Is Fin Food *Really* Good for You,
or
Is That Just Another Fish Tale?

Ed Cox, M.D.

Confucius taught...

"Give a man a fish and feed him for a day.

Teach a man to fish, and feed him for a lifetime".

We now know...

"Give a man a fish and feed him for the day.

Teach a man to fish, and he sits in a boat all day drinking beer."

History – Fish vs. Heart Disease

In 1960s, Bang and Dyerberg studied Greenland Eskimos living in Denmark and compared them to other Danes and to Eskimos remaining in Greenland

Diets in Greenland and Denmark were very different

Transplanted Eskimo adopted typical Danish diet

TABLE 2
Composition of the Eskimo diet and average Danish food

	Eskimos[a]	Danes[b]
Carbohydrate,[c] calorie percent	37	49
Protein, calorie percent	26	11
Fat, calorie percent	37	40
Cholesterol, mg/1,000 kcal	245	139
Saturated fatty acids, percent of total	34	53
Polyunsaturated fatty acids, percent of total	10	13
Essential fatty acids (18:2 + 20:4) percent of total	4.8	10.0
P/S Ratio	0.29	0.25

Fish & CHD - History

CHD rare among Eskimos in Greenland but similar to Danish population among Eskimo in Denmark

Lipid profiles showed similarity of Danish Eskimos, other Danes

Greenland Eskimos had very different lipid profiles: lower cholesterol and triglycerides

TABLE I
Mean values for plasma lipid and lipoprotein concentrations in Greenland Eskimos, Eskimos living in Denmark and Caucasian Danes in Denmark

	Greenland Eskimos	Greenland Eskimos living in Denmark	Danes
Total lipids, g/liter	5.93	7.32	6.55
Cholesterol, mmol/liter	5.58	7.30	6.77
Triglycerides, mmol/liter	0.43	1.12	0.98
Phospholipids, mmol/liter	2.92	3.18	2.91
Chylomicrons, g/liter	0.27	0.24	0.15
β-Lipoproteins, g/liter	4.27	5.00	4.58
Pre-β-lipoproteins, g/liter	0.44	1.10	1.05
α-Lipoproteins, g/liter	3.64	4.24	3.64

Randon sample (5).

Fish & CHD - History

Ancel Keys' observations of low CHD rate related to Mediterranean diet

- Fish are a substantial part of the Med diet
- Perhaps nutrients related to fish consumption are conveying some / much of the benefit

Fish & CHD - History

1980s saw a flood of studies confirming effects of fish-heavy diets

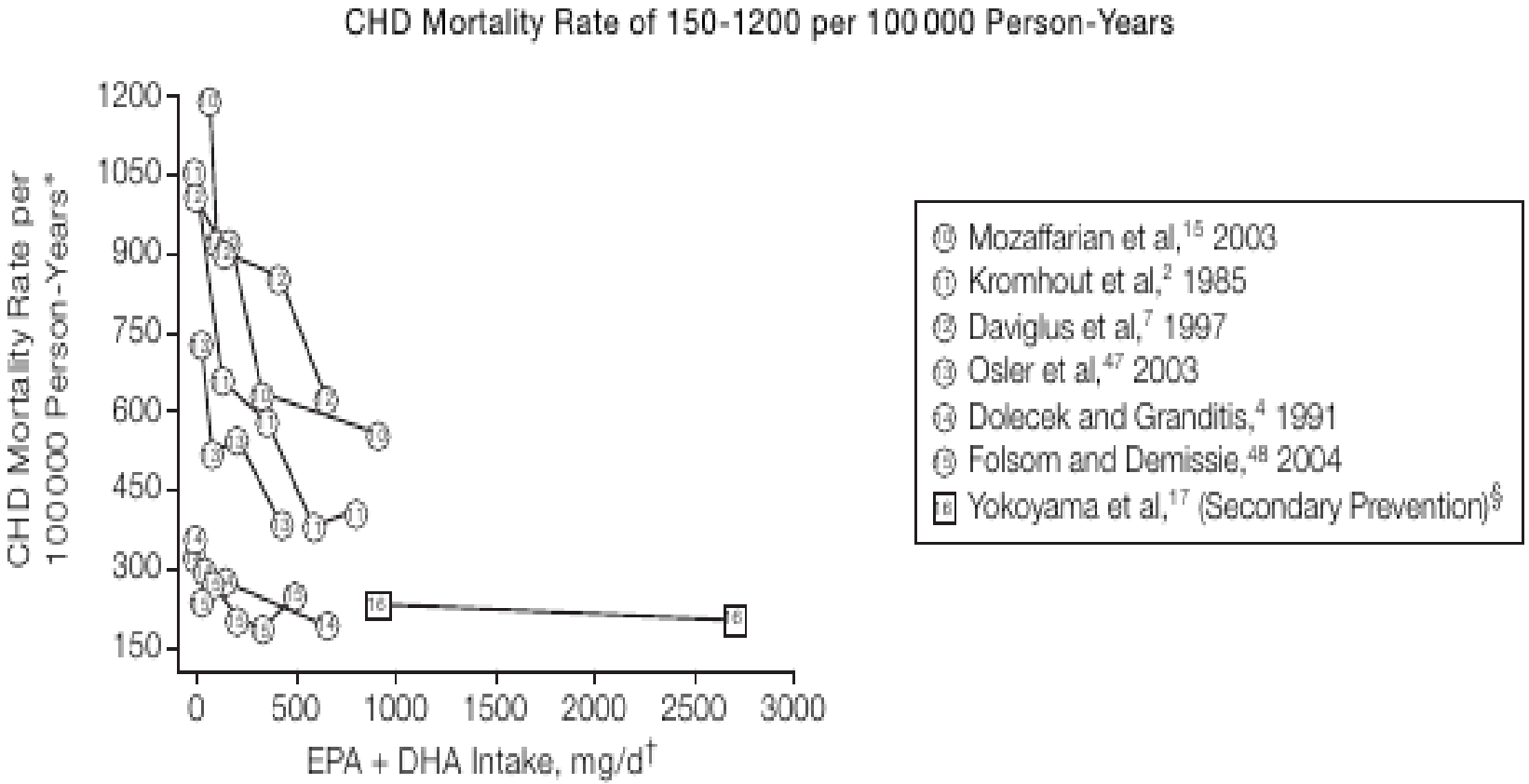
- Lowered cholesterol and triglycerides
- Prolonged bleeding times, reduced platelet aggregation
- Markedly reduced CHD deaths
- Reduced rate of sudden cardiac death

