

Detailed Study Notes: Episode 447

Does Eating Fish Increase Skin Cancer Risk? Study Analysis

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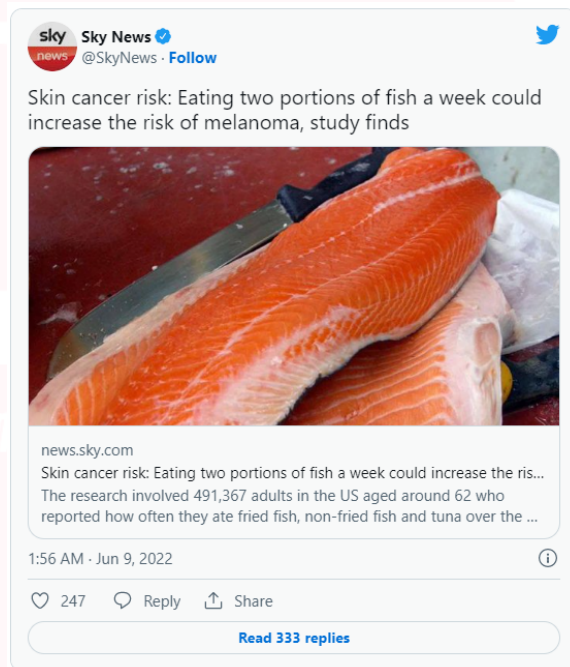
Introduction to this Episode

One of our Sigma Nutrition Premium subscribers, Vern, recently submitted the following question to us via the AMA page:

"What are your thoughts on the recently released study in the US linking 2 servings/week, or more of fish to a 22% increase in risk of developing skin cancer?"

This was referring to a recent study that reported a higher risk of developing melanoma in people who ate a relatively high intake of fish. This study caused headlines and it was picked up by many news outlets (including the New York Times, New York Post, Sky News, etc.).

As you may suspect, some of the headlines would cause deep concern for some readers:



(I will note that a “well done” should go to any outlets you went for more accurate/sensible headlines, such as the New York Times, whose headline read: “Can Your Diet Really Affect Your Skin Cancer Risk?”)

In this episode of the podcast, Alan and Danny dug into the nuances of this study to see if the headlines are justified.

Context

The study in question is one out of Brown University in the US, which reported a higher risk of developing melanoma (a common type of skin cancer) in people who ate a relatively high intake of fish.

The study used data from the [NIH-AARP Diet and Health Study](#) which is a large long-term study involving 3.5 million US citizens (who at the time were members of the American Association of Retired Persons) aimed at improving the understanding of the relationship between diet and health.

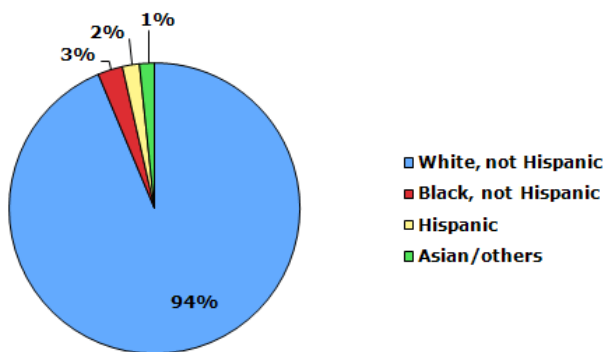


Source: <https://dietandhealth.cancer.gov/>

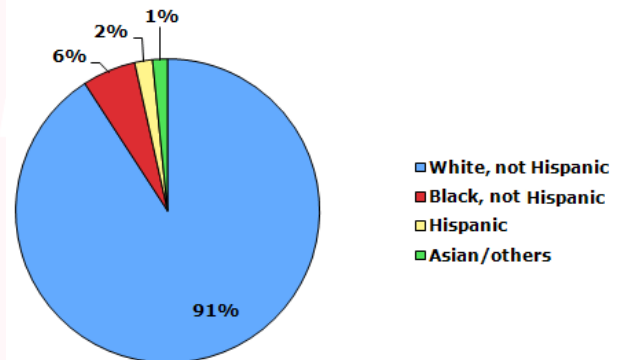
Participants & Study Design

- 490,000 adults in the United States between the ages of 50 and 71
- Participants completed ([reliable](#)) food frequency questionnaires, including information about their fish intake
- Follow-up of 15.5 years (median average)
- Over this time cancer diagnoses among the group were tracked
- Researchers classified melanomas as either:
 - “in-situ” - i.e. on the skin surface
 - “malignant” - i.e. spread deeper
- UV radiation (UVR) exposure was estimated by noon-time ground-level erythemal dose measured in the month of July, based on the latitude and longitude of participants’ residence at baseline.
- Participants were predominantly white, non-Hispanic ethnicity, which is a factor that should be considered given the impact of skin ‘phototype’ (described on next page) on risk.

