

PLOS Science Wednesday: Hi Reddit, my name is Emily Bucholz and I published a study in PLOS Medicine studying the impacts of being underweight after a heart attack, Ask Me Anything!

PLOSScienceWednesday¹ and r/Science AMAs¹

¹Affiliation not available

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Abstract

Hi Reddit, My name is Emily Bucholz. I am a pediatric resident at Boston Children’s Hospital but did my doctorate at Yale School of Medicine. My doctoral research focuses on sociodemographic and clinical predictors of life expectancy after heart attacks. I am particularly interested in how risk factors for the development of coronary heart disease affect long-term survival after heart attacks. I am the lead author of a study recently published in PLOS Medicine titled “Underweight, Markers of Cachexia, and Mortality in Acute Myocardial Infarction: a Prospective Cohort Study of Elderly Medicare Beneficiaries”. In this study, we studied over 50,000 Medicare beneficiaries to examine the effect of underweight on survival after heart attack. We used two techniques (adjustment and stratification) to disentangle the effects of low weight from comorbidity and frailty, which can also lead to weight loss and poor health outcomes. We found that being underweight was an independent risk factor for higher short- and long-term mortality after heart attack. There are several potential explanations for these findings including decreased physiologic reserve, lower rates of guideline-based therapies, and genetic predisposition. Regardless of the mechanism, we conclude that strategies to promote weight gain after heart attack – both in the hospital and after discharge –are worthy of testing. My co-authors were Ms. Hannah Krumholz and Dr. Harlan Krumholz. I will be answering your questions at 1pm ET – Ask Me Anything!

[REDDIT](#)

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PLOSSCIENCEWEDNESDAY [R/SCIENCE](#)

Hi Reddit,

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Did you study patients who were underweight and then had a heart attack, or patients who had a heart attack, then lost too much weight?

[borrax](#)

Thanks for this question. This is an important point to clarify as major cardiac events can certainly cause weight loss and other adverse consequences. Weight status was determined at the time of heart attack so it reflects patients who were underweight and then developed a heart attack.

What is the relative contribution of muscle mass, adipose tissue, and bone to maintaining quality of life (and speeding recovery from acute medical problems like heart attack) at advanced ages?

As a not_naturally_skinny older person, I focus on maintaining/increasing muscle mass, minimizing adipose tissue, and hope for side effects that take care of my bone density (male). An image that motivates me is https://static-content.springer.com/image/art%3A10.1007%2Fs10522-015-9631-7/MediaObjects/10522_2015_9631_Fig1_HTML.gif

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[vtjohnhurt](#)

This is a fascinating question but one that we were not able to examine because we did not have information other than weight, chronic comorbidities, and other markers of frailty. I think this would certainly be a great follow-up question as we start to understand how weight status affects recovery after heart attacks. As you note, it may not simply be about putting on the pounds but also how overall fitness and muscle mass are maintained.

Is there any difference between patients who have always been underweight vs those who have become underweight as older adults?

I do understand that BMI is perfectly valid over large groups, but as an always-underweight adult I would like to know how or if this could apply to me.

[inertia](#)

Unfortunately we weren't able to ask this question because we didn't have information on patients' prior weight. However, there are likely different mechanisms between being underweight throughout life and becoming underweight later on. Patients who meet criteria for underweight throughout life may be so because of genetics, dietary choices, or exercise habits. In contrast, chronic illness or other lifestyle changes are probably more likely to cause a person to become underweight later in life. As to what this means for survival and overall health, we really don't know and were not able to examine this in our study.

My father-in-law was a marathon runner in NYC and had a heart attack. He was very fast, skinny, and seemingly very healthy. He was feeling lousy at work and on his way home decided that maybe he should get checked out at the hospital. He was having an acute MI. He has since taken a break from marathon distances but continues to run around 6 miles regularly. He has also put on a little bit of weight but he appears to be in healthy ranges. Me and my wife have asked him specifically what his diagnosis was and he always backs away from the conversation. Medical stuff scares him. My wife and I are cardiopulmonary lab technicians for the United States Air Force and we asked to see his EKG, in attempts to read his cardiac history. He hasn't gotten around to getting us a copy but I was wondering how much his heart condition had to do with genetics vs his low body weight and intense fitness regiments?