Fish & CHD - History

Omega-3 (ω-3) fatty acids derived from marine sources considered responsible for effects

- EPA (eicosopentaenoic acid)
- DHA (docosohexaenoic acid)
- Principal components of fish oil
- Present in fin and shell fish
- Highest amounts in deep water, ocean fish
- Obtained by eating appropriate fish or by supplements

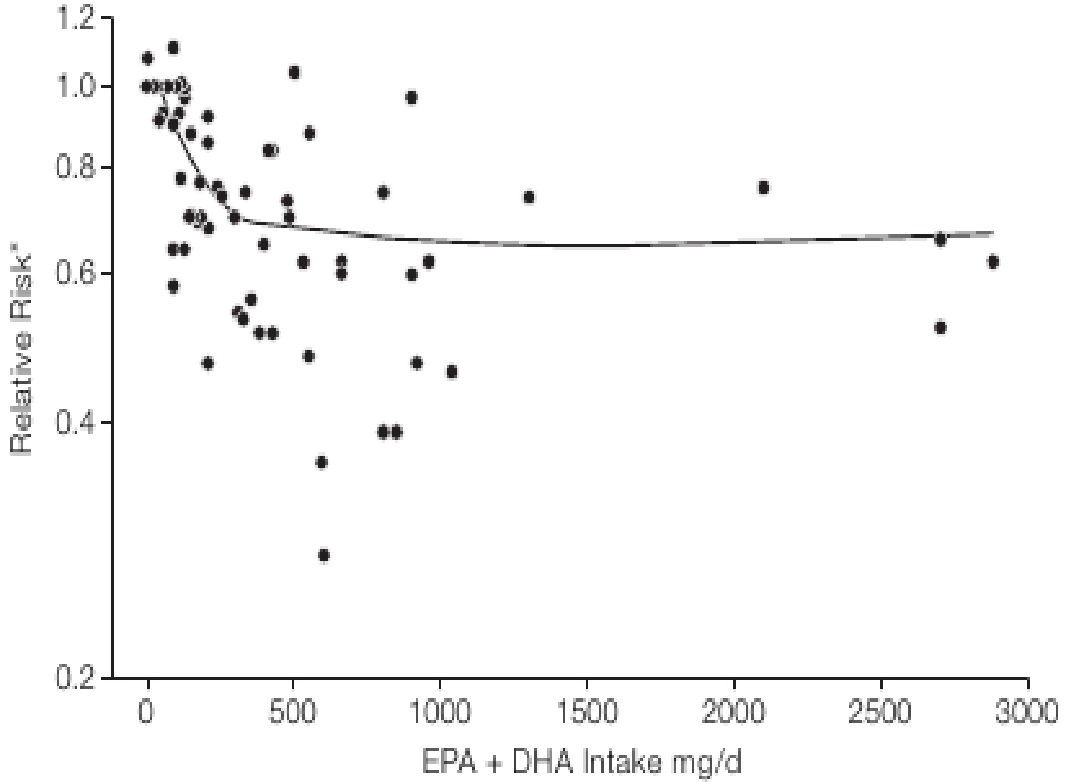
Fish & CHD - History



1990s & early 2000s – RCT and cohort studies relating consumption of marine ω-3 EPA + DHA to CHD mortality – dose-response relationship found