Race/Ethnicity for Men (n=339,669)



Race/Ethnicity for Women (n=226,733)



Skin Phototype

- Skin phototype can be classified using the Fitzpatrick phototype classification, which is a scale of I - VI (1-6)
- Such classification has proven to be useful in indicating photoinduced skin cancer risk
- Different skin phototypes respond differently to the sun
- Compared to light skin, dark skin has a higher quantity of melanin distributed in the upper layers of the epidermis.
- In darker skin, after exposure to UVB, the DNA damage is predominantly seen in the upper layers of the epidermis. But in lighter skin, the deeper basal layers where the stem cells are located are also affected.
- Therefore, active protection against UVB is more important for individuals with light skin as there is a higher risk of sunburn, DNA damage and the development of skin cancers.
- The minimal erythemal dose (MED) is the least amount of ultraviolet (UV) light needed to produce visible reddening of the skin, indicating a mild sunburn.

Fitzpatrick phototype	Description	Individual Typology Angle (ITA)	Skin color (ITA classification)	UVB protection (SPF)	UVA protection (UVA-PF)	High energy visible light protection (VL-PF)
I	Always burns, never tans	ITA° >55°	Very light	SPF50+	UVA-PF +++ (>1/3 labelled SPF)	
II	Burns easily, sometimes tans	41° <ITA° <55°	Light			
III	Sometimes burns, always tans	28° <ITA° <41°	Intermediate			
IV	Rarely burns, tans easily	10° <ITA° <28°	Tan			
V	Rarely burns tans easily; moderately pigmented	-30° <ITA° <10°	Brown			
VI	Rarely burns, tans promptly and intensely; highly pigmented	ITA° <-30°	Dark	SPF30+	UVA-PF +++ (> 2/3 labelled SPF)	VL-PF+++

From: [Passeron et al., J Eur Acad Dermatol Venereol. 2021 Jul; 35\(7\): 1460–1469.](#)

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Overview of Study Results

- Within the cohort, the following diagnoses were identified:
 - 5,034 cases of malignant melanoma
 - 3,284 cases of melanoma *in situ*
- The average amount of fish those in the study ate varied from less than 20 g/week up to about 300 g/week.
- Positive association between higher total fish intake and risk of:
 - malignant melanoma (**HR = 1.22**, 95% CI = 1.11-1.34 for top vs. bottom quintiles)
 - melanoma *in situ* (**HR = 1.28**, CI = 1.13-1.44 for top vs. bottom quintiles).
- This corresponds to a 22% and 28% increase in risk, respectively.
- But as can be seen from the table below, comparing any of the other quintiles to Q1, there is a reported increase in risk.
- So all of the intake categories were associated with statistically significant increased risks, with a linear dose–response relationship, for malignant melanoma and melanoma *in situ*.
- Beyond the positive association between higher intakes of total fish and risk of malignant melanoma and melanoma *in situ*, the authors also reported a positive association for tuna and non-fried fish (after adjusting for other factors).

Table 2 Association of total fish intake with malignant melanoma and melanoma *in situ* in the NIH-AARP Diet and Health Study ($n=491,367$)

	Median (g/day)	Malignant melanoma			Melanoma <i>in situ</i>		
		Cases	Age & sex-adjusted HR (95% CI)	Multivariable HR (95% CI) ^b	Cases	Age & sex-adjusted HR (95% CI)	Multivariable HR (95% CI) ^a
<i>Total fish intake</i>							
Q1	3.23	802	1 (reference)	1 (reference)	510	1 (reference)	1 (reference)
Q2	7.96	973	1.18 (1.08–1.30)	1.15 (1.05–1.26)	632	1.21 (1.07–1.36)	1.18 (1.05–1.32)
Q3	12.93	1035	1.21 (1.10–1.32)	1.18 (1.07–1.29)	693	1.28 (1.14–1.43)	1.25 (1.11–1.40)
Q4	22.38	1122	1.29 (1.18–1.41)	1.24 (1.13–1.36)	720	1.30 (1.16–1.46)	1.25 (1.11–1.40)
Q5	42.79	1102	1.23 (1.12–1.35)	1.22 (1.11–1.34)	729	1.29 (1.15–1.44)	1.28 (1.13–1.44)
<i>p</i> -trend			<0.001	0.001		0.001	0.002

Table from: [Li et al., Cancer Causes & Control volume 33, pages 921–928 \(2022\)](#)

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What Could Explain These Results?

