Diet, Health, and Prevention

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A Revolution in Progress against Chronic Diseases of Lifestyle

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Introduction

Over the last two centuries medical researchers have made hundreds of discoveries about how the body works and what leads to the many deadly and debilitating diseases that afflict humanity. In the nineteenth century Louis Pasteur and other medical investigators discovered that microscopic organisms are responsible for infectious diseases. Decades later these organisms were given the name bacteria and viruses. This discovery led to highly effective ways to massively reduce the burden of sickness and death caused by these diseases. Another great medical discovery came in the first half of the twentieth century with the discovery of different vitamins. It was realized that a deficiency of particular vitamins causes disease, such as scurvy and rickets. This provided an explanation for several diseases that had caused great suffering to millions of people. And like the discovery of bacteria and viruses this led to highly effective interventions. As a result several diseases caused by a severe vitamin deficiency can now be easily prevented.

But no sooner had one family of diseases been conquered than another appeared. This brings us to the fascinating story of how the modern diet has led to many diseases that have become the plague of the modern age.

Several doctors working in Africa in the 1960s noticed that the inhabitants of that continent have a low rate of many of the diseases that are common in Europe and North America. At the same time they turned their attention to the diet as a likely explanation for this. One component of the diet in particular—dietary fiber—was the focus of attention. The researchers hypothesized that the large amount of fiber in the diet eaten by Africans protects them from many diseases. Denis Burkitt, a surgeon working in Uganda, was at the center of this groundbreaking research. The family of diseases that are common in Europe and North America but that were rare in most of Africa in the 1960s became known as Western diseases. Today, they are more commonly known as chronic diseases of lifestyle or non-communicable diseases. In this book we shall use the term chronic diseases of lifestyle or CDL.

One of the greatest privileges of my life was to have jointly edited a book with Denis Burkitt. This book, published in 1994, was titled: *Western Diseases: their Dietary Prevention and Reversibility.* The book reviewed what we know about these diseases, and then explained how a healthy lifestyle can both prevent and reverse these diseases.

The research work carried out in Africa in the 1960s by a small group of medical pioneers sparked enormous interest among doctors and medical researchers. This led to an enormous research effort into the relationship between diet and health. Library shelves now groan under the weight of the accumulated research. As mentioned, a lack of dietary fiber was suspected of playing an important role in CDL. Half a century later the importance of fiber is now well established. But we now have conclusive evidence that several other parts of the diet are also heavily involved in the causation of CDL. This evidence has extended to other aspects of lifestyle beyond diet, particularly smoking and lack of exercise. Much of this book is taken up with looking at the relationship between lifestyle, especially diet, and the major diseases that come under the CDL umbrella.

This information has been delivered to the general public in many different ways. Governments publish food guides that provide detailed advice on the foods that people should eat. They also regulate information that appears on food packages. Governments provide their citizens with huge amounts of other information on lifestyle and health, including smoking and exercise. A great deal of information is also delivered to the public by way of TV, newspapers, magazines, and, of course, social media. People are continuously exposed to this information.

If people gave their health a high priority, they would pay careful attention to this information, absorb it, and then lead a healthy lifestyle. But at this point, alas, we hit two major barriers. The first is that vast numbers of people lack the motivation to follow this advice. The other barrier is that much of the information the public receives is inaccurate or even dishonest. Of particular importance, many corporations spend copious amounts of money promoting harmful products. In particular, the advertising budgets of corporations that promote unhealthy food massively exceeds the government's budget for the promotion of a healthy diet. Because of these two barriers large sections of the population do not lead a healthy lifestyle. Here are some examples that illustrate this problem.