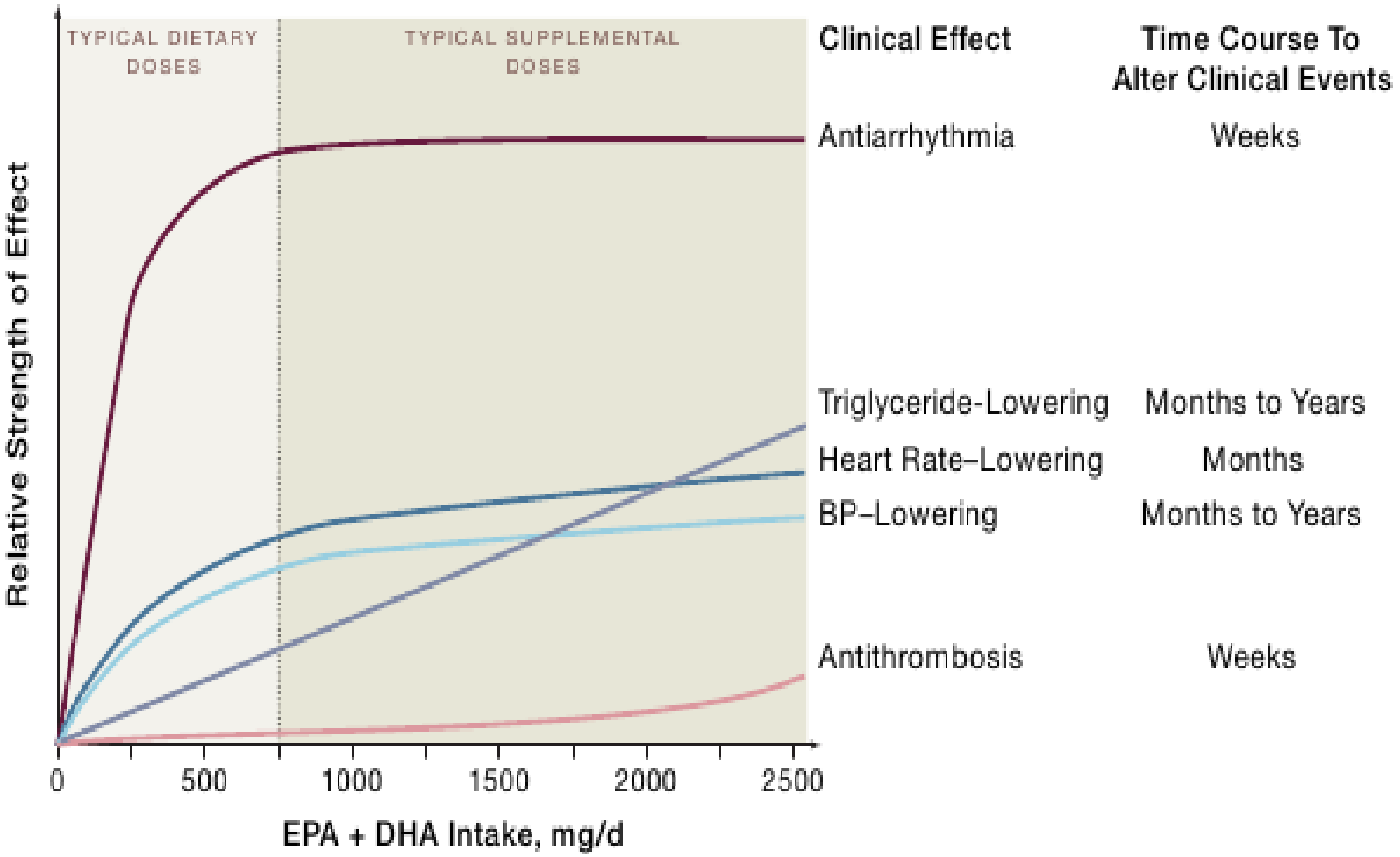
Fish & CHD - History

Figure 2. Relationship Between Intake of Fish or Fish Oil and Relative Risks of CHD Death in Prospective Cohort Studies and Randomized Clinical Trials



CHD mortality (primary prevention) decreases up to 250 mg/d of DHA + EPA, levels off above that

Figure 3. Schema of Potential Dose Responses and Time Courses for Altering Clinical Events of Physiologic Effects of Fish or Fish Oil Intake



CHD and ω-3 Fatty Acids - 2014

REVIEW | Annals of Internal Medicine

Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk

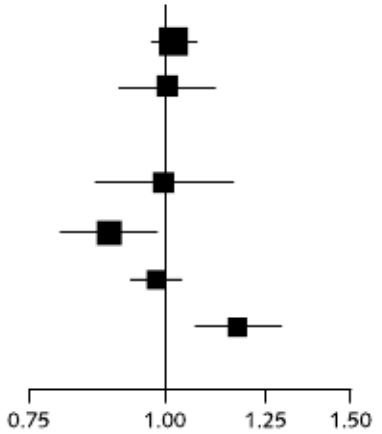
A Systematic Review and Meta-analysis

Rajiv Chowdhury, MD, PhD; Samantha Warnakula, MPhil*; Setor Kunutsor, MD, MSt*; Francesca Crowe, PhD; Heather A. Ward, PhD; Laura Johnson, PhD; Oscar H. Franco, MD, PhD; Adam S. Butterworth, PhD; Nita G. Forouhi, MRCP, PhD; Simon G. Thompson, FMedSci; Kay-Tee Khaw, FMedSci; Dariush Mozaffarian, MD, DrPH; John Danesh, FRCP*; and Emanuele Di Angelantonio, MD, PhD*

CHD and dietary fish ω-3

Figure 1. RRs for coronary outcomes in prospective cohort studies of dietary fatty acid intake.

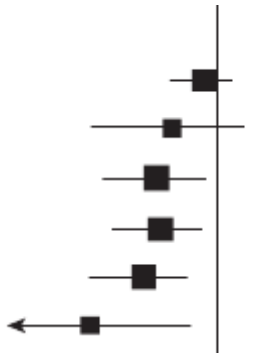
Fatty Acid Intake	Studies, *n*	Participants, *n*	Events, *n*	RR (95% CI)*
Total saturated fatty acids	20	276 763	10 155	1.03 (0.98–1.07)
Total monounsaturated fatty acids	9	144 219	6031	1.00 (0.91–1.10)
Total ω-3 fatty acids				
α-Linolenic	7	157 258	7431	0.99 (0.86–1.14)
Total long-chain ω-3	16	422 786	9089	0.87 (0.78–0.97)
Total ω-6 fatty acids	8	206 376	8155	0.98 (0.90–1.06)
Total trans fatty acids	5	155 270	4662	1.16 (1.06–1.27)



RR (95% CI) Comparing Top vs. Bottom Thirds of Baseline Dietary Fatty Acid Intake

CHD and plasma fish ω-3

Total ϖ-3 polyunsaturated fatty acids				
18:3n-3, α-Linolenic	8	14 945	3426	0.93 (0.83–1.03)
Total long-chain ϖ-3	4	10 558	2753	0.84 (0.63–1.11)
20:5n-3, Eicosapentaenoic	13	23 065	4624	0.78 (0.65–0.94)
22:6n-3, Docosahexaenoic	13	23 065	4624	0.79 (0.67–0.93)
20:5n-3, Eicosapentaenoic + 22:6n-3, Docosahexaenoic	13	20 809	4073	0.75 (0.62–0.89)
22:5n-3, Docosapentaenoic (clupanodonic)	4	7155	2565	0.64 (0.47–0.89)



