein (based on percentage of kcal/day) with risk of mortality from cancer in adults (>18 years of age)aged 19 or older. Black line indicates the linear model; solid purple line indicates a non-linear model with dashed lines representing 95% confidence intervals. ES=effect size. From Naghshi et al., 2020.[10]

Although the data above are purely observational, it's important to note that concerns over the reliability of observational data are far less relevant when results *don't* show a significant association than when they *do* show a significant association. Many variables can artificially create the appearance of an association where one does not, in fact, exist, but consistent *absence* of a signal in epidemiological data – even across studies in different populations and correcting for different covariates – is often quite telling.

An oft-cited and oft-misinterpreted analysis

Perhaps the most frequently cited study supporting a *positive* association between protein intake and cancer mortality was published in 2014 by Levine et al.[5] Although this study was included in both of the meta-analyses summarized above, these particular findings merit a closer look in light of the great extent to which they have been used as evidence in favor of low-protein diets.

Using data from the NHANES III health survey,[11] Levine et al. reported that adults between the ages of 50-65 whose diet consisted of at least 20% calories from protein were more than *four times* more likely to die of cancer than adults of the same age range whose diet consisted of <10% calories from protein (HR: 4.33; 95% CI: 1.96-9.56). Even *moderate* protein intake (between 10-19% of total daily calories) was found to be associated with a three-fold increase in cancer mortality relative to low protein consumption (HR: 3.06; 95% CI: 1.49-6.25). Taken at face value, these numbers might motivate anyone to ditch their protein supplements for good, but here's the catch – among adults *over* age 65, high protein intake was associated with a 60% *lower* risk of cancer mortality relative to low protein intake (HR: 0.40; 95% CI: 0.23-0.71). In an analysis of the combined cohort (all adults aged 50+), protein consumption appeared to have no significant relationship with cancer mortality (HR: 0.89; 95% CI: 0.56-1.44 for the high-protein group relative to low-protein group).

Based on these data, the authors conclude that a low-protein diet may be beneficial for adults below the age of 66 but harmful beyond this age. But in the context of cancer-specific mortality, this interpretation simply doesn't make a great deal of sense, as we have no reason to suspect that the biology of cancer development or progression is drastically different between patients in their 50s and patients in their 70s. (Of note, some might argue that because anabolic responses to dietary protein decline with age, any potential cancer-promoting effects of high protein intake would indeed be expected to dampen with age. However, this explanation cannot account for the apparent *protective* effect of a high-protein diet against cancer over age 65.)

So how *can* we make sense of these results? The most likely (though far less headline-worthy) explanation is a combination of biased data and fluke statistics.

Of the whole study cohort, approximately 630 died of cancer over the follow-up. Based on the rates of cancer mortality across the three defined levels of protein intake, this total included 43 cancer deaths for the low-protein group (9.8% of a cohort size of 437), 485 cancer deaths for the moderate-protein group (10.1% of 4,798), and 103 cancer deaths for the high-protein group (9.0% of 1,146). Though the authors do not provide a further breakdown of cancer deaths by *age group* within their study population, if we consider the numbers of cancer deaths by age group for the *entire* US population (per the CDC),[12] we can safely assume that the 66+ age group likely accounted for the majority (probably between 70-80%) of the cancer deaths for each level of protein intake. This means that Levine et al.'s analysis was likely based on fewer than 35 cancer deaths in the high-protein group and *fewer than 15* cancer deaths in the low-protein group. These numbers are extremely small, making them very susceptible to influences of chance – in other words, the probability that these numbers do *not* reflect true trends in a general population is substantial. And because the numbers of deaths for those 66+ were almost certainly larger, the association observed in the older group can be assumed to be accordingly *more* reliable in predicting a true population trend.

