INTERNATIONAL HEALTH NEWS

William R. Ware, PhD - Editor

NUMBER 252 **NOVEMBER 2014** **23rd YEAR**

In this issue we end the current discussion featured frequently over the past year in IHN concerning diabetes with emphasis on diet and related topics. Diabetes presents an alarming picture. It is described in terms of an epidemic. Many are undiagnosed. Many of those diagnosed are treated, in some cases intensively with a variety of drugs, but the disease progresses. Frequently the diagnoses in older adults do not include investigating the possibility of late onset type 1 diabetes. Diet and exercise generally fail and drugs are started with metformin being the first line of defence. Patients may be told, we will get your blood sugar under control and you will be OK. This is nonsense. In fact, there is little in the guidelines that offer any realistic hope of arresting the relentless progression to insulin dependence. This is very well appreciated by diabetes experts, but not the general public.

As discussed in recent IHN issues, a ray of hope emerged from the UK with the clinical trial by Dr. Roy Taylor and his group. Some might describe it as a thunder bolt, perhaps in the wilderness. A simple dietary intervention worked. Diabetes was reversed over an amazingly short period. One had to be lucky even to learn about this. The success does not appear to have been widely heralded worldwide. But the amazing thing was that a number of diabetic individuals learned about the diet from the UK press and tried it themselves, many without help from their doctor, and for the majority it worked. It is quite possible that for some of those who experienced failure, their problem was late onset type 1 diabetes, which for a considerable period is indistinguishable from type 2, the type for which the diet works. This "do it yourself" experiment is in itself almost unique. It is rare that individuals on their own undertake an intervention where they use a biomarker measured invasively at home to monitor their progress and judge success. The only other examples that come to mind are the use of urine strips to see if a diet produces ketosis, something that was popular after the Atkins Diet became popular, and type 1 diabetics using the finger prick method to help adjust diets they have elected to try.

Those who have found this lengthy discussion of diabetes uninteresting may be pleased it is over for now and hopefully they are certain they do not have diabetes or prediabetes. The emphasis on diabetes was prompted by the fact that it is so common and serious. A significant fraction of you editor's friends are diabetic, and it is almost certain that some additional ones are undiagnosed. In addition, it is hoped that by introducing the work of Taylor and his group, readers will be aware of an "alternative" therapy that seems to work very well. It should even by attractive for those also diagnosed with prediabetes, a red flag that should never be ignored.

In this issue we discuss alcohol, red wine and diabetes, how to determine your approximate risk of developing diabetes, and finally the absolute effectiveness of flu vaccination and a spectacular failure on board a US Navy ship.

Wishing you and your family good health,

William R. Ware, PhD, Editor

Highlights

ALCOHOL, RED WINE AND DIABETES. GOOD, BAD OR INDIFFERENT?

Both the American and Canadian Diabetes Associations take the position that diabetics do not need to avoid alcohol because of this disease. The guidelines contain the usual recommendations concerning moderate, gender dependent drinking and caution against combining alcohol with the anti-hyperglycaemic drugs that act as insulin secretagogues such as sulfonylureas, meglitinides and phenylalanine derivatives as there is the risk of an interaction which might cause hypoglycaemia. A common definition of moderation is a limit of two drinks/day or less than 10 /week for women and less than 3/day or 15/week for men. This recommendation is independent of the presence or absence of diabetes. Beyond this, one must look at the peer-reviewed literature for more details concerning risk vs. benefit. In particular, is there an association between alcohol consumption and the risk of developing type 2 diabetes? Furthermore, what is the impact of moderate alcohol consumption on fasting glucose, glucose tolerance and oxidative stress? Finally, does the source of the alcohol matter and is there a difference between red and white wine? These questions have been reviewed recently by Robertson.[1]

The following follow-up studies examined the incidence of type 2 diabetes (T2D) in individuals with either normal glucose metabolism (tolerance) at baseline or some with prediabetes. Citations can be found in Robertson's review.

