IMMUNE HEALTH:

MICRONUTRIENTS UNDER THE MICROSCOPE

HSIS
THE HEALTH AND FOOD SUPPLEMENTS INFORMATION SERVICE

FOREWORD

Dr Nisa Aslam, Dr Pamela Mason, Dr Gill Jenkins, Dr Emma Derbyshire & Dr Carrie Ruxton

Immune health has increasingly piqued the interest of the public since early 2020, with a heightened awareness born out of the COVID-19 pandemic. It's an observation that's supported by new research commissioned by The Health & Food Supplements Information Service (HSIS),[1] which found that four in 10 Britons (41 per cent) have thought about their own immune health more than usual since the pandemic began.

Overall, it's on the minds of more than three quarters (76 per cent) of us, with younger people aged 18-29 years more likely to consider their immune health compared to those aged 60 and over (83 per cent vs 65 per cent). Unfortunately, however, thinking about it doesn't necessarily translate into immune health knowledge.

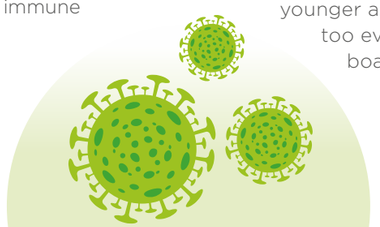
> "FOUR IN 10 BRITONS HAVE THOUGHT ABOUT THEIR OWN IMMUNE HEALTH MORE THAN USUAL"

Nutrition is essential for healthy immune function, with micronutrients (vitamins and minerals) playing a particularly important role. In fact, the European Food Safety Authority (EFSA) even allows manufacturers to make health claims on their product labels in relation to a range of vitamins and minerals which support immune function.

Vitamins and minerals have a wide range of roles in immunity, from supporting immune cell development, growth and energy production processes, to helping protect the body's natural physical barriers, including the skin, gut and respiratory tract lining from harmful microbes (like bacteria and viruses). By helping to maintain the structure of these barriers, micronutrients help to reduce the risk of microbes penetrating the body and causing infection.

Vitamin D has been under the spotlight for its role in immune function during the pandemic, but only just over one third (36 per cent) of Brits are taking a supplement containing Vitamin D. This is of particular concern as dietary sources don't generally provide enough vitamin D. With the main source of vitamin D coming from exposure of the skin to sunlight, this has been worsened by people spending a lot of time indoors during the past 18 months.

It's important not to develop tunnel vision with vitamin D, though, as most (if not all) micronutrients are important for a healthy immune system. With the most recent UK National Diet and Nutrition Survey (NDNS) continuing to show woefully low intakes of minerals and vitamins, particularly in younger adults, shortfalls are all too evident right across the board.



Fewer than six in 10 of those surveyed know how the immune system works, and more than one in 10 (13 per cent) admit they have no idea

Of those surveyed for the HSIS research, 74 per cent agree that nutrient deficiency could compromise immune function, whilst half agree that good nutrition is important to support immune function. The good news is that 51 per cent are actively trying to eat more fruit and vegetables, but that means that half are not. In any case, there's more to a healthy, balanced diet than fruit and vegetables, with wholegrains, low fat dairy or alternatives, and lean protein, all important sources of micronutrients too.

Therefore, this report will delve into how the immune system works, which nutrients it needs to stay healthy and fight off infections, the immune health consequences of vitamin and mineral shortfalls, and how supplements may help bridge the dietary micronutrient gaps facing the UK population.

CHAPTER

1 UNDERSTANDING THE IMMUNE SYSTEM

Good immune health is essential for everyday wellness. According to the HSIS poll,[2] more than three quarters of Brits (76 per cent) think about it, and four in 10 Brits (41 per cent) have thought about it more than usual since the pandemic, with younger people aged 18-29 more likely to consider their immune health compared to Britons aged 60 and over (83 per cent vs 65 per cent).

WHAT IS IMMUNE HEALTH?

Put simply, being in good immune health means that your body's ability to recognise and deal with germs (or pathogens), including viruses, bacteria, fungi, and protozoa (such as the pathogen that causes malaria) is strong.