Additionally, as these are observational data, they are subject to potential biases. In calculating cancer mortality hazard ratios according to level of protein intake, Levine et al. corrected for various demographics, as well as health covariates such as smoking, personal history of cancer, waist circumference, and total caloric intake. But the investigators could not possibly adjust for *every* variable that may have influenced their outcome of interest (i.e., cancer

mortality). They did not, for instance, account for participants' frequency of cancer screening, use of exogenous hormones, family history of cancer, or other variables with implications for risk of cancer death. Combined with the small numbers of deaths in the 50-65 group, these potential sources of bias in baseline cancer risk further increase risk that results are not reflective of the general population.

Protein intake and specific cancer types

While the studies we have described thus far have focused on cancer in broad terms, several studies have alternatively investigated the relationship between protein intake and *specific* types of cancer. Although a handful of individual studies have reported findings favoring either low or high protein intake, larger-scale reviews and meta-analyses generally report no significant association. We won't discuss all of these in detail for an exhaustive list of cancers, but it's worth noting that such systematic reviews and meta-analyses have examined epidemiological data for prostate,[13,14] ovarian,[15] kidney,[16] and pancreatic,[17] and colorectal[18] cancers and have been fairly consistent in their conclusions that protein consumption does *not* correlate with risk.

Why might the hypotheses be wrong?

Given the biochemical mechanisms we've described above, what might explain why epidemiological data do not substantiate any link between dietary protein and cancer? When we look more closely at the mTOR and IGF-1 pathways, critical holes come to light.

There is no question that an influx of amino acids stimulates mTORC1 activity or that the downstream effects of mTORC1 activity include cell growth and proliferation. However, under normal circumstances, activity of mTORC1 is subject to negative regulation by multiple pathways, which ensures that cell growth and division are kept in check and do not occur during unfavorable conditions, such as when nutrient or substrate availability is low.[19] Protein consumption may activate mTORC1, but it does so in a manner that is still subject to negative regulation.[20] That is to say, activation of mTORC1 in response to amino acid availability is part of a *normal, functioning system* for controlling cell growth and metabolism – one that includes an intricate set of checks and balances.

It is the *loss or disruption* of such inhibitory regulation that causes abnormal, chronic mTORC1 activation and permits cell proliferation to proceed in the *uncontrolled* manner characteristic of tumors,[21] just as removing the brakes from a car turns a normally safe and useful mode of transportation into a death trap. Indeed, the reported links between mTORC1 and cancer have involved *aberrant, chronic, hyperactivation* of mTORC1 – such as might result from mutations in genes that mediate mTORC1 inhibition – *not* mTORC1 activity in the context of its usual physiological triggers (e.g., amino acid availability) and functional regulatory pathways. In other words, we have no reason to suspect that normal, protein-induced, acute spikes in mTORC1 activity would promote tumorigenesis on their own.

As further evidence of this point, we can look to the analogous case of muscle-building exercise. Like dietary protein, resistance exercise is a normal, acute trigger of mTORC1 activity, which then mediates the hypertrophy (i.e., cell growth and muscle protein synthesis) that occurs in muscle fibers following training.[22,23] Yet despite this stimulation of mTORC1, high levels of resistance training have consistently been shown to be associated with *reduced* cancer incidence and mortality.[24,25] Of note, strength training also enhances the mTORC1-activating effect of dietary protein,[26] so the finding that this type of exercise is inversely correlated with cancer further underscores how elevated mTORC1 activity alone does not increase the probability of cancer development.

Similar reasoning can be applied to IGF-1 signaling, which is also tightly regulated and, like mTORC1, is acutely triggered by resistance training.[27] Yet, as we discussed in depth in our analysis of the links between protein and aging, an even greater hole in the IGF-1 story is that we simply don't know to what extent – if at all – reducing dietary protein consumption would impact IGF-1 levels, since IGF-1 is affected by many variables apart from protein intake, including age. Indeed, in the Levine et al. paper detailed above, circulating IGF-1 levels were found to have *no association* with protein intake among individuals over the age of 65.[5]

Cancer development versus cancer progression

Understanding the difference between normal and aberrant mTORC1 activity brings us to another vital point of distinction: the impact of dietary protein and mTORC1 on cancer *development* or *initiation* versus their impact on cancer *progression*. It is plausible that even if protein-induced mTORC1 activation does not promote cancer *on its own*, in a setting of *existing* cancer – in which mutations have already caused checks on cell proliferation to become dysregulated – even normal, otherwise harmless triggers of mTORC1 activity may fuel tumor growth. With this distinction in mind, does evidence point to any benefit to limiting protein intake while battling cancer?