TL/DR : father in law was a marathon runner, very healthy. Had heart attack. Could it be genetics that caused MI or fitness regiment/underweight?

[ThePrizeKeeper](#)

Thanks for this question and sharing. From your description, it sounds as though your father-in-law was very healthy and athletic without weight issues. There are many, many factors that influence the risk of heart disease including (but not limited to) genetics, diet, exercise, behaviors, stress. Weight and body mass index are only a few factors that may influence risk of heart disease and recovery. It is not uncommon for athletic, normal weight patients to develop heart disease. However, there is usually another risk factor that can be pinpointed either through diagnostic work-up or on personal/family history. That said, this is not always the case

In our study, we looked at survival after heart attack but not risk of heart disease. And we are increasingly learning that risk factors for development and recovery are very different. Our findings show that underweight patients have worse survival than normal weight patients after a heart attack. However, it's not clear why. The next steps are to understand whether nutritional supplementation or strategies for gaining weight are beneficial in underweight patients after heart attack. Based on other

literature, the most important things to do after heart attack appear to be maintaining a healthy weight, keeping cholesterol and blood pressure in check, exercising frequently but not too much, and avoiding unhealthy behaviors like smoking. I hope this is helpful!

We always get the advice that losing weight is good for your cardiovascular health; the thinner the better. Is this bad advice, or are the under weight patients in your study mostly elderly people in poor health, who have lost a lot of muscle mass?

[random_testaccount](#)

We are increasingly learning that risk factors for the development of heart disease do not necessarily predict survival after heart attack. Several "paradoxes" have been found in which risk factors that increase your risk of heart disease actually improve survival after heart attack. The classic examples of these include smoking and obesity. Using the example of obesity, we know that obese patients are more likely to have heart attacks than normal weight patients; however, studies have consistently shown that obese patients actually fare better after heart attacks than non-obese patients. This is confusing as we might expect that the risk factors are the same.

There are several theories as to why this paradox exists including greater physiologic reserve in obese patients to overcome the stress caused by heart attacks, more intensive treatments delivered to obese patients, differences in age or other risk factors between obese and non-obese patients, and confounding by cachexia or other chronic illnesses that lead to weight loss.

In our study, we focused specifically on underweight and normal weight patients and found that underweight patients had poorer survival after heart attack than normal weight patients. We adjusted for many comorbidities and measures of frailty that might reflect disease processes that cause cachexia and could explain why these patients were underweight. However, we found that underweight patients were still at increased risk even after we took these variables into account. This would suggest that underweight patients are at increased risk even if they don't have diseases that we typically think of as causing cachexia.

While we cannot comment on how being underweight influences your risk of developing heart disease, it would appear that these patients are at higher risk of bad outcomes after heart attack.

I'm a dietitian at an acute care facility who frequently sees underweight elderly patients. We have triggers set up to fire on patients with documented weight loss, low BMI, etc so we can focus on these high risk cases.

Did you do any study into the cause of their malnutrition? I feel like much of the time the battle is already lost before they make it to me.

[argonplatypus](#)

Unfortunately we did not look specifically at the cause of malnutrition in the patients in our study. Our results show that underweight patients with heart attacks were significantly more likely to be smokers, to have comorbidities like heart failure, COPD, stroke, Alzheimer's disease, and to have markers of poor nutrition (i.e. low albumin levels). Low weight in these patients is almost assuredly multifactorial so it is hard to say why these patients were underweight.

I have two questions - first, for the categorical (BMI) analysis, what threshold (s) did you use for BMI?

Second, I don't really follow why, in the sensitivity/sub-group analysis, you would exclude all patients

with significant comorbidity (instead of just adjusting for the presence of comorbidities, either individually, or with something like a Charlson score).

[ar_604](#)

1. We used the CDC defined thresholds for BMI. Underweight patients had a BMI <18.5kg/m² and normal weight patients had BMIs ranging between 18.5 and 25kg/m².
2. The sensitivity analysis was performed because we wanted to ensure that confounding by significant comorbidities or frailty were confounding our findings. We were concerned that adjustment for these factors was insufficient to remove confounding because underweight status is so closely linked to comorbidity and frailty. Indeed we found that even after adjustment for the "sickest" patients, underweight was still significantly associated with worse survival after heart attack.