Just under three quarters of the HSIS survey respondents (74 per cent) said you can catch more viruses if the immune system is weak, whilst more than four in 10 (41 per cent) said you can catch COVID-19 if you're in poor immune health. Research shows that immunological differences across the population (for example, poorer immune function after the age of 50) go part way to explaining differences in severity of COVID-19.[3]

SIGNS YOU'RE STRUGGLING WITH A WEAKENED IMMUNE SYSTEM INCLUDE:

- Constantly catching colds
- Battling frequent infections, such as ear infections or thrush
- Needing several courses of antibiotics over a year
- Taking longer than normal for your cuts and grazes to heal.

While frequent tummy troubles such as diarrhoea and bloating or feeling tired all the time can be signs of various illnesses, they may also indicate weakened immune health. More than six in 10 (63 per cent) of HSIS survey participants correctly said you may feel run down or fatigued when your immune system is under stress.

Allergies can also be linked to poor immune health. However, the relationship here is complex, as the immune system can go into overdrive when presented with an allergen but poor immune health can also increase risk of allergies and inflammation.

WHAT IS THE IMMUNE SYSTEM?

The immune system exists to protect us against germs and other harmful substances, such as toxins made by germs and allergens (for example, pollen, animal fur, and dust mites). It's incredibly complex, consisting of a diverse network of cells and proteins, each of which has a specific job at recognising or reacting to harmful material.

IMMUNE CELLS AND PROTEINS

As GP Dr Nisa Aslam explains, "Immune cells and proteins work together throughout the body to provide a defence against infection. If the immune system meets harmful material such as germs, it mounts an immune response. It does this by distinguishing between our own body cells and harmful invaders. In short, a healthy immune system can tell what's part of the body and what isn't. It recognises proteins on the surface of invading pathogens (viruses and bacteria, for example) and ignores the proteins on its own cells."

A healthy immune response depends on the activity of several different types of white blood cells (or leucocytes). In the HSIS research poll, 72 per cent of respondents knew this. Six in 10 also correctly said red blood cells are important too. Red blood cells contain haemoglobin, which helps defend the body by producing anti-infection reactive oxygen species (ROS).[4]

> "IMMUNE CELLS AND PROTEINS WORK TOGETHER THROUGHOUT THE BODY TO PROVIDE A DEFENCE AGAINST INFECTION"

PATHOGEN PATROL

White blood cells constantly patrol the body, seeking out pathogens, in both the blood vessels and the lymphatic vessels that run in parallel with the veins and arteries. They're stored in our lymph glands, including those in the spleen, thymus, bone marrow, and lymph nodes. When they detect an invader, white blood cells multiply and signal to other immune cells to do the same.