This question has been investigated in a small number of studies in laboratory mice using human xenograft models, in which immunodeficient mice are implanted with human tumor cells to initiate cancer, but results have been inconsistent. A 2013 study in xenograft mouse models of human breast cancer and prostate cancer, for instance, reported that for both cancer types, restricting dietary protein to 7% of total daily calories inhibited tumor growth relative to mice on a 21% protein diet, as shown by smaller tumor size.[28] However, despite a trend in this direction, results failed to achieve statistical significance until very late in the study (>3 months, or the equivalent of 20-30 human years) and only when mice also began to diverge in *body weight*. Mice on 7% protein exhibited lower body weights than mice on 21% protein, suggesting lower calorie intake or increased energy expenditure which might have impacted tumor growth independently of protein concentration. Indeed, a subsequent study involving many of the same investigators reported that intermittent fasting had a far greater impact in limiting tumor growth than protein restriction.[29] Additionally, work by a separate research group on a genetic mouse model of breast cancer found that even at very high dietary protein concentrations (up to 69% of total calories) tumor growth was significantly slower than the growth rates observed among mice consuming far less protein (23% of total calories), but again, the slower tumor

growth correlated with lower body weights. Together, results from these three studies suggest that differences in overall energy intake – not protein intake *per se* – underlie apparent "effects" of dietary protein on cancer progression.

But as we indicated earlier, the extent to which mouse models of cancer translate to human cancer is not always clear, particularly when considering the complex and often subtle effects of dietary variables. In addition to the fact that these animals are undergoing severe manipulations to induce cancer in a manner that humans would never experience, the mice are not being *treated* for cancer as humans would be. Typical cancer treatments such as surgery, chemotherapy, and radiation all present their own unique stresses on the body which certainly alter the impact and importance of various nutrition-related factors. Indeed, concerns related specifically to cancer treatments often complicates the task of assessing the effect of dietary variables in human cancer patients, yet accounting for such concerns is critical for any meaningful evaluation of the impact of protein on cancer progression.

