Institution: University of Ulster

Unit of Assessment: 3B Allied Health Professions, Dentistry, Nursing and Pharmacy – Biomedical Sciences

Title of case study: Benefits and risks of fish consumption in pregnancy

1. Summary of the impact (indicative maximum 100 words)

Research undertaken at the University of Ulster has had a global impact on public health advice about fish consumption during pregnancy. Ulster's international collaborative research has been used by the Food and Agriculture Organisation (FAO) of the United Nations and the World Health Organization (WHO), and also by industry, to promote greater fish consumption during pregnancy. The work has also been evaluated by the European Food Safety Authority (EFSA) in its assessment of the public health risk of methyl-mercury in food.

2. Underpinning research (indicative maximum 500 words)

The Seychelles Child Development Study (SCDS) is a series of epidemiological studies in mother-child cohorts recruited in the high fish-eating population of the Seychelles. The key Ulster researchers are Professor JJ Strain, Dr E McSorley (née Duffy), Dr Maria Mulhern (née Barnes) and Dr Alison Yeates (née McAfee) who were employed at the University of Ulster at the time the research was carried out, from 1999 onwards. The research programme was undertaken in collaboration with the University of Rochester, New York and the Department of Health, Republic of Seychelles. The results have been published in top nutrition and toxicology journals

It is crucial that pregnant women receive accurate advice on diet. Fish exposes mothers to potentially high amounts of methyl-mercury, an environmental pollutant and toxicant to which the developing foetal brain is particularly sensitive. Government advisories worldwide have cautioned pregnant women to limit their fish consumption. This advice is based on limited epidemiological evidence; for example, in the Faroe Islands a study which found detrimental effects on children's neurodevelopment, was linked to maternal consumption during pregnancy of pilot whalemeat which is high in methyl-mercury.

However fish is an excellent source of protein and essential nutrients. It is the primary source of n-3 (omega-3) polyunsaturated fatty acids (PUFA), particularly docosahexaenoic acid (DHA), which are important for brain development. Limiting maternal fish intake could therefore pose a threat to children's optimal neurological development. Moreover, in many communities worldwide, fish is the predominant source of protein and other essential nutrients.

A resolution of this dilemma comes from studies involving the high fish-eating population of the Republic of Seychelles. The Seychelles Child Development Study (Main Cohort), originally set up in 1989, recruited pregnant women and continues to follow their offspring. It was designed to determine if prenatal exposure to methyl-mercury had a detrimental effect on offspring's neurodevelopment. In fact it found positive associations between maternal methyl-mercury exposure and developmental outcomes in the children, but the reasons for this association were unclear given that methyl-mercury is a toxin. A further study (SCDS Nutrition Cohort) was set up to see if nutritional factors could explain this positive association. This study involved the recruitment of 300 mothers during pregnancy and has continued to observe 229 mother-child pairs. It measured the women during pregnancy both for methyl-mercury exposure and a number of nutritional factors which are known to influence child development; the cognitive development of the offspring has been measured at various stages of their childhood.

The study found positive associations between the maternal intakes of n-3 PUFA (and especially DHA) from fish consumption during pregnancy, and the developmental outcomes in the children. These associations were shown in the children at 9 months, 30 months and 5 years of age and these findings may also explain the positive associations between maternal methyl-mercury exposure and developmental outcomes found in the SCDS Main Cohort. Our conclusion was that maternal nutrition has played a confounding role in these epidemiological studies.

Potentially detrimental effects of maternal methyl-mercury exposure (negative associations with developmental outcomes in the child) in the SCDS Nutrition Cohort were only evident at 30 months of age and only when the n-3 PUFA measures were included as covariates in the

regression analyses. Such negative associations have not been found up to 17 years of age among the offspring from the SCDS Main Cohort.

The work indicates that the beneficial effects of the n-3 PUFA present in fish can outweigh any adverse effects of prenatal methyl-mercury exposure on neurodevelopmental outcomes in children. Indeed, these beneficial effects were observed with fish intakes up to two meals per day. This level of fish consumption in this sentinel population is much higher than that consumed by pregnant women in Western countries.

Key Researchers at Ulster:
Key staff: Professor JJ (Sean) Strain (Professor of Human Nutrition and Director of NICHE; 1981-present); Dr Emeir McSorley (née Duffy) (Senior Lecturer; 2002-present); Dr Maria Mulhern (née Barnes) (Lecturer; 2007-present); Dr Alison Yeates (née McAfee) (Research Associate 2009-present); Professor Julie Wallace (Professor; deceased)

3. References to the research (indicative maximum of six references)

Strain, J.J., Davidson, P. W., Thurston, S. W., Harrington, D., Mulhern, M. S., McAfee, A. J., van Wijngaarden, E., Shamlaye, C. F., Henderson, J. and Watson, G. E. (2012). Maternal PUFA status but not prenatal methylmercury exposure is associated with children's language functions at age five years in the Seychelles. *Journal of Nutrition,* 142(11): 1943-1949.
DOI:10.3945/jn.112.163493.
Times Cited: 6 SJR: 1.505 SNIP:1.555 Impact Factor: 3.916