We shall start with the diet, and what a sorry story it is:

- Salt is liberally added to processed foods. As a result the quantity of it in the typical American diet far exceeds the recommended levels. Salt intake is usually stated in terms of sodium, which constitutes about 40 percent of salt. It is generally recommended that sodium intake should not exceed 2000 mg per day but the actual median intake is close to 3400 mg per day (Cogswell et al., 2012).
- Another unhealthy substance present in many foods is sugar. Here we only consider added sugar (such as the sugar added to coffee or present in soft drinks and cakes) but not the sugar naturally present in such foods as fruit, fruit juice, and milk. American adults obtain roughly 14 percent of their calories (energy intake) from added sugars (Newens & Walton, 2016). Teenagers, predictably, consumer more—about 17 percent of their calories
- Whole grain cereals are an important part of a healthy diet. The average intake by American adults is about 0.7 oz (20 grams) per day (Albertson et al., 2016). This is equivalent to less than a slice of bread, only a fraction of the recommended intake.
- Fruits and vegetables are also central to a healthy diet. Americans eat, on average, around 2 to 3 servings per day, about half the recommended intake (Krebs-Smith et al., 2010).

It is recommended in the USA that young people engage in at least 60 minutes of daily exercise. A survey across the USA reported that only 15 percent of high school students met this objective (CDC, 2011). The majority of American adults also fall well short of achieving the recommended amount of exercise (King et al., 2009).

In one important area, however, lifestyles have seen a dramatic improvement. In 1965 about 42 percent of American adults smoked but by 2008 this had fallen by a bit more than half to about 20 percent (Cokkinides et al., 2009). Nevertheless, smoking is still the single largest preventable cause of disease and premature death in the USA (though obesity may be moving into first place).

Actions have consequences. And the consequence of an unhealthy lifestyle is, of course, poor health. By way of illustration we look at two major health problems, namely the epidemics of obesity and type 2 diabetes.

The USA is a world leader in many areas, but not all of them are positive. Obesity stands out as an area where the USA is a world leader for all the wrong reasons. An epidemic of obesity appeared in the country around 1980 and shows no sign of loosening its grip. Roughly 40 percent of adult men are classed as being overweight and an additional 35 percent are obese (Yang & Colditz, 2015). Fewer women (30 percent) are overweight but slightly more (37 percent) are obese. In total, therefore, about seven out of ten adult Americans are overweight or obese.

The epidemic has hit all age groups. In one major survey it was revealed that 21 percent of adolescents aged 12 to 19 years are obese (Ogden et al., 2016). An especially alarming finding is that the prevalence of obesity for this age group doubled in the 23 years from 1991 and 2014. Valuable information came from another survey. Among 11 to 15 year-old American children 32 percent of boys and 26 percent of girls are overweight or obese (Ahluwalia et al., 2015). The survey also presented findings for Canada and 23 European counties. The numbers for those other countries were only about half or two-thirds of the American numbers.

As obesity is a major risk factor for type 2 diabetes, it is anything but surprising that the obesity epidemic has been closely followed by a diabetes epidemic. This was confirmed by a large survey carried out across the USA (Menke et al., 2015). Roughly 13 percent of American adults have diabetes. In addition, 38 percent have prediabetes. This label is applied when the blood sugar level is abnormally elevated but to a lesser degree than we see with diabetes. The presence of prediabetes indicates that a person is en route to developing actual diabetes. Another finding from this survey is that for every four cases of diabetes in 1990 there were five cases by 2012. This demonstrates, not surprisingly, that the prevalence of diabetes has been rising in parallel with the prevalence of obesity.

In summary, chronic diseases of lifestyle (CDL) are the dominant family of diseases in the USA and across the Western world. As the name suggests, these diseases are closely related to an unhealthy lifestyle. A healthy lifestyle—especially a healthy diet, adequate exercise, and abstinence from smoking—can, to a great extent, prevent these diseases, or at least delay their appearance by many years.

This book explores CDL, their causes, and most especially the role of diet. The first goal is to enable the reader to achieve a healthy lifestyle and thereby add years to his (or her) life and life to his (or her) years. But the book goes much further. Many aspects of health are, to a greater or lesser extent, beyond the rather limited capabilities of regular people. The overall aim is to describe the **big picture**. Towards that goal other important topics are also explored including:

- Food labels. The design of commonly used food labels are described. Alternate, and often superior, designs are evaluated.
- Health promotion is a strategy where health experts try to persuade the population to follow a healthier lifestyle, including eating a healthier diet.
- Government policy. Because health promotion achieves only limited success, health experts have searched for more effective strategies. Increasing attention has been turned to the development of government policies as a way to enhance the health of the population.
- The role of the food industry is of great importance as it is responsible for the mass marketing of unhealthy foods.
- The population are continually exposed to large amounts of false and misleading information in the area of diet and health. This creates endless confusion.