One treatment effect that creates significant challenges for addressing protein's impact is the anorexia that typically accompanies chemotherapy, as results related to *protein* intake are often confounded by differences in *total energy* intake – an issue which, in a cancer setting, tends to bias results in favor of higher protein intake. However, a multivariate analysis of data from pancreatic cancer patients undergoing chemotherapy (n=40) found that protein intake levels of <1.1 g/kg body weight/day was a *stronger* predictor of mortality than low total energy intake (<25 kcal/kg body weight/day),[30] suggesting that protein intake is *positively* correlated with cancer survival, even independent of overall energy intake (**Figure 2**).
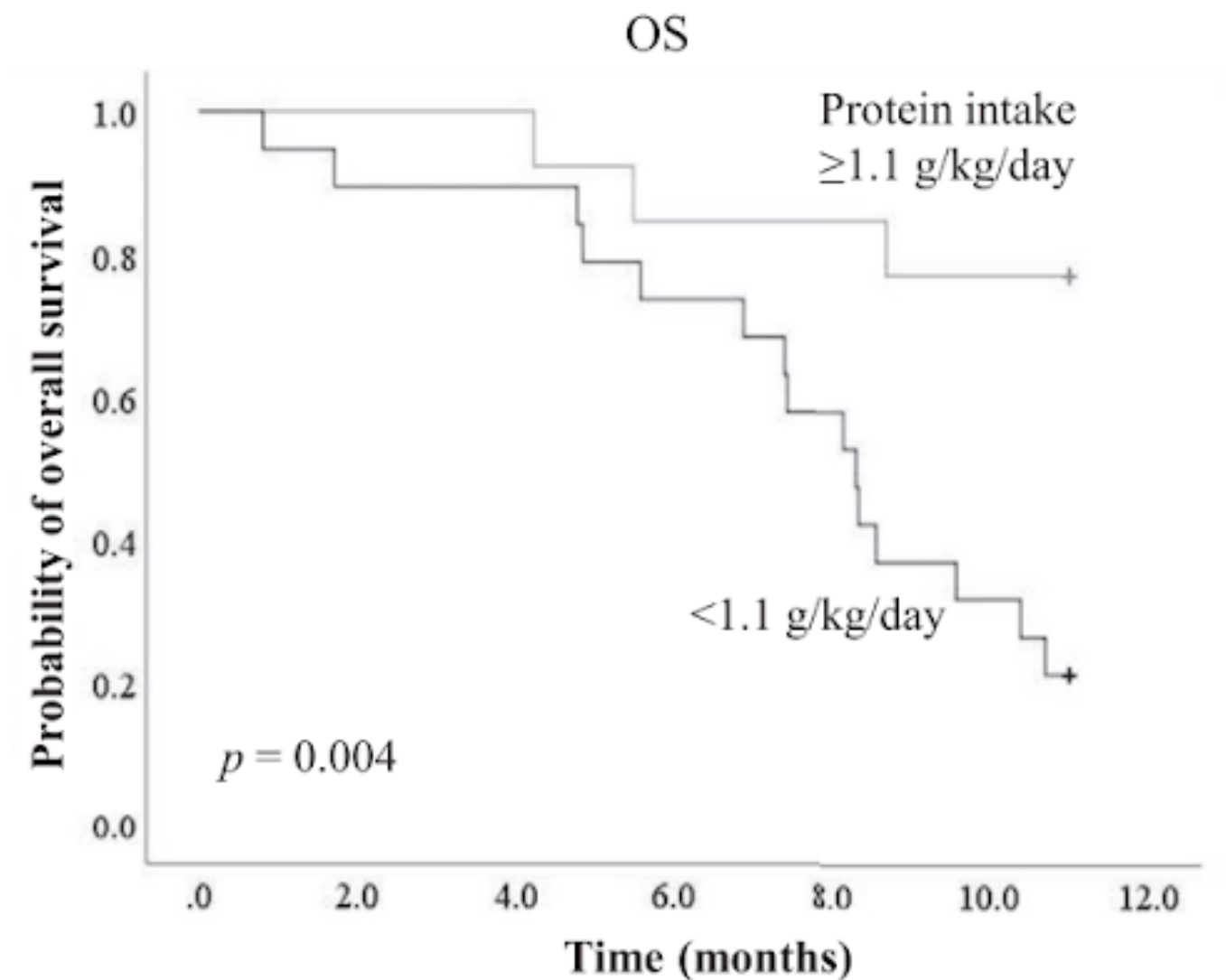
Figure 2: Kaplan-Meier curve of overall survival for pancreatic cancer patients consuming more (light gray) or less (dark gray) than 1.1 grams of protein per kilogram of body weight per day. From Hasegawa et al. 2021.[30]

This conclusion is corroborated by a handful of studies that examined the relationship of dietary protein and cancer survival and recurrence *following* primary cancer treatments. For instance, in an analysis of data from 6,348 women from the Nurses' Health Study who had been diagnosed with breast cancer between 1976 and 2004, those in the highest quintile of daily protein intake (mean intake=88.3 g protein/day) were at a 16% *lower* risk of distant breast cancer recurrence (RR=0.84 (95% CI: 0.69-1.03) than those in the lowest quintile (mean intake=61.5 g/day) after adjustment for covariates, including total energy intake and body mass index (BMI).[31]