- Over 3100 men and women 40—69 years of age were followed for 4 years. No association was found between moderate alcohol consumption and T2D. Wine was the most common source and was associated with lower risk of T2D in both men and women.
- Approximately 2000 men and 3000 women were given baseline oral glucose tolerance tests to identify type 2 diabetics and followed for 8—10 years. Wine was not associated with the occurrence of either T2D or prediabetes in men with normal glucose tolerance. Women of normal glucose tolerance experienced reduced risk with wine consumption higher than occasional drinkers.
- A very large cohort of men and women was followed for 10 years. Moderate alcohol consumption reduced the risk of T2D, wine more so than other forms of alcoholic drinks.
- Comparison of red wine with beer consumption in 90,000 individuals revealed reduced risk of diabetes in those who drank wine.

While there was considerable variation in study design and the cohorts examined in these studies, the results can be generalized. Moderate drinking does not appear to increase the risk of T2D and specifically drinking wine appears to be associated with reduced risk.

Nevertheless, it is common to see alcohol listed as a risk of developing type 2 diabetes, and one sees a recent study cited (second study in the above summary)[2]. In this study, for high alcohol consumption, the fully adjusted model gave insignificant risk for either pre diabetes or type 2 diabetes for men and protection for women. When the groups were combined, the fully adjusted model still contained the null result (no effect) in the confidence interval. Hardly compelling evidence when considered along with the other studies discussed above. Cherry-picking studies in reviews can lead to widespread misconceptions.

The second question concerns the impact on existing T2D of moderate wine consumption and in particular red wine which has received almost all the research attention.[1] Robertson's review discusses

four items of interests. There does not appear to be a significant effect on fasting blood glucose (FBG) or HbA1c with red wine intake in the range of 120 to 240 mL/day. Significant changes appear to occur in insulin resistance which was found to decrease 43% over 2 weeks with 360 mL of red wine consumption. In addition, another study found that 300 mL of red wine taken with a meal negated the decrease in antioxidant capacity caused by the food.

An interesting study by Marfella *et al*[3] examined the impact of 118 mL of red wine and a 2000 calorie/day Mediterranean style diet for one year. The subjects were randomized to wine or no wine but had roughly the same diet. The subjects were all type 2 diabetics with a recent history of heart attack (MI). In both groups almost identical changes in FBG and HbA1c occurred over the year, with both groups regressing to the prediabetic ranges. Thus these changes were independent of the wine intervention. The big and significant differences between the intervention and control groups were seen in insulin resistance as measured by a calculation based on fasting insulin and glucose (HOMA-IR), the inflammation markers CRP, TNF-α, and IL-6, and markers of oxidative stress and myocardial performance. The authors suggest that red wine may have a beneficial effect on the prevention of cardiovascular complications after MI in type 2 diabetics through the reduction of pro-inflammatory cytokines and the reduction of oxidative stress.

It is noteworthy that the amount of red wine in the above study corresponded to one average glass per day and that moderate wine consumption is a component of the Mediterranean diet and also by itself, an important component of a lifestyle pattern associated with dramatic reduction in mortality from all causes, heart disease, cardiovascular disease and cancer in elderly men and women. The pattern involved the Mediterranean diet, moderate alcohol consumption, physical activity and not smoking. The 30% absolute risk reduction yielded a number needed to treat over 10 years of 3 to prevent one fatal event. [4]

Robertson concludes that drinking red wine in moderation has no adverse effects on individuals with T2D and in fact may prevent this disease in people at risk. Both epidemiologic and metabolic studies appear consistent. He also points out that considerable evidence suggests that the red wine effect comes from the skins of the grapes rather than the juice or the alcohol, since the skins contain the polyphenols which are well known to have antioxidant effects. It is not surprising that red wine has a 12-fold higher level of polyphenols compared to white wine.