There have been many changes in recent years in our understanding of the story of diet, health, and prevention. Several of the topics discussed in this book have been well known for decades, but others have only emerged in recent years and have received little attention outside of academic circles. In order to properly understand the **big picture** it is essential to take a close look at all the topics discussed here.

When we ascend to 30,000 feet and view the **big picture**, we see that the whole field of diet, health, and prevention is now in the midst of a revolution. That is the explanation for the title of this book.

This book can be likened to the rivers of Montana. One river flows west to the Pacific, a second goes north through Canada to Hudson Bay and thence to the Arctic Ocean, and the third joins the Missouri, then the Mississippi, and continues to the Gulf of Mexico. These rivers resemble the world of nutrition and health: many streams flow into major rivers of ideas, action, and direction, but these rivers can flow in opposite directions and interact in complex ways with the total landscape of nutritional health. These opposing thoughts and actions are sometimes seen in the chapters of this book.

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CHAPTER 1

How Nutrition Scientists Carry Out Research on Diet and Disease. Why is there so much Confusion?

There is a strong relationship between foods, the substances present in food, and the risk of a spectrum of diseases and assorted health problems. Diet also has an important place as a treatment for various conditions. Examples include losing weight and treating diabetes and high blood pressure.

Enormous progress has been made over the last several decades in unravelling the myriad of connections between diet and health. But progress does not go in a straight line. Rather, it's a series of what appear to be important new findings, often followed by new evidence that refutes those findings. Then, a few years go by and new findings are made but this time they survive being checked in follow-up research. The process is like peeling back the layers of an onion. This chapter should help the reader gain some insight into this confusing subject.

Many methods are employed to figure out the relationship between diet, health, and disease. In this chapter we examine these methods. Why, the reader may ask, should I bother myself with the methods employed by nutrition researchers? There are two reasons. The first is because new findings coming from research studies are constantly being announced. In some of these studies fairly reliable research methods have been used while other studies have used methods that are much less reliable. Understanding the strengths and weaknesses of different types of research allows people to better judge how much credence should be given to a new claimed discovery. The second reason for the reader to learn a few things about this subject is because it is very interesting (though here I declare a strong personal bias).

RANDOMIZED CONTROLLED TRIALS (RCT)

A RCT is a type of study in which the subjects are given some type of intervention. RCTs are hugely important in many areas of research related to health and disease. But like all methods, RCTs have both strengths and weaknesses. RCTs are well suited for testing drugs and produce reliable results, but are prone to many problems when used in nutrition research, especially in the area of the prevention of disease.

We first look at the use of RCTs in the testing of drugs. Most drug studies are focused on symptoms (such as depression, pain of arthritis, or blood pressure) and last for just a few weeks or months. Let us suppose that researchers wish to test whether Drug X is an effective treatment for Disease Y. Scores of such studies are carried out every year. The researchers recruit patients who all have Disease Y and who agree to take part in the study. The patients are then randomly divided into two groups. One group receives the drug while the other group receives a placebo (dummy pill). An essential feature of this type of study is that neither the patients nor the researchers who have direct contact with the patients know which patients are taking the actual drug and which ones the placebo. For that reason the study is described as "double blind". This is important in order to avoid bias, for the following reasons. In the case of the patients they are more likely to respond positively if they believe they are receiving an effective drug. This phenomenon is known as the placebo effect. The researchers may have other biases. If they believe the drug is effective, they may inadvertently transmit this opinion to the patients, but only to the ones receiving the actual drug. The researchers are, in effect, giving the patients an extra dose of placebo effect. Researchers may also be biased in how they record the results. When asking patients whether they feel better, it is easy to record answers in a biased way. For example, the researchers may ask subjects if they have less pain, and then record the responses. It is very easy to interpret what the patients say in such a way that those receiving the drug appear to have less pain. This in no way implies dishonesty by the researchers, but rather that people, even trained researchers, are unconsciously biased in how they hear and interpret statements.