Paper also selected for pubcast:
Video Pubcast, Scivee (in association with American Society of Nutrition) (October 2012): Maternal Polyunsaturated Fatty Acid Status but not Prenatal Methylmercury exposure is associated with Children's Language Functions at Age Five Years in the Seychelles
Available at: http://www.scivee.tv/node/53926 1024 views (as of 08/09/2013)

Davidson, P. W., Cory-Slechta, D. A., Thurston, S. W., Huang, L.-S., Shamlaye, C. F., Gunzler, D., Watson, G., van Wijngaarden, E., Zareba, G., Klein, J. D., Clarkson, T. W., Strain, J. J. and Myers, G. J. (2011). Fish consumption and prenatal methylmercury exposure: Cognitive and behavioral outcomes in the main cohort at 17 years from the Seychelles child development study. *Neurotoxicology,* 32(6): 711-717.
DOI: 10.1016/j.neuro.2011.08.003
Times Cited: 14 SJR: 0.998 SNIP: 1.113 Impact Factor: 3.096

Lynch, M. L., Huang, L.-S., Cox, C., Strain, J. J., Myers, G. J., Bonham, M. P., Shamlaye, C. F., Stokes-Riner, A., Wallace, J. M. W., Duffy, E. M., Clarkson, T. W. and Davidson, P. W. (2011). Varying coefficient function models to explore interactions between maternal nutritional status and prenatal methylmercury toxicity in the Seychelles Child Development Nutrition Study. *Environmental Research,* 111(1): 75-80.
DOI: 10.1016/j.envres.2010.09.005
Times Cited: 7 SJR: 1.424 SNIP: 1.472 Impact Factor: 3.398

Stokes-Riner, A., Thurston, S. W., Myers, G. J., Duffy, E. M., Wallace, J., Bonham, M., Robson, P., Shamlaye, C. F., Strain, J. J., Watson, G. and Davidson, P. W. (2011). A longitudinal analysis of prenatal exposure to methylmercury and fatty acids in the Seychelles. *Neurotoxicology and Teratology,* 33(2): 325-328.
DOI: 10.1016/j.ntt.2010.11.003
Times Cited: 12 SJR: 0.783 SNIP: 0.968 Impact Factor: 2.983

Davidson, P. W., Strain, J. J., Myers, G. J., Thurston, S. W., Bonham, M. P., Shamlaye, C. F., Stokes-Riner, A., Wallace, J. M. W., Robson, P. J., Duffy, E. M., Georger, L. A., Sloane-Reeves, J., Cernichiari, E., Canfield, R. L., Cox, C., Huang, L. S., Janciuras, J. and Clarkson, T. W. (2008). Neurodevelopmental effects of maternal nutritional status and exposure to methylmercury from eating fish during pregnancy. *Neurotoxicology,* 29(5): 767-775.
DOI: 10.1016/j.neuro.2008.06.001

Times Cited: 51 SJR: 0.998 SNIP: 1.113 Impact Factor: 3.096

Strain, J. J., Davidson, P. W., Bonham, M. P., Duffy, E. M., Stokes-Riner, A., Thurston, S. W., Wallace, J. M. W., Robson, P. J., Shamlaye, C. F., Georger, L. A., Sloane-Reeves, J., Cernichiari, E., Canfield, R. L., Cox, C., Huang, L. S., Janciuras, J., Myers, G. J. and Clarkson, T. W. (2008). Associations of maternal long-chain polyunsaturated fatty acids, methyl mercury, and infant development in the Seychelles Child Development Nutrition Study. *Neurotoxicology,* 29(5): 776-782.
DOI: 10.1016/j.neuro.2008.06.002
Times Cited: 52 SJR: 0.998 SNIP: 1.113 Impact Factor: 3.096

Grant income obtained to undertake the studies was from the US National Institutes of Health (NIH) and the European Commission (EC):
Strain, J. J., Wallace, J. M. W., Duffy, E. M., Mulhern, M. and McAfee, A. Methyl mercury effects on adolescent development. Funded by grant 5-R01- ES008442 US National Institute of Environmental Health Sciences, NIH; 2011-2015; £200k.

Strain, J. J., Chang, C. K., Wallace, J. M. W. and Duffy, E. M. Toxicity of methyl mercury in a fish-eating population. Funded by grant 5-R01-ES010219 US National Institute of Environmental Health Sciences, NIH; 2010-2014; £710k.

Strain, J. J., Bonham, M. P., Wallace, J. M. W., Duffy, E. M., Rowland, I. and Livingstone, M.B.E. Public health impact of low-level mixed element exposure in susceptible population strata (PHIME). Funded by grant from the EC through its Sixth Framework Programme for RTD (contract no FOOD-CT-2006- 016253); 2006-2011; £445k.