A study recently published in the journal *Diabetes Care* examined the relationship between alcohol consumption and vascular complications and mortality in type 2 diabetics.[5] Over 11,000 men and women mean age 66 years with information on alcohol consumption were followed for 5 years. This report was based on data from a study which had other major objectives. Moderate consumption was defined as ≤ 21 drinks/week for men and ≤14 for women. Exceeding these limits constituted heavy consumption. For the three endpoints of cardiovascular events, microvascular events and all-cause mortality, the relative risk reductions associated with moderate consumption were 118% 17% and 14% where the reference was abstinence. The results for heavy consumption were not significant, suggesting a J-shaped response curve. When the type of alcoholic beverage was examined, somewhat larger effects were seen with red wine vs. abstinence than with other sources of alcohol for cardiovascular events and all-cause mortality, but with the latter giving statistically non-significant results. The hazard ratios leading to the relative risk reductions were adjusted in the research for a large number of confounding factors. The authors suggest that a plausible explanation for the better results with red wine might be that red wine drinkers are typically less overweight, exercise more, and drink with meals, but BMI and exercise were among the confounding factors used in the statistical analysis. Thus drinking with meals might be a factor.

There is some evidence that red wine with meals influences adverse post-meal (postprandial) effects related to cardiovascular and other vascular problems which are particularly prevalent in diabetics.

- Red wine prevents the postprandial increase in plasma cholesterol oxidation products. These modified cholesterol molecules present after eating are thought to be associated with cardiovascular risk.[6]
- Impaired endothelial function (inner surface cells of blood vessels for example) is thought to be associated with vascular disease. Red wine and olive oil, components of the Mediterranean diet have been found to improve endothelial function, presumably acting as antioxidants.[7].

- It has also been found that red wine mitigates the postprandial increase in LDL cholesterol susceptibility to oxidation. The conventional wisdom regards oxidized LDL as a particularly bad cholesterol.[8,9]

One might wonder why all the research interest in red wine. The answer is that it is a very rich source of a large number of phytochemicals including polyphenols which have been independently associated with health benefits. These are extracted during the long exposure of the juice of the grapes to the skins during fermentation process. With the recent increasing interest in more full-bodied reds, it is probably true that the levels of these beneficial chemicals are increasing in many of the popular wines. These wines incidentally tend to come with 1% to 2% higher alcohol content.

Wine consumption has always been part of the explanation for the so-called French Paradox, a paradox derived from the belief that fat and cholesterol are bad and yet important components of the traditional French diet. The paradox disappears when one abandons the above dogma based beliefs and adds the beneficial aspects of the traditional manner of eating and as well the higher level of activity common to at least some members of this population. Unfortunately, these healthy cultural aspects of living may be disappearing in this population.

Thus, it can be concluded that in the context of diabetes, red wine in moderation appears to be beneficial and there is no evidence of enhanced risk of either prevalence or the serious consequences associated with the inevitable progression of this disease. As pointed out by Robertson in his review, one should not ignore the benefits of red wine associated with merely "relaxing with good friends during a savoury meal with a great cabernet."

Mainstream medicine has historically shown reluctance to recommend any alcoholic beverage as part of healthy living although wine is consistently mentioned when the Mediterranean diet is described. Alcohol was also an important component of a lifestyle and dietary pattern that produced sensational 10-year cardiovascular absolute risk reductions.[4] The reason for the reluctance of course is the dark side of alcohol consumption which presumably is at least theoretically know to all readers of this newsletter. Adverse drug reactions must be added to addiction when considering the reasons to abstain or proceed with great caution. Potentially fatal drug Interactions such as with Tylenol and heavy alcohol consumption to potentially produce fatal cerebral enema are probably not as appreciated as they should be, and excess mortality associated with alcohol related accidents is of course common. One must be sure of their own ability to control alcohol consumption to the level of moderation before embracing what appear to be compelling benefits.

Disclaimer and conflict of interest. Your editor is a great fan of good red wines, and this appears to be the case with Professor Robertson whose review is cited above.

RISK OF DEVELOPING TYPE 2 DIABETES AND INDICATED ACTIONS

Avoiding diabetes should be a top priority of everyone. The serious long-term effects of having this disease and their significant impact on the quality of life should provide sufficient motivation for aggressive action to prevent its development.