Hi! Recently in the UK there was some coverage that said the health guidelines (that have been in place for decades) which tell us that a diet high in saturated fat can lead to heart disease was based on one flawed study carried out a long time ago, and that a diet high in saturated fat does not have a correlation with heart disease. What are your thoughts on this research?

[JXG88](#)

Unfortunately I don't have the expertise to comment on dietary cholesterol or saturated fat in heart disease.

Hello and thank you for taking the time to do this AMA.

Your results and study as a whole are very interesting. Generally we focus on the overweight when it comes to heart attacks. It's great to see the other side of this issue as we lose muscle mass, bone density and adipose tissue as we age and many otherwise healthy adults become under weight.

What was the most significant factor affecting mortality after heart attack?

Was there a significant difference between males and females, both in rate and factors?

Thank you again, we appreciate your time and answers.

[Alantha](#)

Thanks for your interest!

1. For this study, we focused explicitly on weight status as a predictor of mortality after heart attack. We did not directly compare other factors, although this has been done in other studies. We do know that survival after heart attack depends on many factors (sociodemographic, clinical, treatment, post-hospitalization care), so it is nearly impossible to isolate a single factor. And we also know that risk factors for survival change over time!! Your risk factors change as you get farther out from the event.
2. More woman than men were underweight at the time of heart attack. However, underweight appeared to be a more potent risk factor for mortality in men than in women. We hypothesized that this may be because lower BMI in men reflects a more malnourished or cachet state since men typically have higher BMIs than women.

Does the Fat free mass / Fat distribution have an impact on recovery after a heart attack?

For example:

190cm @ 90kg with 7% fat.

This could be a healthy strength training individual that is looking good for the summer, but he does not have a lot of fat. Though, he's at a very nice total weight. Does this matter at all, as opposed to him having more fat / less muscle?

[Kaluro](#)

This would be an interesting area to explore. Unfortunately we only had information on weight but did not have information on fat distribution. Certainly an area for future research!

Which is worse for recovery, being under- or over-weight?

[exarkun108](#)

We did not directly compare underweight to overweight or obesity as we limited our study to underweight and normal weight patients. However, previous literature has suggested that underweight patients are at the highest risk of poor outcomes after heart attack across all BMI groups (10.1016/j.ijcard.2009.12.029; 10.1161/ CIRCOUTCOMES.113.000421)

Are underweight people less likely to get heart attacks to begin with?

What about ethnic differences? (e.g. what if one is an underweight Asian?)

Could it be that underweight people who get heart attacks are generally a "different type" of underweight people than those who don't get them?

[inquilinekea](#)

1. There is certainly literature to suggest that underweight patients are less likely to have heart attacks than heavier patients because excess weight is associated with risk factors (diabetes, hypertension, high cholesterol) for heart disease. However, we did not study this question in our study.
2. Unfortunately we did not look at interactions between ethnicity and body mass index. We simply did not have enough patients across multiple races/ethnicities to look at this issue.
3. Yes, we lay out several reasons as to why underweight patients may be at higher risk for poor survival after heart attack. Among these, we suggest that the pathophysiology of heart attacks may be a fundamentally different process in underweight patients than normal weight patients. Underweight patients may have an underlying genetic predisposition to coronary artery disease which could be associated with poorer prognosis. Consistent with this hypothesis, there is some literature to suggest that underweight patients with heart attacks have more severe and extensive coronary disease than normal weight and overweight patients (Reeves et al, J Am Coll Cardiol, 2003; Shirzad et al, Minerva Chir, 2009)

- How much residual confounding by smoking do you believe there could be?
- How did you test the proportional hazards assumption?

- Tobias et al. published findings from the Nurses' Health Study using a similar methodology but among T2DM patients instead of AMI patients (<http://www.nejm.org/doi/full/10.1056/NEJMoa1304501>). They found that when they excluded early deaths, there was no survival disadvantage in the underweight group. Do you think there could be a similar shift in results had you excluded early deaths in your analysis?
- You found that underweight appeared to be less harmful in older patients. A well-known analysis by Berrington de Gonzalez et al. found the opposite (<http://www.nejm.org/doi/full/10.1056/NEJMoa1000367>). Granted, this was in healthy never-smokers, which raises the question of whether there is some higher order interactions by age x sickness x BMI. Could you comment?
- This is not really discussed in your paper, but do you believe that a normal weight individual who becomes overweight after AMI truly has a longer survival time compared to if that individual had remained normal weight? The normal -> over seems to be a much more common and controversial scenario that everyone wants to know about.