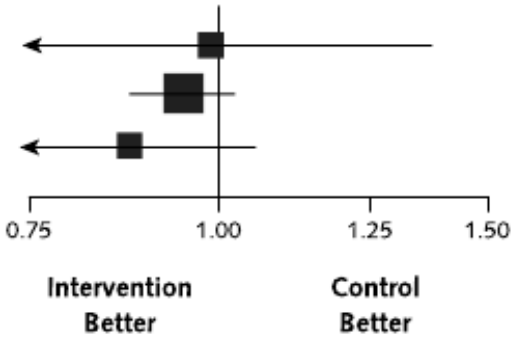
EPA and DHA are the fish-derived ω-3

Amount present in blood reflects dietary intake

CHD and ω-3 supplements

Figure 3. Effect of fatty acid supplementation on risk for coronary event, derived from available randomized, controlled trials.

Fatty Acid Supplement	Studies, *n*	Events/Participants, *n/N*		RR (95% CI)*
		Intervention Group	Control Group	
α-Linolenic acid	4	199/9444	220/9422	0.97 (0.69–1.36)
Long-chain ω-3 fatty acid	17	2426/38 303	2548/38 277	0.94 (0.86–1.03)
ω-6 fatty acid†	8	459/7245	515/7231	0.86 (0.69–1.07)



EPA and DHA supplements have not been demonstrated to reduce coronary events significantly in randomized controlled trials

Fish & CHD - Conclusion

Marine n-3 PUFA, EPA + DHA, confer substantial benefits in primary prevention of CHD in a graded dose-response

Maximum benefit occurs at 250 mg/d, the amount of ω-3 in 2 servings per week of ω-3 rich fish

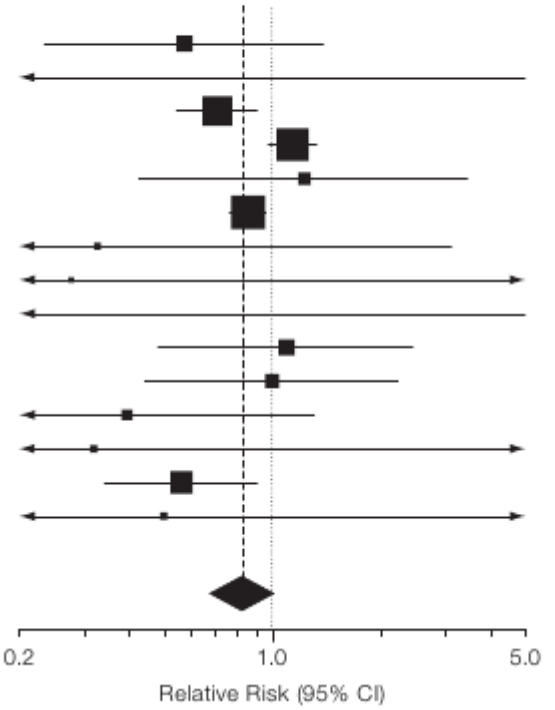
Secondary prevention is also effective, though benefits continue up to 1000 mg/d

More recent randomized clinical trials have cast some doubt on efficacy of omega-3 supplements

Fish Consumption & Mortality

Figure 4. Risk of Total Mortality Due to Intake of Fish or Fish Oil in Randomized Clinical Trials

Source	% Weight	Relative Risk (95% CI)
Brouwer et al,[62] 2006	3.9	0.57 (0.24-1.38)
Brox et al,[87] 2001	0.3	0.17 (0.01-4.05)
Burr et al,[3] 1989	18.7	0.71 (0.55-0.92)
Burr et al,[51] 2003	24.4	1.15 (0.99-1.34)
Eritsland et al,[88] 1996	2.9	1.23 (0.43-3.51)
Gruppo Italiano,[9] 1999	26.0	0.86 (0.76-0.97)
Johansen et al,[89] 1999	0.7	0.33 (0.03-3.18)
Kaul et al,[90] 1992	0.3	0.28 (0.01-6.78)
Leaf et al,[91] 1994	0.4	0.20 (0.01-4.18)
Leaf et al,[61] 2005	4.6	1.09 (0.49-2.46)
Nilsen et al,[92] 2001	4.6	1.00 (0.45-2.24)
Raitt et al,[60] 2005	2.3	0.40 (0.12-1.32)
Sacks et al,[56] 1995	0.3	0.32 (0.01-7.57)
Singh et al,[93] 1997	9.9	0.56 (0.34-0.91)
von Schacky et al,[57] 1999	0.6	0.50 (0.05-5.39)
Overall	100.0	**0.83 (0.68-1.00)**



Fish consumption and mortality

Fish consumption and all-cause mortality in a cohort of Swedish men and women

A. Bellavia, S. C. Larsson & A. Wolk

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J. Intern. Med 2017

Swedish Cohorts Fish Study

Swedish Mammography Cohort (F)

Cohort of Swedish Men (M)

Subjects: 72,522 (33,973 F 38,549 M)

Enrolled: 1997 Follow up: 17 yrs.