Together, the research cited above refutes the notion that protein restriction would slow cancer progression and, to the contrary, highlights the *importance* of adequate protein intake for cancer survival. Though the "highest protein intake" categories in most of these studies would more accurately be described as "moderate," individuals with cancer diagnoses are widely regarded as having *greater* protein requirements than healthy individuals. Depletion of muscle mass is a classical feature of cancer cachexia, compromising patients' quality of life and their ability to tolerate cancer treatments, as well as reducing the probability and duration of

survival.[32] Such muscle wasting is exacerbated by protein restriction and counteracted by dietary protein-induced stimulation of muscle protein synthesis. Indeed, current guidelines from the European Society for Clinical Nutrition and Metabolism note a strong consensus among clinical nutritionists that protein intake should be *increased* – not decreased – during cancer to increase quality of life and odds of survival.[33]

Does protein source matter?

A number of studies have taken the question of dietary protein and cancer risk a step further, investigating how correlations might change when considering protein from animal-based sources versus plant-based sources. Animal protein typically stimulates mTOR more potently than plant protein due to the former's higher proportions of essential amino acids (and leucine in particular), which are most instrumental in driving mTORC1 activity. But as discussed above, the effect of this activation on cancer risk is questionable, and when we look at epidemiology data, once again, these studies have largely failed to identify any significant associations.

In a 2016 analysis of diet and mortality data from 131,342 US adults, those who consumed the most animal protein (>18% of total daily calories) did not differ significantly from those who consumed the least (≤10% of total daily calories) in risk of cancer-related death (HR=1.02, 95% CI: 0.94-1.11), and each 10% increase in animal protein intake was associated with zero increase in risk (HR=1.00; 95% CI: 0.95-1.06).[34] Likewise, plant protein intake was reportedly unrelated to cancer mortality, as those who consumed the highest (>6% of total daily calories) levels were found to be at a statistically equivalent risk to those who consumed the lowest (≤3%) levels (HR=0.97; 95% CI: 0.90-1.05). In a separate study (n=102,521, women only) that analyzed specific *types* of animal protein sources, no significant associations were observed between cancer mortality and intake of total red meat, processed red meat, poultry, fish/shellfish, or dairy, though increasing consumption of protein from eggs was reported to correlate with a 13% increased risk for each additional ounce of intake per day (HR=1.13; 95% CI: 1.07-1.20; *P*=0.05).[35] Again, this study also found no correlation between total intake of animal-based (HR=0.98; 95% CI: 0.94, 1.03; *P*=0.73) or plant-based (HR=1.05; 95% CI: 0.92-1.19; *P*=0.11) proteins (per every 5% increment in total energy intake) and cancer mortality. Collectively, these results indicate that high protein intake is not associated with elevated cancer risk *regardless* of whether the protein is derived primarily from animal or plant sources.

Still, a fairly large body of research has suggested that this isn't the case – that consumption of animal protein, and red meat in particular, is indeed a significant risk factor for various cancers. Long-time readers may [recall](#) [previous](#) [rants](#) on the many reasons why this research is heavily flawed, but since this alleged link nevertheless continues to receive so much attention, we'd be remiss not to reiterate a few key points here.

First and foremost, correlation is not causation – an inherent limitation of observational data, and one that applies to nearly *all* of the studies we have discussed throughout this piece. Although causality can sometimes be inferred from observational data that meet certain criteria (known as Bradford Hill criteria, discussed in detail in our recent examination of the [health effects of sauna use](#)), the body of literature on animal protein and cancer risk simply doesn't measure up in this respect. Results are highly inconsistent, and where positive correlations are

reported, they are generally weak. The "plausible mechanism" is, as we've seen above, not quite as plausible as it first appears, and the few *interventional* studies on this subject (i.e., randomized trials comparing low vs. high red meat consumption) have, according to a 2019 meta-analysis, collectively shown no effect of meat intake on cancer mortality.[36]

So if meat consumption is not *causally* related to cancer, what might explain the apparent correlation? This question brings us to key point #2: observational research on meat consumption and cancer risk is heavily confounded by the fact that high consumption of these foods (and red meat in particular) is closely associated with *overall* poor diet and health habits.