A list of risk factors includes genetics, lifestyle factors such as lack of activity and exercise, smoking, the influence of dysfunctional gut microbes, and certain vitamin deficiencies, in particular vitamin D. Certain dietary patterns are also associated with enhanced risks.[10] One also sees alcohol mentioned, but when one checks the citations given in a recent review of risk factors, the evidence is not significant. This is discussed elsewhere in this issue. The success of lifestyle modifications, except for the strict adherence to a Mediterranean diet, has been disappointing. While typical absolute risk reductions of 15% in diabetes incidence are impressive,[11] 85% experience no benefit, which is not good enough. At the opposite extreme, the Newcastle Diet appears to successfully bring nearly *all* diabetics to normal, reminiscent of the early successes of antibiotics for infectious diseases, and in sharp contrast to the lack

of success of modern medicine in reversing the chronic diseases of aging where absolute benefit is almost negligible across the board.

The above risk factors that are modifiable are similar to a second set of factors studied in the Framingham Offspring Study.[12] Using a large database, the Framingham researchers examined the importance of a wide variety of factors on the 8-year incidence of type 2 diabetes. The most important factors found were then assigned points reflecting their relative importance. The factors and the assigned points are given in the table. The points resulted from a standard logistic multivariable analysis of the significant factors. In the table, the risk is the absolute risk of developing type 2 diabetes over 8 years associated with the points score is given.

PREDICTIVE FACTORS FOR MIDDLE-AGED ADULTS	PTS
Fasting glucose 5.5 to 7.0 mmol/L (100-126 mg/dL)	10
BMI 25.0 to 29.9 (overweight)	2
BMI ≥30 (obese)	5
HDL (M) < 1.0 mmol/L (40 mg/dL) and (W)< 1.3 mmol/L	5
Family history of diabetes	3
Triglyceride level > 1.7 mmol/L (150 mg/dL)	3
Blood pressure > 130/85 or treated	2
Total Points	30

PTS	RISK
≤ 10	≤3%
12	4%
14	6%
18	13%
20	18%
24	33%
≥25	>35%

The factors in the table provide a useful check list since all are known to most health conscious individuals, some of routine blood tests. They may be regarded as thresholds for significant concern and targets for intervention. Factors omitted in the final analysis because of small influence were gender, waist circumference and the results of the 2-hour glucose tolerance test. Thus if one is prediabetic but almost diabetic by fasting blood glucose, overweight, has a low HDL and high triglycerides, then the risk is 18% over 8 years. Change the weight to obesity and one jumps to nearly 33%. The factors in this table are common to the metabolic syndrome which for some is the unintended consequence of a low-fat, high carbohydrate diet with positive energy intake.

What is interesting in this table is the weight given to elevated fasting blood glucose (FBG). The range given applies to prediabetes. When one crosses this threshold, action is indicated and can include the ketogenic or low carbohydrate diets discussed in the November 2013 discussion of treating diabetes, or the 800 calorie diet discussed last month which was designed for diabetics but applicable to prediabetics. Both will reduce BMI, increase HDL and decrease triglycerides. The focus should be on the FBG since it carries the most weight as it approaches 7 mmol/L (126 mg/dL). Dietary intervention which forces the FBG back into the normal range will almost certainly favourably impact the triglycerides, HDL and BMI. It will be noted that the factors in the table are also important in identifying the metabolic syndrome, which is also of course a risk factor for diabetes. The reduced HDL and elevated triglyceride levels are the hallmark of the dyslipidemia associated with both the metabolic syndrome and the risk of diabetes. These factors, aside from the hereditary one, tend to cluster, although the impact on FBG would appear to be a following rather than a leading indicator, to borrow from economists' lingo. It is noteworthy that elevated triglycerides and depressed HDL are also almost invariably the result of a low fat, high carbohydrate diet but this is an oversimplification since simply consuming energy well above that needed can impact all of the factors in the table, although they will not all change at the same rate.

By dealing with the BMI problem, one is also dealing with the waist to hip ratio, one of the commonly discussed risk factors for diabetes, i.e. belly fat. Dramatically decreasing weight almost always significantly decreases triglycerides and increases HDL.