Every human is different from every other human. For that reason they vary in their response to such external influences as drugs. Some patients may respond well to a particular drug while others have no response and may even get worse. To overcome this problem the researchers recruit enough subjects so that the results are clear. For many drug studies it may be enough to have 400 people of whom 200 receive the drug and 200 the placebo. At the end of the study the findings may reveal that the symptoms of 60 percent of those given the drug improved whereas an improvement was seen in only 20 percent of those given a placebo.

If the results of a double-blind study on a drug show that many of the patients given the drug had an improvement in their symptoms while only a few of those given the placebo improved, then it is reasonable to conclude that the drug is an effective treatment. RCTs are a powerful tool as they generate trustworthy results regarding whether a drug really is an effective treatment for the disease being studied. For that reason, the double-blind RCT is the standard method for testing whether drugs are effective.

RCTs are also carried out in order to determine whether a drug can prevent a disease. We see an excellent illustration of this with a class of drugs known as statins. These drugs lower the blood cholesterol level. They are a common treatment for patients who are at high risk of heart disease because of an elevated blood cholesterol level. Giving statins to such patients is intended to help prevent heart disease. The effectiveness of statins has been demonstrated in numerous RCTs.

An especially famous series of RCTs were carried out during the years 2020 and 2021 in order to test whether several newly developed drugs are effective at preventing the COVID-19 virus from causing sickness in persons infected with the virus. Based on the successful findings from these RCTs the new drugs were approved for use across entire populations.

RCTs are also used to test many other interventions, including dietary changes that are intended to prevent or treat a disease. First we look at RCTs that investigate the effectiveness of diet in *treatment*. Whether the study is testing a dietary treatment for lowering blood cholesterol in people with high blood cholesterol, lowering blood pressure in people with high blood pressure, or for improving blood glucose control in people with diabetes, it makes perfect sense that all subjects recruited for the study already have the condition being studied. Such studies are comparable to drug studies. Accordingly, the study may need to include only a few hundred subjects and last just a few weeks or months. However, studies of this type that investigate whether a dietary treatment is effective for weight loss in overweight people may need to follow the subjects for two years. This is important as weight that is lost in the first few months of a new diet is often regained over the next year or two.

For obvious reasons, the subjects in a RCT know if they have made changes to their diet. For that reason most RCTs that investigate dietary changes cannot be done double blind. This is a significant problem as it can lead to biased results. In particular, subjects given the changed diet may improve as a result of the placebo effect. That can easily be the case with studies of such conditions as migraine, arthritis, and irritable bowel syndrome (IBS) where symptoms are subjective. For example, four weeks after a person has changed his diet in order to relieve the symptoms of arthritis, he might be convinced that there is less pain, regardless of whether the state of the diseased joints has actually improved.

A large part of nutrition research is concerned with whether a change in the diet prevents a disease. Unfortunately, RCTs are far less reliable in this area than is the case with the testing of dietary interventions or drugs for the *treatment* of disease. The reasons for this are as follows.

Most diseases develop very slowly over many years. The diet change, even if effective at preventing a disease, may only affect a small proportion of people. These factors create several major challenges in the design of a RCT. Let us suppose a team of researchers wish to investigate whether a supplement of vitamin D helps prevent cancer. The first problem is that only a small fraction of the population develop cancer over a period of a few years. The second problem is that vitamin D, even if effective, may only prevent a small fraction of new cases of cancer. An optimistic prediction might be that it prevents one out of every 20 new cases of cancer. The researchers will then carefully plan the study with the goal that the findings will reliably tell us whether or not vitamin D prevents cancer. The study must be large enough so that the effects of chance do not overshadow the results. The researchers will consult with a statistician to figure out how many subjects are needed. She may then estimate that for this goal to be achieved, the study must be designed so that around 800 people would be expected to develop cancer in each group. Then, if vitamin D cuts the risk of cancer by one in 20, we would expect to see around 800 people develop cancer in the group given placebo but only about 760 in those given vitamin D. With those numbers the results of the study might be judged to be meaningful (the technical term for this is "statistically significant"). But in order for 800 people in the placebo group to develop cancer it would have to include many thousands of subjects and keep track of them for perhaps five years. This means that the study will inevitably be many times larger (and more expensive) than a study that investigates whether a dietary change or a drug is effective for treatment. This obviously creates a huge problem.