[qyll](#)

1. It is difficult to comment on the degree of residual confounding by smoking. Rates of smoking in underweight and normal weight patients in our study were 21.4% and 17.0%, respectively. We did adjust for smoking in our analyses but there may be some degree of residual confounding, particularly since we did not evaluate how long or how much patients were smoking.
2. We tested the proportional hazards assumption using graphical and formal testing of Schoenfeld residuals.
3. This is an interesting question. Thank you for this reference. It is difficult to say whether our results are biased by the exclusion of early deaths as we only included patients who actually presented to the hospital. However, I have trouble thinking of reasons as to why normal weight patients may be more likely to die out of hospital from heart attack than underweight patients.
4. The interactions between underweight and age are interesting. As we hypothesize in the paper, this may be due in part to our ability to detect differences in survival at older ages since life expectancy is universally shorter. You raise an interesting point about sickness or comorbidity. As it may be that older patients have significantly more comorbidity in both underweight and normal weight patients and thus there are fewer differences between groups. Although we did adjust for several comorbidities, they may also have non-cardiac comorbidities that were not included in our analyses. We also hypothesized that older patients generally have reduced physiologic reserve to overcome acute events like heart attacks and thus age may act as equalizer of risk.
5. We did not look at trajectories of weight gain after heart attack; however other papers have looked at weight changes and their association with outcomes. Most notably, data from the ENRICH trial (Lopez-Jimenez et al, Am Heart J, 2008) suggest that weight loss is a predictor of poorer survival after heart attack, but little is known about weight gain, particularly in underweight patients. This would be the next step for research in this area.

In your research what have you discovered in regards to what kind of person frequently has the least amount of heart attacks and the least severe when they do? I'm looking for attributes that an individual can control such as: Bodyfat percentage, muscle mass, overall weight, cardiac fitness (and to what degree, do people with Athletic heart syndrome get heart attacks?) social connections, etc.

Thank you!

[UrGunCremeUrKhakis](#)

We focused specifically on underweight and its effects on survival after heart attack, that is after heart disease has occurred. We were not able to study risk factors for the development of heart disease. We do know from other literature that it is a multifactorial process and it is impossible to isolate one type of individual at lowest risk for heart attacks because so many factors, including genetics, play a role.

Did you study or have you studied myocarditis in the same way? Particularly the post MI mortality risks in the younger, generally healthier population who have suffered from a myocarditis related MI?

[courtneylovesmerkin](#)

We did not study myocarditis.

I'm a Cath lab specialist and I find that many of my skinny STEMI patients (which is relatively rare, most are obese) are smokers or into drug use, or they are old and frail. I see that your study took these factors into account.

My question is, how did you find define normal weight - a BMI of 18.5-24? I rarely see AMI patients that are a normal weight and I would love to see the comparison of underweight, normal weight, overweight and obese patients that suffer MIs. How did you find so many people at at normal weight?

[carolinablue199](#)

We did take smoking into account but only found moderate differences between underweight and normal weight patients in rates of smoking. These rates are likely much smaller overweight or obese patients but they were not included in our study.

As you note, excess weight and obesity are certainly risk factors for coronary disease and heart attacks. We were fortunate to use a dataset that included over 230,000 Medicare fee-for-service patients with heart attacks that included rich, chart-abstracted data as well as long-term follow-up for this study. With these numbers, we were able to identify over 50,000 normal weight (i.e. BMI 18.5-25kg/m²) and underweight patients (i.e. BMI <18.5kg/m²) to study but you are right that the majority of patients had BMI >25.

Are you concerned that the following will happen: 1) BuzzFeed-style sites take your study and summarize it into a single quote about how being skinny can give you heart attacks. and then 2) This being cited by overweight people, and used as a reason to avoid improving their health.

[Bog_warrior](#)

We hope that this is not how our study will be interpreted. Our study is specific to underweight and normal weight patients and there is significantly more research to be done in order to understand why underweight patients are at increased risk and whether strategies to promote weight gain in these patients is beneficial.