Deaths: 16,730 (7,168 F 9,562 M)

Cofactors: BMI, activity, smoking, alcohol, education, dietary fruit, vegetables, meat, total energy

Swedish Cohorts Fish Study

Characteristics

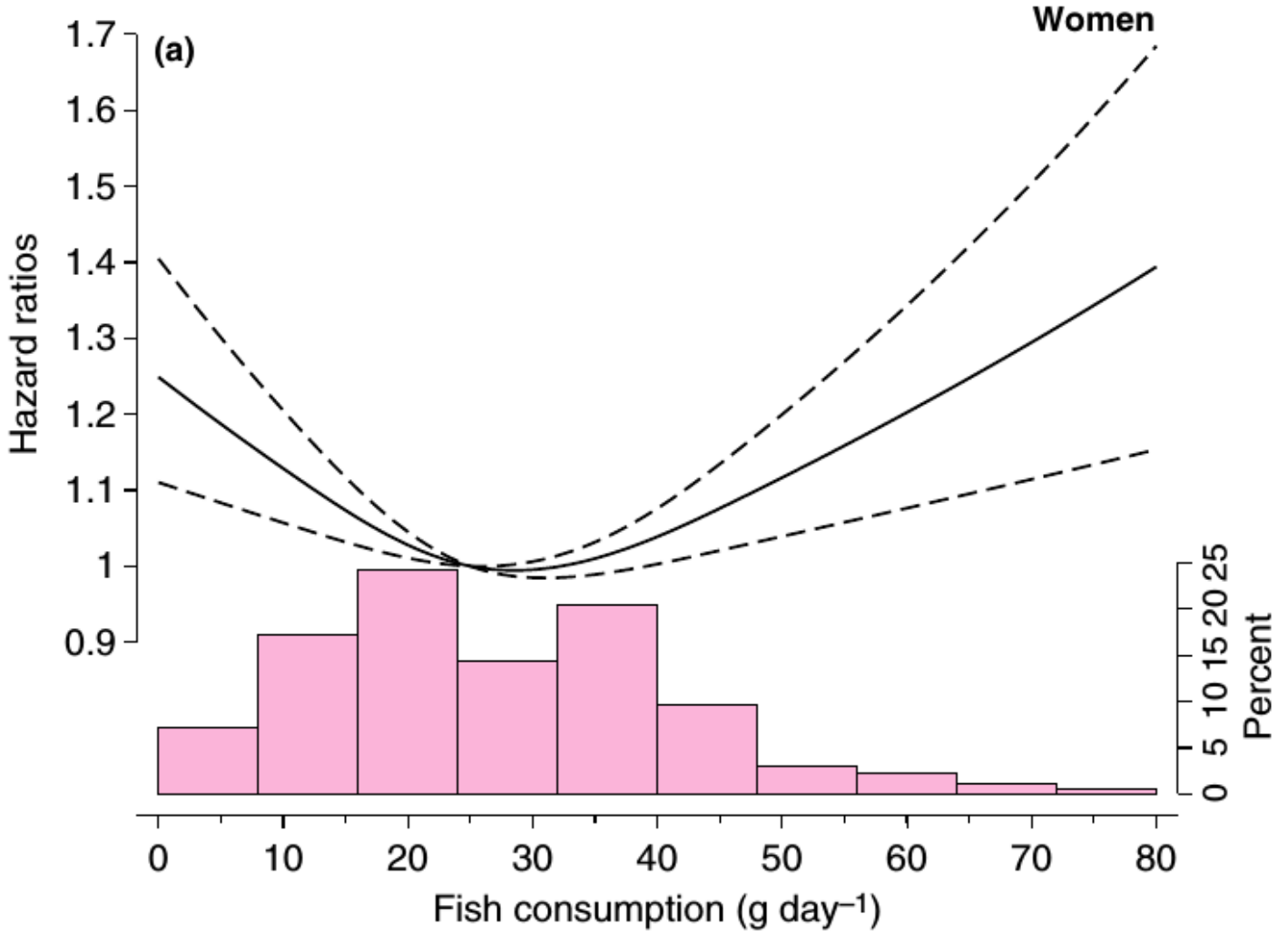
- Average fish consumption 30 g/d (1 oz/d)
- Higher fish consumption associated with higher intake of alcohol, fruit, vegetables, meat and total calories
- Fish consumption not associated with BMI, activity, smoking, education

Swedish Cohorts Fish Study

All-cause mortality and total fish intake

- Lowest mortality at median consumption level
- Higher mortality (compared to median intake) at lowest intake (increased 19% M, 25% F)
- Increased mortality in woman (compared to median intake) at highest intake – 39% higher at 80 g/d