How does our clever team of researchers get around this problem? The easiest way to reduce the huge size of the study and its prohibitive cost is to recruit subjects at high risk of cancer. By that means a much higher proportion of the subjects will develop cancer during the study than if they recruited only subjects at relatively low risk of cancer. This greatly reduces the number of subjects who must be recruited by a factor of four or five. But solving one problem creates a new problem. Cancer is a disease that usually develops slowly over many—perhaps 20 or 30—years. Suppose vitamin D is effective at an early stage, but not at a late stage, in the development of cancer. If the study includes only subjects at high risk of cancer and they are studied for only five years (as is the case in this example), then it may already be too late for vitamin D to achieve a preventive benefit. In that case the results will wrongly lead the researchers to conclude that vitamin D is of no value in the prevention of cancer.

Many RCTs have been carried out with the goal of determining if a particular change to the diet helps prevent a disease. Only a minority of those RCTs have produced positive results. It is strongly suspected that a major reason for this is because the subjects in the RCTs have mostly been at high risk of the disease being investigated and were studied for only a few years. I explained this problem in detail in my paper on the subject (Temple, 2016). So, for example, a RCT on whether a dietary supplement prevents cancer may use subjects who have been smokers for 20 years while a RCT on whether fish oil prevents heart disease may use subjects who have previously had a heart attack. In each case the study period may have a duration of around three or four years. What these RCTs are really studying is whether a dietary change can block the late stages of the disease process. Many of these RCTs may therefore be doomed to failure before the first human guinea pig has been recruited.

As is the case with most RCTs that test whether a dietary change is an effective treatment, most studies of dietary change in prevention cannot be done double blind. As before this can lead to biased results. Not all nutrition studies have this problem. Sometimes the dietary change takes the form of giving a pill. This is the case with studies that investigate whether vitamin C prevent colds or whether beta-carotene prevents cancer. Such studies can be done double blind, much like drugs studies.

EPIDEMIOLOGY

Epidemiology is a powerful tool for studying the causes of many diseases. It embraces a family of related methods.

RCTs are generally considered a type of epidemiology. But epidemiology also includes studies where the researchers study a population but without trying to make any changes to how people eat and behave. This means studying the number of cases of different diseases within a population and then searching for the factors that help explain this. Such studies are often referred to as “observational”.

The findings from this type of epidemiological study may tell us, for example, that high levels of air pollution are associated with increased rates of heart disease. The reader should note the use of the words “*associated with*”. All we can say for sure after we examine the results of this study is that people who are exposed to air pollution have a higher risk of developing heart disease. But we must be very hesitant before jumping to the conclusion that the air pollution actually *causes* heart disease; there are probably other possible explanations for the findings. For example, poor people may live in areas of a city with the worst air quality and they are most prone to heart disease for reasons unrelated to air quality. To put it another way, this may be a case of guilt by association. We must therefore be cautious before jumping to the conclusion that the findings from studies of this type reveal cause and effect.

In this section three major types of epidemiological study are described.

Cohort Studies

This is a powerful method for uncovering the relationship between diet and disease. In a typical cohort study a large number of reasonably healthy people are recruited. The number may be a few thousand or as many as several hundred thousand. Every subject is questioned about their diet as well as other relevant factors, such as their smoking habits, how much exercise they carry out, and their body weight. The researchers keep track of every subject and record all cases of the diseases of interest and of deaths. Then, after anywhere from four to 20 years, the researchers carefully analyze which factors are associated with which disease. As the lifestyle-related information is recorded at the start of the study and the subjects are then tracked, this type of study is often called a *prospective* cohort study. Cohort studies obviously involve storing and analyzing enormous amounts of information. For that reason they are a child of the computer age.