Strain, J. J., Wallace, J. M. W., Robson, P. J., Rowland, I. and Livingstone, M. B. E. Factors modifying the toxicity of methyl mercury in a fish eating population. Funded by grant 5-R01 – ES010219 US National Institute of Environmental Health Sciences, NIH; 2010-2014; £467k.

4. Details of the impact (indicative maximum 750 words)

Experts and global leaders in health matters have used the collaborative research undertaken in the Seychelles by researchers at Ulster to revise the guidelines on fish intake during pregnancy.

A report of the Joint FAO/WHO Expert Consultation on the Risks and Benefits of Fish Consumption **[1]** concluded that maternal fish consumption contributes to optimal neurodevelopment in their offspring and that the neurodevelopment risks of not eating fish exceed the risks of eating fish for up to at least seven 100g servings per week and methyl-mercury concentrations up to at least 1 µ/g. Data from studies undertaken in the SCDS were central to these conclusions and the work of Davidson *et al.* 2008, Strain *et al.* 2008 and Lynch *et al.* 2011 was cited in the report. This report was a landmark in global recommendations for maternal advice on fish consumption during pregnancy. Maternal advice in most countries has recommended that fish intake should be limited during pregnancy because of the concerns of methyl-mercury neurotoxicity to the foetus. The report recognised that eating fish is part of the cultural traditions of many peoples and in some populations fish is a major source of food and essential nutrients. This report was the first time in an official advisory publication that the direct benefits of the n-3 fatty acids, from fish eaten during pregnancy, were indicated to outweigh any possible risks of methyl-mercury on child development

Following the FAO/WHO report, the European Food Safety Authority (EFSA) **[2]** was asked by the European Commission (EC) to consider these new developments regarding methyl-mercury toxicity and evaluate whether the Joint FAO/WHO Expert Committee on Food Additives (JECFA) provisional tolerable weekly intakes (TWI) for methyl-mercury were still appropriate. This request recognised that the SCDS Nutrition Cohort had indicated that n-3 PUFA in fish may counteract any potential negative effects from methyl-mercury exposure. It also recognised that beneficial nutrients in fish may be the confounding factor that accounts for the positive outcomes in the SCDS study compared with the adverse outcomes in previous child cohort studies. In light of these findings, the Panel on Contaminants in the Food Chain (CONTAM) established a revised

TWI for methyl-mercury. The Panel also concluded that, if measures to reduce methyl-mercury exposure are considered, the potential beneficial effects of fish consumption should also be taken into account. All six key references in section 2 were evaluated and used in this scientific opinion, which is being used by the EC to update European recommendations.

In the most recent Dietary Guidelines for Americans 2010 **[3]**, it was appreciated that a variety of seafood in the amounts recommended outweigh the health risks associated with methyl-mercury. There was some relaxation, compared with the Advisory from the Environmental Protection Agency (EPA), with respect to the advice given to pregnant women on fish consumption. Women were still advised not to consume the fish with the highest methyl-mercury content and limit consumption of white tuna because of its methyl-mercury levels.

The work of the SCDS has also been cited in various websites associated with industry **[4]** and websites giving advice to clinicians **[5]** and health professionals **[6-9]**, albeit citations to the specific key references in section 2 are not always given.

The Seychelles Child Development Study is the largest epidemiological prospective study of nutrition and toxicology. The results continue to inform policymakers on the risk-benefit analysis of fish consumption during pregnancy.

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. FAO/WHO (2011). Report of the Joint FAO/WHO Expert Consultation on the Risks and Benefits of Fish Consumption. Rome, Food and Agriculture Organization of the United Nations; Geneva, World Health Organization, 50 pp.

Executive Summary available at: http://www.who.int/foodsafety/chem/meetings/RBfish_exec_summary.pdf . Accessed March 2011.

2. EFSA Panel on Contaminants in the Food Chain (2012) Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Journal, 10(12):2985

3. Dietary Guidelines Advisory Committee. (2010). *Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2010, to the Secretary of Agriculture and the Secretary of Health and Human Services.* U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

4. Food Product Design (08/01/13)Prenatal exposure to fish boosts child's brain power http://www.foodproductdesign.com/news/2013/01/prenatal-exposure-to-fish-boosts-child-s-brain-po.aspx

5. UpToDate (April 2012) Risks and benefits of fish consumption and fish oil supplements during pregnancy. http://www.uptodate.com/contents/risks-and-benefits-of-fish-consumption-and-fish-oil-supplements-during-pregnancy

6. Fats of Life (December 2012) Higher maternal PUFAs, not methylmercury, associated with language scores at age 5. PUFA Newsletter 17(3) 16-18.

7. Fats of Life (April 2012) Maternal and infant health: Unimpaired neurodevelopment in adolescents of mothers with high prenatal fish and methylmercury intakes. PUFA Newsletter 17(1) 5-6.

8. Fats of Life (September 2008) Maternal and infant health: Interplay between nutrients and methylmercury in child neurodevelopment. PUFA newsletter 13(3) 15-17.

9. Omega-3 Centre (December 2012) Nutrients in fish can boost brain development The Omega-3 Centre: e-newsletter 11.