All-cause mortality and fish intake

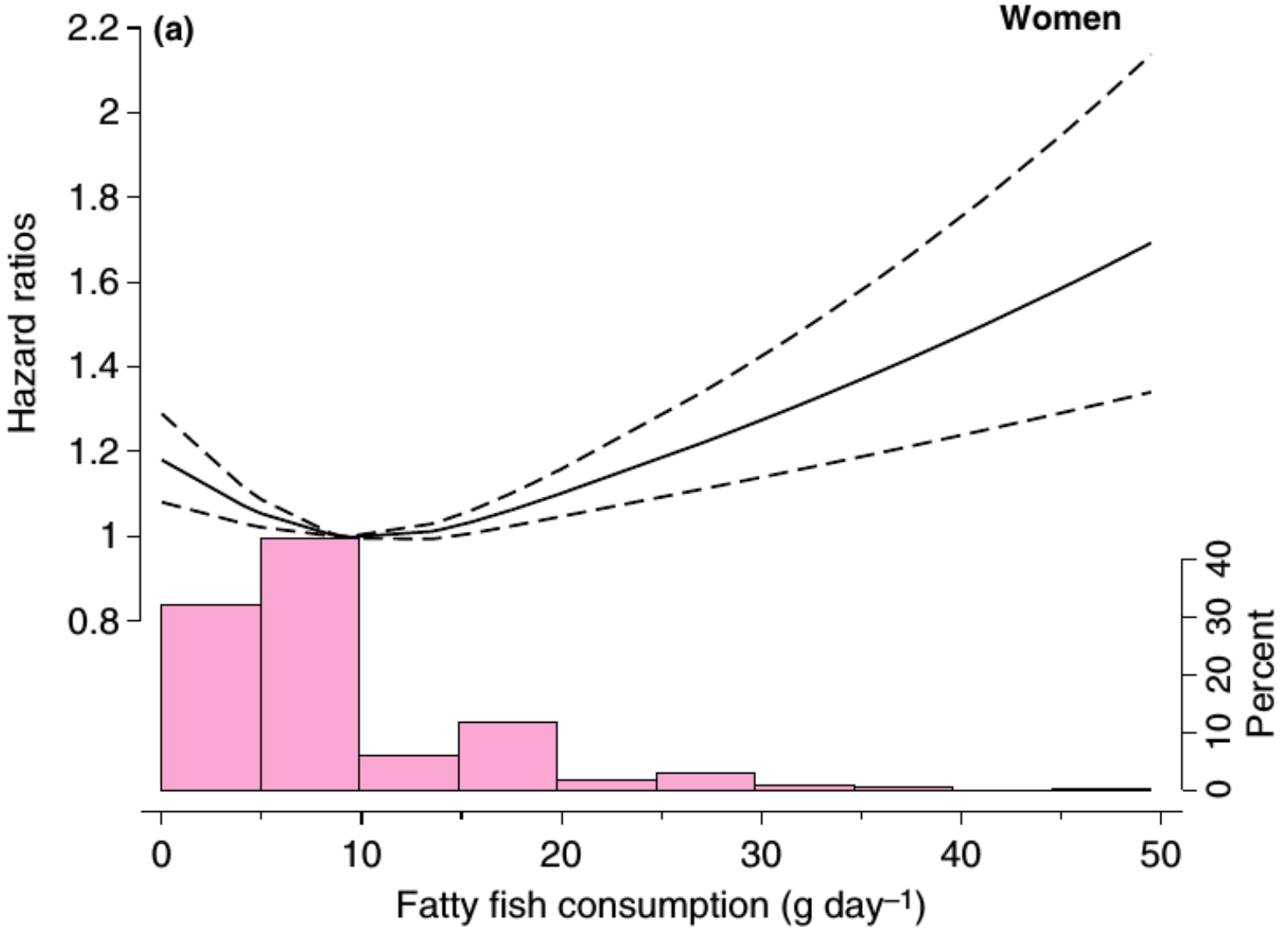


Swedish Cohorts Fish Study

All-cause mortality and fatty fish intake

- Lowest mortality at median consumption level (10 g/d)
- Higher mortality (compared to median intake) at lowest intake (increased 10% M, 20% F)
- Higher mortality (compared to median intake) at highest intake (50 g/d) (increased 30% M, 68% F)

All-cause mortality and fatty fish intake



Specific causes of death

Cardiovascular mortality was associated with fish intake, with U shaped curve

Cancer mortality was not associated with fish intake

Conclusions – Swedish Cohorts

Moderate fish consumption (1 oz/d) was associated with lower mortality (all-cause, cardiovascular) compared to no or little fish consumption

Increasing fish consumption beyond the optimum was associated with increasing mortality in women

Increasing fatty fish consumption beyond the optimum was associated with striking increased mortality in women and, to a lesser extent, men

EPIC Fish Study

Eur J Epidemiol (2015) 30:57–70
DOI 10.1007/s10654-014-9966-4

NUTRITIONAL EPIDEMIOLOGY

Fish consumption and mortality in the European Prospective Investigation into Cancer and Nutrition cohort

Dagrun Engeset · Tonje Braaten · Birgit Teucher · Tilman Kühn ·

EPIC Fish Study

Objective: Mortality vs. fish consumption

Subjects: 480,535 (337,352 F 143,183 M)

Ages: 35-70

Enrolled: 1992-99

Follow-up: 2006-2010

Events (death): 32,587 (17,603 F 14,984 M)

EPIC Fish Study: Methods

10 countries, 23 centers

- Spain, Greece, France, Italy, Germany, Netherlands, UK, Denmark, Norway, Sweden

Food-frequency questionaires

- Tailored to each country
- Considerable variation in level of detail

Recruitment

- Tailored to each country
- Variation in personal characteristics

EPIC Fish Study: Findings

No association was seen between fish consumption and mortality

- By lean, fatty and total
- By country
- By gender
- Unadjusted or adjusted
- All-cause or cause specific