Cohort studies have strengths and weaknesses. First, the weaknesses. Making an accurate record of a person's diet is much more difficult than most people realize. When subjects in a research study are asked to describe their typical diet, they will try to be honest but will typically give responses that are only a rough approximation of the truth. This is because of the fallibility of the human memory. This problem is compounded by a second problem. Many cohort studies measure the diet of the subjects only once, namely at the start of the study. The researchers are assuming that this reflects the habitual diet of the subjects over the next decade or longer. But, of course, people change their diet over time. They may cut down on their alcohol intake, switch from beef to chicken, from butter to margarine, or from regular cola to diet cola.

What is the impact of this on the results of cohort studies? Let us suppose that people who regularly eat beef have a 10 percent higher risk of developing heart disease. Errors in making an accurate measurement of people's diets will tend to reduce the strength of this association. So instead of the findings indicating to the researchers that the risk is increased by ten percent, the researchers may end up concluding that the risk increases by only five percent. The more sophisticated cohort studies attempt to reduce the impact of this problem by repeating the diet assessment every few years. This produces a more accurate picture of a person's diet.

There is a second important weakness inherent in cohort studies. Suppose a cohort study discovers that people whose diet is quite rich in vitamin C have a low risk of cancer. What does this mean? The obvious message from the study is that vitamin C prevents cancer. If the results were reported in the media, this might lead to a spike in sales of vitamin C supplements. But a closer look at the results will tell a different story. Vitamin C is obtained from fruits and vegetables. A high intake of vitamin C is therefore a clear indication of a high intake of fruits and vegetables. But these foods contain literally thousands of substances in addition to vitamin C. So what the study really found is that people who eat plenty of fruits and vegetables have a low risk of cancer. This probably means that fruit and vegetables are protective against cancer. But we cannot say that with any certainty. Perhaps people who eat generous amounts of fruit and vegetables are more health conscious and follow a number of healthy lifestyle habits. This problem is called confounding and is a frequent problem in cohort studies.

Despite these problems cohort studies have enormous value. This is best demonstrated by comparing cohort studies with RCTs. As was explained above, RCTs that investigate the role of diet in disease prevention have mostly used subjects who were at high risk of the disease being studied and were studied for only around three or four years. The results of these studies do not reliably tell us whether the dietary change truly prevents the disease but rather whether it blocks the late stages of the disease process. But cohort studies are completely different. They usually recruit only subjects who are reasonably healthy. In the better cohort studies the subjects are then followed for upwards of ten years. This time period is sufficiently long that it will probably cover most of the stages of disease development from start to finish. With this study design, therefore, the findings tell us whether the dietary change truly prevents the disease.

There is an official dogma in medical research. RCTs are considered highly reliable. That is true for many types of study such as the effectiveness of drugs. For that reason RCTs are often referred to as the "gold standard". Epidemiological studies, by contrast, have a lower status.

Textbooks that cover this subject tell students that epidemiology shows "association not causation". But for the reasons explained above, the situation is quite different when it comes to investigating whether a particular dietary change prevents disease. Here, cohort studies are arguably at least as reliable as RCTs and may even be more reliable (Temple, 2016).

Here are two examples that illustrate this.

Dietary fiber is thought to be protective against colon cancer. This has been tested in both RCTs and cohort studies. Ideally, an RCT would study healthy people (free of colon disease) and then test whether a fiber supplement prevents colon cancer over the next ten years or longer. But such a study would need huge numbers of subjects and would be almost impossible to carry out because of cost. Quite apart from cost it would be an immense challenge to recruit enough volunteers who would agree to follow a specified diet every day for ten years. Instead of that highly impractical study design what investigators have done is to use subjects who had colon adenomas (a benign tumor that is believed to be a stage on the road to actual colon cancer). The subjects were given a supplement of wheat bran, a rich source of fiber, for between two and four years. The investigators did not measure actual cancer but rather the appearance of new adenomas in the colon. No evidence was seen that wheat bran reduced the risk of this. How reliable are these results? The answer is: not very. This is because the subjects already had colon adenomas meaning that they were well down the road leading to colon cancer. Adding to the problem, the study did not measure actual colon cancer but rather a disorder associated with it. For that reason the RCTs cannot be seen as a proper test of whether fiber prevents the development of colon cancer. Cohort studies, in stark contrast, recruited healthy people and then tracked them for between five and 17 years. This long time period covers most of the timeframe needed for a healthy colon to develop cancer. Several cohort studies have reported that persons whose intake of fiber was relatively high had a reduced risk of developing colon cancer. These studies are far more informative than the RCTs as they suggest that foods rich in fiber prevent the development of colon cancer in healthy people. The cohort studies do, however, have one important limitation. Rich sources of fiber include fruits, vegetables, and whole grain cereals. So the most scientifically accurate conclusion from the studies is not that "fiber prevents colon cancer" but rather that "foods rich in fiber prevent colon cancer". This is an important distinction; we cannot say with any confidence what substances in fiber-rich foods deserve the credit. Despite the limitations of these cohort studies, from a practical point of view the findings are hugely important as they provides strong evidence on how to prevent a serious and deadly disease.