With regard to diet, some guidelines now feature the Mediterranean food pattern as the ideal healthy diet. However, obviously even adherence to this diet pattern while consuming considerably more calories than needed will result in fat storage and weight gain in most individuals, thus negating the benefits. It

appears, especially based on Taylor's view of how diabetes develops,[13] that one must place primary emphasis on not consuming more than is absolutely necessary for the required metabolic processes determined by activity and basal metabolism. Another way of putting this is simply that it is important to maintain a BMI of 25 or less through adult life.

The actions necessary of course depend where one is in the continuum of normal, prediabetes and diabetes, and thus the aggressiveness of the action needed to return to a healthy state. The factors in the above table actually pertain to more than just the risk of diabetes, but diabetes carries so many additional risks of chronic disease and disability. Thus is reasonable to give great weight to maintaining a normal FBG. It is also noteworthy that it is not uncommon for the overweight and obese to have perfectly normal glucose metabolism and FBG. However, elevated BMI carries other risks, but the magnitude is still being debated.

NEWCASTLE 800-CALORIE DIET ELIMINATES THE METABOLIC SYNDROME

The success of the Newcastle 800-calorie diet along with variations in reversing (eliminating) diabetes was discussed in the last issue of IHN. The original 2011 report of the clinical trial also indicates that the subjects all had the metabolic syndrome which is not surprising given that it is a major risk factor for diabetes. The diet eliminated the metabolic syndrome at the same time it eliminated the diabetes. This is clear from the following table, which includes the defining characteristics of the syndrome. Three or more must be present to qualify. In the clinical trial, no blood pressure data was given, but this has no bearing on these conclusions. Data from the clinical trial are given at the beginning and after the 8-week diet.[14] Since three characteristics were present at baseline, the subjects, (9 male, 2 female so the definition is given for men) qualified for the diagnosis of metabolic syndrome.

CHARACTERISTIC	DEFINITION	BEFORE	AFTER
Waist Circumference (cm)	≥103	107	94
Triglycerides (mmol/L)	≥ 1.7	2.4	1.3
HDL Cholesterol (mmol/L)	≤1.0	1.1	1.1
Diastolic BP (mm Hg)	≥ 130	-	-
Fasting glucose (mmol/L)	≥ 5.6	9.2	5.7

Along with the elimination of the metabolic syndrome, it is probably true that the associated health risks are also eliminated. It is noteworthy that all four of the measured characteristics normalized in 8 weeks. Large randomized trials have found that lifestyle and dietary interventions over a year or more are capable of reducing the number in the treated group who qualify for the metabolic syndrome diagnosis, but never to zero.[15]

HOW WELL DO FLU VACCINES WORK? FALL CAMPAIGN IS IN FULL SWING

One easily gets the impression that the answer is very well indeed. Get your shot and you will be protected. Flu vaccination has become mandatory in many health care institutions. No shot and either wear a mask or quit. One would expect that most would be protected. The efficacy (relative risk reduction in controlled trials) is typically 50-60 % and can go higher, especially for children. Vaccine manufacturers and promoters would of course like it close to 100% which would justify the claim if one gets their shot, they won't get the flu. If one took an exit poll was taken from a vaccination clinic at a local mall, probably a surprising number would say just that. Thus it is of interest to look at two recent meta-analyses and examine the other side of the coin, the absolute benefits, a taboo subject in this field.

Recently, Ossterholm e*t al*[16] examined the efficacy of influenza vaccination as indicated by studies that were randomized, placebo controlled and where the cases were laboratory verified as viral influenza. It was required that vaccine efficacy be reported for all circulating influenza strains. Meta analyses of qualifying trials were conducted separately for adults and children or just adults

A second recent study by Tricco *et al*[17] compared the efficacy of influenza vaccines depending on whether or not they were matched to at least one of the strains circulating that year. Both matched and unmatched randomized controlled trials involving either trivalent inactivated vaccine (TIV) or nasal spray containing live attenuated influenza vaccine (LAIV) were analyzed. All the meta analyses had a mixture of studies involving children and adults in varying proportions, but more than half of the studies using LAIV involved children. The results of these two studies are given in the table below. Both papers provided enough information to calculate absolute results, actually by two methods which gave very close to identical results. The published papers ignored absolute results.