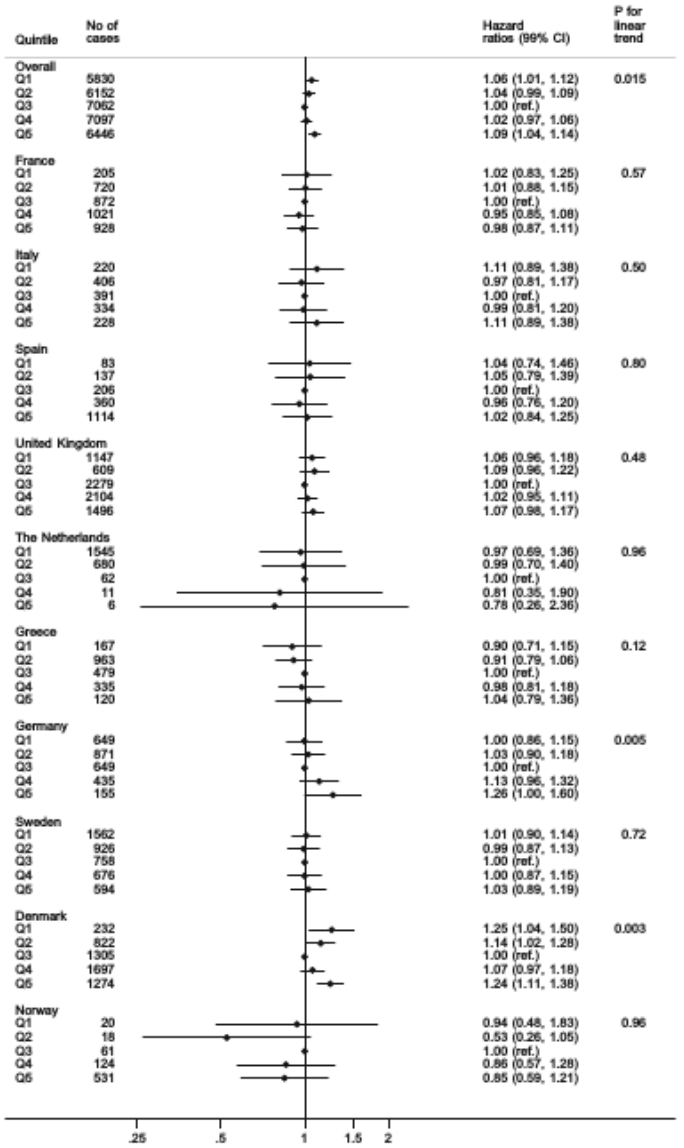
Exceptions

- All-cause unadjusted: Weak U-shaped association
- Denmark unadjusted: U-shaped association

Mortality vs. fish - EPIC

Quintile	No of cases	Hazard ratios (99% CI)	P for linear trend
Overall			
Q1	5830	1.06 (1.01, 1.12)	0.015
Q2	6152	1.04 (0.99, 1.09)	
Q3	7062	1.00 (ref.)	
Q4	7097	1.02 (0.97, 1.06)	
Q5	6446	1.09 (1.04, 1.14)	
Denmark			
Q1	232	1.25 (1.04, 1.50)	0.003
Q2	822	1.14 (1.02, 1.28)	
Q3	1305	1.00 (ref.)	
Q4	1697	1.07 (0.97, 1.18)	
Q5	1274	1.24 (1.11, 1.38)	

Unadjusted



EPIC Fish Study: Conclusions

This study does not support a protective - or deleterious - effect of fish consumption on death from all causes, or specific causes

Consumption of fish may usefully substitute for intake of other demonstrably less-healthy foods, such as processed meats

Study limitations, including heterogeneity of subjects and questionaires, may have obscured relationships between fish and mortality, though there is no specific indication that is the case

Fish oil supplements

Findings of benefits from consuming n-3 rich fish spawned the hypothesis that fish oil extracts might have the same benefit, without the cost or bother of eating fish

Preliminary findings were encouraging

Further investigation has cast serious doubt that supplements have the same benefit as fish in the diet

Fish contaminants & their risk

Most common threat is methylmercury

- MM bioaccumulates through the acquatic food chain, reaching highest-levels in large, long-lived predators (swordfish, shark)
- MM poses particular threat to cause delayed cognitive and neuromuscular development in children exposed *in utero*
- MM may be especially problematic in localities following industrial accidents or pollution (power plants, mining)

Fish & mercury – FDA guidelines for pregnant women, children

1. **Do not eat:**
   - **Shark**
   - **Swordfish**
   - **King Mackerel**
   - **Tilefish**

They contain high levels of mercury.

Fish & mercury – FDA guidelines for pregnant women, children

2. Eat up to 12 ounces (2 average meals) a week of a variety of fish and shellfish that are lower in mercury.

- Five of the most commonly eaten fish that are low in mercury are shrimp, canned light tuna, salmon, pollock, and catfish.

- Another commonly eaten fish, albacore ("white") tuna has more mercury than canned light tuna. So, when choosing your two meals of fish and shellfish, you may eat up to 6 ounces (one average meal) of albacore tuna per week.

Fish & mercury – FDA guidelines for pregnant women, children

3. **Check local advisories about the safety of fish caught by family and friends in your local lakes, rivers, and coastal areas.**

If no advice is available, eat up to 6 ounces (one average meal) per week of fish you catch from local waters, but don't consume any other fish during that week.

Fish & mercury – guidelines for other adults of all ages

No special precautions need be taken in regard to consumption of fish as regards its mercury content, with the exception of when knowledge exists that locally caught fish contain exceptionally high levels of methylmercury contamination

Fish contaminants & their risk

PCBs and dioxins – organochlorines

- Industrial process compounds which persist for long times in the environment
- Evidence suggests exposure increases cancer risk in humans
- Exposure due to fish consumption generally very low
- Benefit – risk analysis concludes ratio of benefit (CHD reduction) to cancer risk is very favorable (1000:1 or better)

Fish – Which ones, how much?

Different types of fish differ dramatically in their ω-3 content

ω-3 content can differ in a given fish by wild vs. farmed, and by preparation (fresh, frozen, canned)