The second example looks at fish, fish oil, and heart disease. Again, we will compare cohort studies and RCTs. Many cohort studies have revealed that people who eat fish regularly have a 20 percent lower risk of cardiac death compared with those who seldom eat fish. As with the previous example, the subjects in these studies were healthy at the start of the study and were carefully tracked for many years. RCTs were altogether different. The large majority of the subjects already had a history of heart disease. They were given a supplement of fish oil and followed for around two years. The treatment appears to cause some reduction in risk of heart disease but far less than what was seen in cohort studies. We can summarize the findings as follows:

- Cohort studies provide strong evidence that fish prevents heart disease.
- RCTs provide weak evidence that fish oil supplements prevent heart disease.

Which type of study is more reliable? The cohort studies examined the relationship between diet and the risk of cardiac death over the many years it takes for the disease to develop. But the RCTs looked narrowly at the risk of recurrence of heart disease in people who had already reached an advanced stage in disease development. If fish stops the progression of heart disease but only during its early stage, we will only see this in cohort studies, not in RCTs. This leads us to the same conclusion as in the previous example: it is cohort studies rather than RCTs that provide the far more valuable information.

Case-control Studies

This type of study can be viewed as a simplified and speeded up version of a cohort study. A direct comparison is made between people with and without the disease being investigated. Here is an example of how it works. A team of researchers wishes to investigate the role of diet in kidney cancer. They recruit 200 patients who were recently diagnosed as having kidney cancer. For comparison they also recruit 200 people free of the disease. They then ask all 400 people to describe their past diet. The results might reveal, for example, that the cancer patients eat more processed meat but less citrus fruit than do the folks who are free of cancer. These findings suggest that processed meat makes kidney cancer more likely whereas citrus fruit lowers the risk.

Case-control studies have two major advantages over cohort studies. First, they require far fewer people (hundreds rather than many thousands). Second, an entire study can be done much more quickly. Unfortunately, case-control studies do have their downside. It is widely believed that the findings that come out of case-control studies are generally less reliable than are those from cohort studies.

Population Studies

The Introduction described how a group of medical investigators working in Africa in the 1960s noticed that the inhabitants of that continent seldom developed many of the diseases that are common in Europe and North America. These diseases are now commonly referred to as the chronic diseases of lifestyle. Based on this pioneering research we now know that these diseases are closely associated with the Western lifestyle. This is an example of a population study.

Like all types of research that investigates the relationship between diet and disease, population studies have their inherent strengths and weaknesses. On the plus side population studies are fairly cheap to carry out and can be done using data that are based on millions of people. The flip side is that there are typically a great many differences besides diet between different populations which makes it hugely challenging to figure out which factors are truly responsible for the variations in the risk of the disease being studied. Is it a component of the diet (fat, vegetables, meat)? Or perhaps it is another component of lifestyle, such physical activity or smoking. These differences are much greater when comparing countries from different parts of the world.

Population studies also suffer from serious problems with the accuracy of the raw data. Many less developed countries do not collect accurate data, including for health statistics such as cause of death, and for food intake. Consider the following example. A researcher wishes to compare the intake of meat with the risk of death from cancer in various countries in Europe and Africa. While the numbers coming from Europe are likely to be reasonably accurate, the data from Africa are likely to be riddled with serious errors. If the researcher works on the assumption that all numbers that appear in government reports are accurate, this can easily lead to the well-known problem of "junk in, junk out". For that reason researchers must be extremely careful when using data collected in less developed countries.