- The researchers speculated their results may be due to levels of contaminants in some fish species. These contaminants include polychlorinated biphenyls (PCBs), arsenic, mercury, etc.
 - Manufacture and processing of PCBs was prohibited in 1977.
 - Regulation has largely led to dioxin emissions decreasing by more than 90% since the late 80s.
 - But as PCBs and dioxins can persist in the environment for a long time, they continue to be present in low concentrations in many foods.
- However, levels of contaminants in the subjects' bodies were not measured. So, from this study, we don't know if such contaminants are the reason for these results.
- Other research has suggested people who eat more fish have higher levels of heavy metals such as mercury and arsenic in the body.
- And while most skin cancer is caused by ultraviolet (UV) light damaging DNA in skin cells, occupational exposure to specific chemicals used in the plastic and chemical industries (PCBs) are another known risk factor.
- In 2019, the [World Cancer Research Fund \(WCRF\) Expert Panel](#) reported that there is strong evidence that drinking water contaminated with arsenic increases the risk of skin cancer.
- But whether the amount present in fish confers a similar risk is unknown.
- Data on 20,000 women from the [Swedish Mammography Cohort](#), with a follow-up of 4.5 years, suggested there could be an increased melanoma risk for the highest dietary intake of PCBs. However, those results also showed a huge reduction in risk based on EPA and DHA intake. Something to note for a later discussion on weighing up the net effect of including fish in the diet.

Finally, one big unknown is whether the results of the discussed study actually accurately capture the relationship between fish intake and skin cancer risk. In other words, there are a number of limitations of this study that should be taken into account, and should prevent strong conclusions being made based on this one study. Let's discuss some of these limitations...

Limitations

Diet Assessment

- Diet was only assessed once at baseline and fish intakes may have changed over time.

Adjustment for Relevant Factors

- NIH-AARP study was originally designed to track many types of cancers, not melanoma specifically. So adjustment may not have been as robust..
- Researchers adjusted their analyses for some factors, E.g. physical activity, smoking, family history of cancer and alcohol intake
- But... the adjustment for daily UV exposure was only based on the average UV index for the suburb they lived in.
 - I.e. there was no adjustment for UV exposure related to a person's occupation.
 - No information on several melanoma risk factors, such as:
 - mole count, hair color, history of severe sunburn or individual sun-related behaviors, lifetime UV exposure

Demographics

- Predominantly white ethnicity, who were 50-70 years of age at enrolment
- Could potentially point to UV exposure contributing to risk

Difficulting in Assessing Impact of Diet on Cancer

- Very difficult to make clear connections
- Associations are easy to make, but many are weak or even odd...
 - E.g. Eating more citrus fruit has been associated with a greater melanoma risk in [some](#), but [not all](#), studies

Considering Net Impact of Fish Intake

- Regular fish consumption has consistent evidence of benefit across a range of outcomes.
- Even with some contamination, what is the net impact?
- It's possible any risk from 'two portions of fish a week' may be outweighed by the benefits.

Summarized well in a number of reviews:

- [Mozzafarian & Rimm review](#): *"Levels of dioxins and polychlorinated biphenyls in fish are low, and potential carcinogenic and other effects are outweighed by potential benefits of fish intake and should have little impact on choices or consumption of seafood"*
- [Mozzafarian & Rimm, 2006](#): *"Based on strength of evidence and potential magnitudes of effect, the benefits of modest fish consumption (1-2 servings/wk) outweigh the risks among adults and, excepting a few selected fish species, among women of childbearing age. Avoidance of modest fish consumption due to confusion regarding risks and benefits could result in thousands of excess CHD deaths annually and suboptimal neurodevelopment in children."*
- [Gil & Gil, 2015](#): *"Despite risks of mercury, PCBs and Dioxins for major health outcomes among adults, the vast majority of epidemiological studies have proven that the benefits of fish intake exceed the potential risks with the exception of a few selected species in sensitive populations."*

Connection to Previous Episodes

One of our Premium-exclusive episodes, titled ["Fish is Bad For You"](#), covered some similar themes. In that 'Quack Asylum' episode, we took a video made by a medical doctor as an example of where quackery can raise its head on this topic. Specifically, there are four claims made in the video that we investigate and see if there is any basis to them.

Of perhaps most relevance to the current episode is the 4th claim tackled: *"When you are eating fish, you are eating pollution, which is toxic"*, which you can listen to at the 47:53 mark of the "Fish is Bad For You" episode.

Pragmatic Conclusions

1. Reasons for this link with melanoma are still unexplained. There could be an effect, but there may not be.
2. *If* there is an effect, it's unknown what component of fish is responsible. One hypothesis is contamination with PCBs, arsenic, etc., which is far more likely than anything in fish *per se*.
3. However, there are other clear health benefits to fish consumption. And for most outcomes there is a positive effect.
4. Still recommended to consume 1-2 servings of fatty fish per week. Noting the exception in pregnancy where the amount and type of fish consumed should be accounted for.
 - a. See episodes [#441](#) and [PRE#2](#) for more details.
5. *"I wouldn't discourage people from having fish just because of our finding,"* one of the study authors, Dr. Eunyoung Cho, said (source: [NYT](#))
6. DON'T TAKE HEADLINES AT FACE VALUE! ;-)