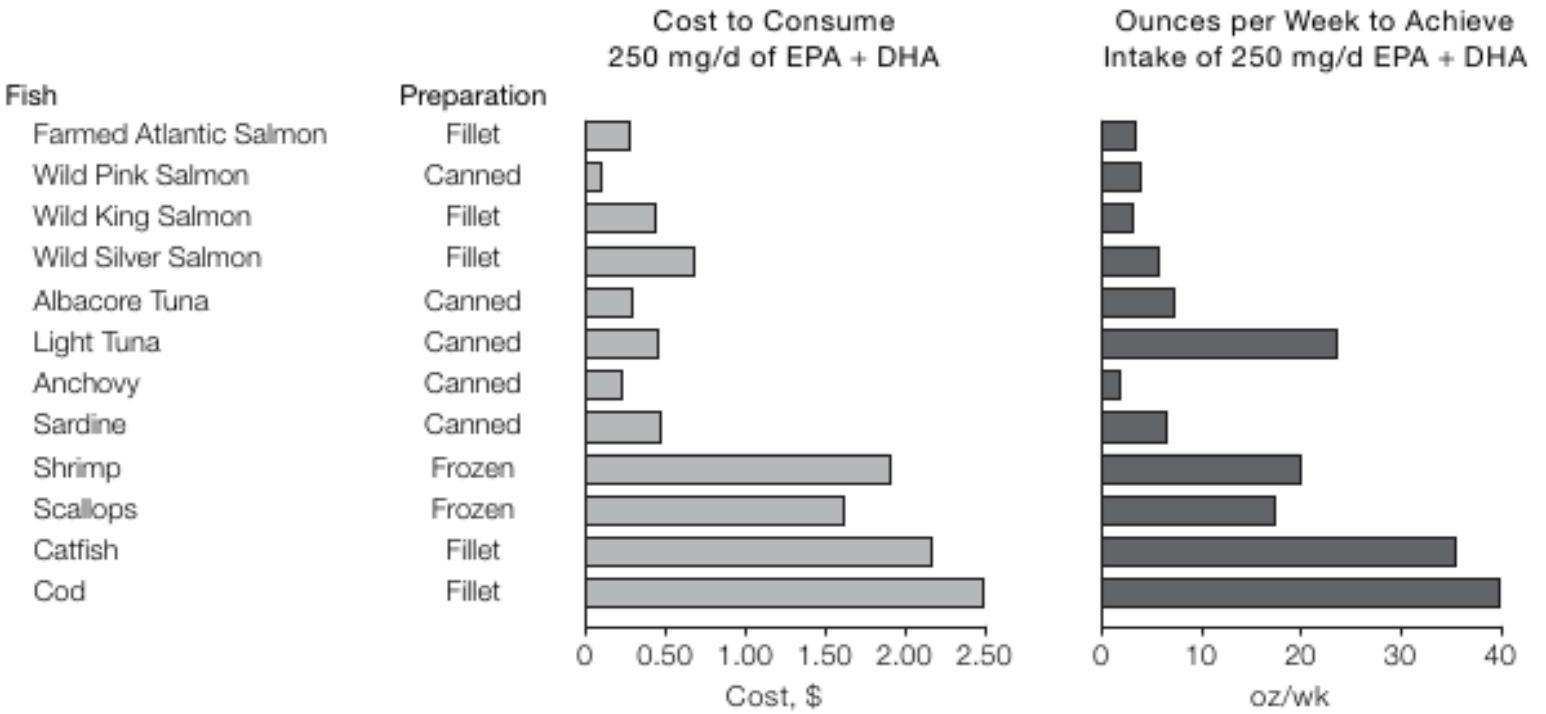
Other considerations – environmental impacts (overfishing with depletion of stocks, line vs. netting, fish farming effects)

- Www.foodandwaterwatch.org for Smart Seafood Guide

TABLE 1 Major dietary sources of long-chain (n-3) PUFA

	EPA	DPA[2]	DHA	Combined EPA
			mg/100 g	
Anchovy	763	41	1292	2055
Herring, Atlantic	909	71	1105	2014
Salmon, farmed	862	393	1104	1966
Salmon, wild	411	368	1429	1840
Mackerel, Atlantic	504	106	699	1203
Bluefish	323	79	665	988
Sardines, Atlantic	473	0	509	982
Trout	259	235	677	936
Golden bass (tilefish)	172	143	733	905
Swordfish	127	168	772	899
Tuna, white (albacore)	233	18	629	862
Mussels	276	44	506	782
Striped bass	169	0	585	754
Shark	258	89	431	689
Pollock, Atlantic	91	28	451	542
Oysters, wild	274	16	210	484
King mackerel	174	22	227	401
Tuna, light (skipjack)	91	17	237	328
Snapper	48	22	273	321
Flounder and sole	168	34	132	300
Clams	138	104	146	284
Grouper	35	17	213	248
Halibut	80	20	155	235
Lobster	117	6	78	195
Scallops	72	5	104	176
Blue crab	101	9	67	168
Cod, Pacific	42	5	118	160
Shrimp	50	5	52	102
Catfish, farmed	20	18	69	89
Eggs	0	7	58	58
Chicken breast	10	10	20	30
Beef	2	4	1	3
Pork	0	10	2	2

Figure 6. Estimated Costs of Consuming the equivalent of 250 mg/d EPA + DHA From Fish



Costs were calculated for commonly consumed seafood species, based on retail prices (averaging the most commonly sold items in each of 6 US cities in the east, midwest, and south from a national online grocery store[181] or, for wild king and silver salmon, from online retailers[182-184]) and on species-specific eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) content.[121] Least expensive was canned pink salmon (9 cents/250 mg of EPA + DHA); the average cost per 250 mg of EPA + DHA for these 12 types of seafood was 92 cents. The corresponding ounces per week needed to achieve 250 mg/d of EPA + DHA is also shown.

Fish & Health - Summary

Regular consumption of fish containing adequate amounts of ω-3 PUFAs DHA & EPA is associated with reduced all-cause and CHD mortality

Full benefit to healthy individuals can occur with two servings of carefully-selected fish per week

Fish oil supplements do not convey the same benefits, at least as we understand at this time

Fish & Health - Summary

Women who are pregnant, might become pregnant, or are nursing, as well as children, should observe precautions in the amount and type of fish to minimize methylmercury exposure

Much variation exists in the amount of different fish that must be consumed to obtained these benefits, as well as in the cost

- Canned albacore tuna, canned pink salmon, anchovies and sardines are especially cost-effective

Environmental concerns should be considered in choosing fish