A classic example of a population study is the relationship between the amount of selenium in the soil in the states of the USA and the risk of cancer. American states with relatively high amounts of selenium in the soil (and therefore in the local diet) tend to have lower rates of cancer than states where the soil has a poor content of selenium (Shamberger et al., 1976). The same observation was made when different countries were compared

(Schrauzer et al., 1977). This led to the discovery (which is still being investigated) that selenium offers some protection against cancer. A similar finding concerns sunshine. The sunnier states of the USA tend to have lower rates of cancer compared to states with less sunshine. The favored explanation for this is that the people who live in sunny states produce more vitamin D in their skin which then helps prevent cancer.

ANECDOTAL OBSERVATIONS

Charlie gets flu most winters. A friend told him about Echinacea, a herbal product, which is claimed to help prevent flu. Charlie bought a large bottle and took a pill every day before and during flu season. He did this again the following year. Charlie was pleasantly surprised that both those years he did not succumb to flu. The obvious conclusion, Charlie concluded, was that Echinacea had prevented him from getting flu. It is possible that Charlie was right and that Echinacea does indeed deserve the credit. But the facts are also consistent with other explanations. Possibly, Charlie was immune to the strain of flu viruses that appeared during the years he was taking Echinacea. Or perhaps luck was on Charlie's side and he was not infected by the flu virus. The information available to us is so limited that we can only guess as to the correct explanation.

This little story is known as an anecdotal observation. It is universally accepted in all areas of medicine that such observations have very limited value. This type of "evidence" (using the term very loosely) is the source of endless confusion when it comes to trying to figure out connections between diet and health. The central problem with anecdotal observations is that they are often a manifestation of chance. The placebo effect may also be at work. For example, Mary might go to a health food store and ask for advice on how to treat her poor level of energy. Mary is persuaded to take a vitamin B supplement. Over the next few weeks Mary notices that she seems to have more energy. Mary is delighted: the supplement has restored her energy level, or so she believes. In reality, it is most unlikely that the supplement had any direct effect on Mary's energy level. A more plausible explanation is that her improvement might have been due to the placebo effect (the supplement merely created the illusion that she had more energy). It is also entirely possible that Mary's improved energy was simply a chance occurrence (she did improve but this was going to happen anyway for one of a dozen different reasons). What the two examples (Charlie and Mary) illustrate is the very limited credence that can be given to anecdotal observations.

One danger of anecdotal observations is that people often refer to them in a highly selective way so as to prove a point. There are plenty of people who have smoked for 50 years with few apparent ill-effects and many others who died of lung cancer despite having never smoked. Such so-called evidence can be used in a very misleading way to demonstrate that smoking is not harmful. This could even be taken to an extreme as exemplified by the story of Tsutomu Yamaguchi. In 1945 this unfortunate man was on the receiving end of not one but two atom bombs. Yet he survived for the next 65 years until his death at the age of 93 (Wikipedia). This proves that atom bombs are good for the health!

MEASURING BIOMARKERS

Research studies often measure what are called "biomarkers". These are measures of substances in the body that have been shown to be reliable indicators of disease risk. For example, the blood level of LDL-cholesterol is a reliable indicator of a person's risk of heart disease. Another valuable biomarker is the blood glucose level. Measuring the blood level of these substances is often done in nutrition research as it provides a good indication of whether a dietary change is likely to increase or decrease the risk of a particular disease. So a dietary change that causes a decrease in the blood level of LDL-cholesterol implies a reduced risk of heart disease. Similarly, a dietary change that causes a decrease in the blood level of glucose indicates a lower risk of diabetes. The great advantage of measuring biomarkers is that it is a quick and relatively cheap method of deducing if a dietary change is likely to help prevent a disease. These studies are usually done as part of a RCT.

STUDIES OF BODY MECHANISMS IN HEALTH AND DISEASE

Enormous numbers of research studies are carried out that investigate the intricate details of body mechanisms. The rationale for this research strategy