VACCINE EFFICACY IN RECENT META-ANALYSES						
Study	STUDIES	Age	NNT	RRR	No Benefit	Vaccine
Osterholm[16]	8	18-64	64	60%	98.4%	TIV
Osterholm [16]	7	0.5-7	8	84%	87.3%	LAIV
Trico[17]	12	A&C	93	62%	98.9%	TIV-Matched
Tricco[17]	11	A&C	204	51%	99.5%	TIV-Mismatched
Tricco[17]	15	A&C	18	77%	94.4%	LAIV-Matched
Tricco[17]	15	A&C	48	60%	97.9%	LAIV-Mismatched

TIV—Trivalent inactivated vaccine. LAIV—Live attenuated influenza vaccine.
NNT—Number needed to treat. RRR—Relative risk reduction. A&C—adults and children.

Note that most of the relative risk reductions (RRR) are impressive. Those who do not understand relative risk reduction will assume that for example, a RRR of 60% means that 60% of those vaccinated will not get the flu. However, only 1.6% will actually benefit whereas 98.4 will not. The magnitude of the relative risk reduction is related to the absolute risk reduction divided by the absolute risk in the control group, and thus can be very large for small absolute benefits in the case of disorders or diseases that have a low population incidence, which is the case with the flu in adults. Children have a higher untreated population risk, but it is still only generally only a few percentage points. Risk reductions are generally adjusted for confounding, and but these can be used to calculate the adjusted absolute risk reduction and number needed to treat. Note also that the RRR correlate rather poorly with the NNT, something at the very heart of the problem of using the RRR.

The above table suggests that independent of the type of the vaccine or how well it matches the strains during a given year, most vaccinated individuals do not benefit but must simply hope they are lucky. For TIV, a very common vaccine, mismatching does not seem to make much difference. However, the benefit for children from the LAIV is quite strong, as seen in the analysis involving LAIV by Osterholm *et al* and in the two by Tricco *et al* involving both LAIV which had heavy representation of children in the studies included, since it is the popular vaccine type for children. While numbers needed to treat of 8 are not common in clinical trials or their pooled analyses, it is unfortunately still true, as shown in the table, that even with such a low number, most do not benefit. There is very little data for those over 65 of age.

The analysis by Osterholm *et al* prompted a number of comments in the literature. It is interesting in these comments that the focus was universally on relative risk reduction, never on the percentage treated that do or do not benefit, i.e. the absolute results. This appears to be a taboo point of view. Commentators worried that the “modest” relative risk reductions in the 50% range would be used by critics to discourage vaccination, but if this is the case, the more realistic view based on absolute benefit would rightly terrify proponents of this popular public health intervention and the related desire to develop herd immunity. Furthermore, there is always the worrisome problem that adverse effects have been suppressed by the industry, certainly far from an unheard of approach to doing business; therefore one cannot do a risk/benefit analysis.

The above results are a nice example of how a given set of trial results can be presented in different ways (another term is spin) that either accentuate the positive or provide a more realistic view. For those who find this hard to believe, an appendix at the end of this issue is included which gives a sample calculation. The potential for creating unrealistic expectations is obviously great and an almost universally used approach.

It seems worth mentioning in passing that pregnant women, if they decide to get a flu shots, should demand the mercury free one which generally comes in a single dose vial not a septum capped little bottle. Live attenuated influenza vaccine which is delivered as a nasal spray, in generally mercury free. However, given that the vaccine preparation may have other dangers to the fetus aside from mercury toxicity which may be unknown or suppressed, perhaps the dismal percentage of adults benefiting should be given considerable weight by this special group.