Because this point is best illustrated with an example, let's look at a study we haven't yet examined in past newsletters – a 2022 investigation comparing cancer risks associated with moderate to high meat intake (self-reported consumption of processed, beef, pork, lamb, or poultry >5 times per week, n=247,571), low meat intake (self-reported consumption of these meats ≤5 times per week, n=205,385), meat intake restricted only to fish (pescetarianism, n=10,696), and vegetarianism (n=8,685, including 446 vegans).[37] The researchers reported that, relative to the group that consumed meat most frequently, those classified as low meat intake, pescatarian, or vegetarian were all at lower overall cancer risk (HR=0.98, 95% CI: 0.96-1.00; HR=0.90, 95% CI: 0.84-0.96; and HR=0.86, 95% CI: 0.80-0.93, respectively) after adjusting for several covariates, including physical activity level, smoking status, alcohol consumption, diabetes, and various demographic and socioeconomic variables.

But if we take a closer look at baseline data for these covariates, a clear pattern emerges across diet groups. Those with the highest meat intake were also more likely than any other group to have diabetes and be current or former smokers, and they had higher average BMI and daily alcohol intake. All together, these disparities signal a trend of *poorer overall health* among those consuming the most meat – a trend which was also generally sustained in comparing the low meat intake group to the pescatarian and vegetarian groups – suggesting that those consuming more meat were likely at higher risk of cancer regardless of their meat consumption habits. And while it's true that the authors corrected for these *particular* health-related variables, their models did not factor in countless *other* health-related variables which might have biased results.

Putting aside potentially relevant variables such as family history of cancer or access to healthcare, the issue becomes clear when we focus solely on other *dietary* variables which are likely to co-vary with meat intake. Many Americans with the highest meat intake – and particularly the highest non-seafood meat intake – are consuming it in the form of fast food burgers, hot dogs, and other highly processed foods with loads of calories but minimal nutritional value in the form of essential vitamins, minerals, and fiber. By contrast, many who adopt a pescatarian or vegetarian diet choose to do so specifically as part of a *broader effort* to "eat healthy" and are accordingly more likely to opt for fresh, whole food sources. In other words, meat intake tends to correlate with *overall poor diet*, but the apparent negative "effects" of higher meat intake might not be related to the meat *per se*, but rather to *lower fiber or micronutrient intake*. If this is the case, then we would expect that a *healthy* omnivore diet (i.e.,

one that includes ample fresh vegetables and whole grains in addition to high-quality meats and minimal processed foods) would not differ from a healthy pescatarian or vegetarian diet in their respective associations (or lack thereof) with cancer risk.

For most people, too little protein is a greater risk than too much

Although the hypothesis of protein-induced mTORC1 activation leading to increased cell proliferation and thus increased cancer risk initially appears to make some sense, epidemiological data has failed to substantiate such a link between protein intake and cancer. Under closer inspection, we find that even the proposed mechanism has considerable flaws – suggesting that this hypothesis is more "guess" than "educated" – and it becomes clear that concerns over cancer risk with high protein intake are largely unfounded and should not discourage individuals from making conscious efforts to ensure sufficient daily protein consumption.

Adequate protein intake is required for building and keeping muscle mass, which in turn is essential for avoiding frailty (and associated injury risks) and for maintaining metabolic health. We recently [covered](#) recommendations for protein quantity, distribution, and quality in significant detail, and although protein needs across individuals differ based on activity level, age, and other factors, existing evidence generally favors erring on the side of more, not less. Most individuals struggle to get *enough* protein in their diet (let alone *more* than the 1.6 to 2 grams of protein per kg of bodyweight we recommend), in part due to the very satiating effects of this particular macronutrient (a topic we will cover in an upcoming "Ask Me Anything" episode on *The Drive*). And while we lack any clear evidence that it's possible to *overdo* protein intake, ample evidence reveals the detrimental effects of having too little – effects which include higher injury risk (and worse prognosis for recovery), poorer glucose tolerance, increased weight gain, limited mobility – and indeed, poorer prognosis following a cancer diagnosis.

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