What should one do? There do not appear to be studies that have provided strong evidence concerning actions found to dramatically reduce the risk of the flu. Mainstream medicine regards the problem solved with vaccination. While maintaining a vitamin D status that is sufficient or more than just sufficient can be justified from a number of studies and is easy and inexpensive to accomplish and justified for a large number of other reasons, definitive studies have yet to appear. The subject of maintaining a high level of immune response will have to wait for a future issue of IHN.

CDC REPORTS INFLUENZA OUTBREAK IN A VACCINATED POPULATION

On October 24, 2014 the Centers for Disease Control in its *Morbidity and Mortality Report* described a flu outbreak among the crew of a navy ship moored in San Diego. In February of 2014, 25 cases of influenza, of which 20 were influenza A, occurred over a short period among a crew of 102. Ninety-nine percent of the crew had been vaccinated with a vaccine very well matched with the flu viruses circulating in 2013-14. The fact that it was influenza was documented by laboratory tests. The headline in the New England Journal of Medicine's daily online *Journal Watch of* October 24 read as follows: *Flu Outbreak Aboard Navy Ship Highlights Possibility of Illness in Vaccinated Populations.* The interesting word is "possibility." Reference to the above table indicates that 94.4% to 98.9% of vaccinated populations are not protected with a matched vaccine, depending on the type of vaccine, and the 94.4% is due in part to heavy weighting from children. These results apply to large pooled populations and studies covered a number of years. Of the 25 flu cases, 16 received the TIV form, 8 the LAIV and one was unvaccinated. Using the term "possibly" seems rather an understatement.

According to the CDC report, Tamiflu was given to the crew to "reduce the impact and spread of the disease." This is the same antiviral that has been discredited and found virtually useless after huge amounts of government funds throughout the world were spend stockpiling it. See the February 2013 issue of IHN for the full story of the shocking Tamiflu saga.

Reference List

1. Robertson RP. Red wine and diabetes health: getting skin in the game. *Diabetes.* 2014;63:31-38.
2. Cullmann M, Hilding A, Ostenson CG. Alcohol consumption and risk of pre-diabetes and type 2 diabetes development in a Swedish population. *Diabet Med.* 2012;29:441-452.
3. Marfella R, Cacciapuoti F, Siniscalchi M et al. Effect of moderate red wine intake on cardiac prognosis after recent acute myocardial infarction of subjects with Type 2 diabetes mellitus. *Diabet Med.* 2006;23:974-981.
4. Knoops KT, de Groot LC, Kromhout D et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. *JAMA.* 2004;292:1433-1439.
5. Blomster JI, Zoungas S, Chalmers J et al. The relationship between alcohol consumption and vascular complications and mortality in individuals with type 2 diabetes. *Diabetes Care.* 2014;37:1353-1359.
6. Karatzi K, Karatzis E, Papamichael C, Lekakis J, Zampelas A. Effects of red wine on endothelial function: postprandial studies vs clinical trials. *Nutr Metab Cardiovasc Dis.* 2009;19:744-750.

7. Karatzi K, Papamichael C, Karatzis E et al. Postprandial improvement of endothelial function by red wine and olive oil antioxidants: a synergistic effect of components of the Mediterranean diet. *J Am Coll Nutr.* 2008;27:448-453.
8. Natella F, Macone A, Ramberti A et al. Red wine prevents the postprandial increase in plasma cholesterol oxidation products: a pilot study. *Br J Nutr.* 2011;105:1718-1723.
9. Natella F, Ghiselli A, Guidi A, Ursini F, Scaccini C. Red wine mitigates the postprandial increase of LDL susceptibility to oxidation. *Free Radic Biol Med.* 2001;30:1036-1044.
10. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk Factors Contributing to Type 2 Diabetes and Recent Advances in the Treatment and Prevention. *Int J Med Sci.* 2014;11:1185-1200.
11. Li G, Zhang P, Wang J et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet.* 2008;371:1783-1789.
12. Wilson PW, Meigs JB, Sullivan L, Fox CS, Nathan DM, D'Agostino RB, Sr. Prediction of incident diabetes mellitus in middle-aged adults: the Framingham Offspring Study. *Arch Intern Med.* 2007;167:1068-1074.
13. Taylor R. Type 2 diabetes: etiology and reversibility. *Diabetes Care.* 2013;36:1047-1055.
14. Lim EL, Hollingsworth KG, Aribisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. *Diabetologia.* 2011;54:2506-2514.
15. Yamaoka K, Tango T. Effects of lifestyle modification on metabolic syndrome: a systematic review and meta-analysis. *BMC Med.* 2012;10:138.
16. Osterholm MT, Kelley NS, Sommer A, Belongia EA. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. *Lancet Infect Dis.* 2012;12:36-44.
17. Tricco AC, Chit A, Soobiah C et al. Comparing influenza vaccine efficacy against mismatched and matched strains: a systematic review and meta-analysis. *BMC Med.* 2013;11:153.

****

APPENDIX

Pooled data from 8 studies, adults 18-64 years of age, given trivalent inactivated influenza vaccine compared to unvaccinated controls. Cases laboratory-validated as viral influenza. Taken from Figure 2.[16]

THE RAW DATA

	Vaccinated	Control
Cases of flu	221	357
Total in group	18,797	13,095

CALCULATIONS

Flu Case %: (221/18,797) X 100 = 1.180%, No Flu % (357/13,095) X 100 = 2.730%,

Percentage who benefited: 2.730% -- 1.180% = 1.55% or 1.55 per 100

Percentage with no benefit: 100% – 1.55% = 98.4%

The absolute risk reduction produced by vaccination was the percentage that benefited, 1.55% is the difference between the flu rates in the two groups, expressed as a percentage rather than probability, i.e. 0.0155.

If 1.55/100 had benefit, how many must be vaccinated for one to benefit?

It is calculated from 1.55/100 = 1/x and thus x = 64. This number needed to treat for one individual to benefit, i.e. not get the viral flu, and is the NNT. Put another way, it is the reciprocal of the absolute risk reduction expresses as a probability (range 1.0 to 0), not a percentage, i.e. NNT = 1/0.0155. The time interval is approximately the flu season.

The unadjusted risk ratio 0.4 is obtained from the ratio 1.118/ 2.730 = 0.4 and the relative risk reduction (RRR) was 1 -- 0.4 = 0.60 or as a percentage 60%. Why is this true?

Details. Risk ratio = (case % in treated group)/(case % in untreated group) = T/U. But 1 = (T/U) = (U – T)/U = RRR, the relative risk reduction obtained comparing the % of cases prevented to the case % in the untreated (control) group. The same calculation can be done without expressing the numbers as percentages, since the 100 cancels out.

Thus the four numbers, i.e. the cases and size of the groups, constitute the input data that produce these various final results used to express how well the treatment works. The 60% RRR looks great, the number who do not benefit looks terrible. Same data, just different presentations, both correct.

Some think that by getting the vaccination they will not get the flu, some think that their risk is reduced by 60%, but interpret this by thinking that if a group of 100 are vaccinated, 60 will not get the flu. In fact, if 100 are vaccinated, between 1 and 2 individuals will be protected and 98% to 99% will not be protected. This is what the critics of the use of relative risk reductions are talking about, but no one is listening. Why spoil a nice picture based on a perfectly valid calculation.

It is also noteworthy that when a disease or disorder has a very small population prevalence reflected by the percentage of cases in the control group, this forces the NNT and the percentage that do not benefit into the range seen in this example. This is the consequence of treating a group where the vast majority will not become cases, treatment or no treatment. One can argue that treatment is still desirable, but one must not have unrealistic expectations, and now the risk of adverse side effects becomes a major issue.

Small absolute benefits and large NNT should stimulate research to find something better. Instead the RRR becomes a powerful marketing and public health tool.

Editor: William R. Ware, PhD

INTERNATIONAL HEALTH NEWS is published 10 times a year by
Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@yourhealthbase.com World Wide Web: http://www.yourhealthbase.com

ISSN 1203-1933

INTERNATIONAL HEALTH NEWS does not provide medical advice. Do not attempt self-diagnosis or self-medication based on our reports. Please consult your healthcare provider if you are interested in following up on the information presented.