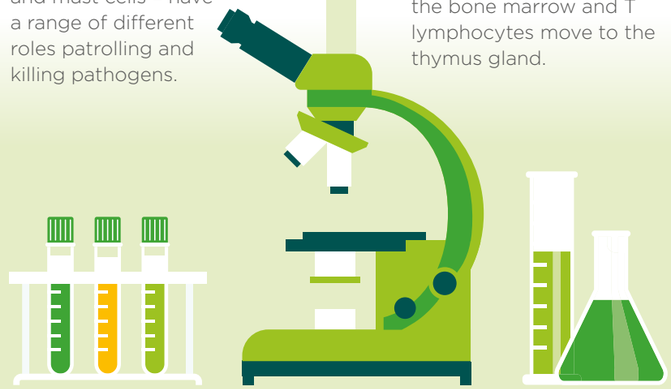
TYPES OF WHITE BLOOD CELLS

PHAGOCYTES

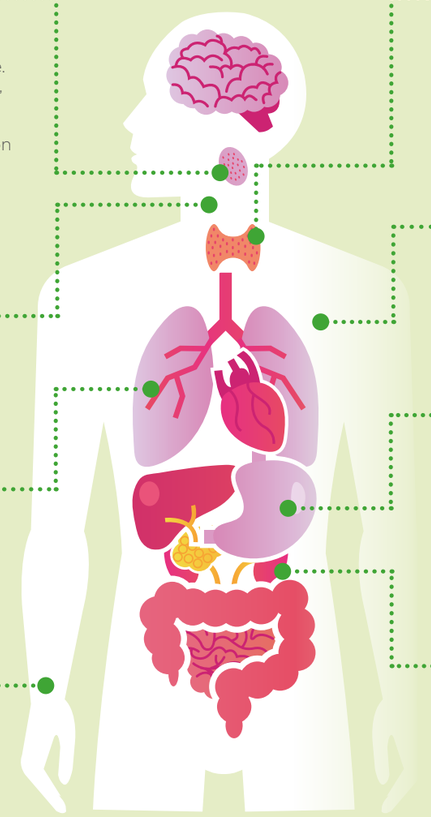
- Surround and 'eat' pathogens
- Neutrophils are the most common type – they destroy bacteria
- The other three types – macrophages, monocytes, and mast cells – have a range of different roles patrolling and killing pathogens.

LYMPHOCYTES

- Help the body to remember previous harmful invaders and recognise them if they come back
- Start life in the bone marrow and develop into two types – B lymphocytes stay in the bone marrow and T lymphocytes move to the thymus gland.



THE BODY'S IMMUNE DEFENCE SYSTEM:



ADENOIDS

Adenoids are a patch of tissue that is high up in the throat, just behind the nose. They, along with the tonsils, are part of the lymphatic system. The lymphatic system clears away infection and keeps body fluids in balance. The adenoids and tonsils work by trapping germs coming in through the mouth and nose.

LYMPH NODES

In the lymph nodes are the cells (lymphocytes) of the immune system. These recognise and eliminate invading pathogens.

RESPIRATORY SYSTEM

The Cilia (fine hair-like projections) line the airway and move mucus and contaminants upwards out of the repiratory tract.

SKIN

The skin forms a very effective barrier against invading pathogens.

THYMUS GLAND

The thymus glad trains and differentiates T cells into specialised categories. This includes Cytotoxic T cells., T helper cells and T regulatory cells.

WHITE BLOOD CELLS

White blood cells attack pathogens both in the blood itself and in other tissues of the body.

STOMACH AND INTESTINES

Stomach acid kills most harmful bacteria. Antibodies secreted by the intestinal cells attack viruses and other pathogens that have landed in the intestinal tract.

SPLEEN

The Spleen assists the body in protecting itself against bacterial infections.

BUILDING YOUR DEFENCES

B lymphocytes produce antibodies when they spot a harmful invader. Once an antibody has been produced, a copy stays in the body, so if the same pathogen appears again, it can be dealt with more quickly. Apart from making antibodies, B lymphocytes also send signals to T lymphocytes, which have the job of destroying harmful material in the body and sending signals to other immune cells.

"With some diseases, such as chickenpox, immunity can be life-long, whilst in other cases, including the common cold and flu, immunity doesn't last forever. This is often due to the arrival of different strains of a virus, which the immune system must learn to deal with," says dietitian Dr Carrie Ruxton.

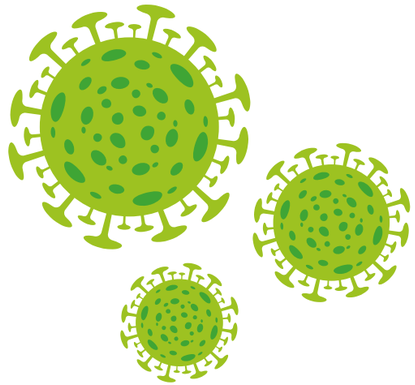
Everyone's immune response is different but broadly speaking it gets stronger as we move from childhood through to our teens and young adulthood. This is why young adults tend to catch infections less often than young children. Immune function generally remains at its most effective until we reach about 50, but this does vary and also depends on the presence of other illnesses the person may have, as well as lifestyle factors like smoking, drinking alcohol, exercise, sleep, and nutrition.

FIGHTING INFECTION FROM DAY ONE

Babies are born with some ability to fight infection using what is known as the innate immune response. This works fast but doesn't have the ability to target specific invaders. The innate immune system consists of physical barriers (for example, the skin and the mucous membranes of the nose, mouth, and gut), which physically stop pathogens from entering the body.

ADDING TO YOUR IMMUNITY LIBRARY

As we get exposed to viruses and bacteria and/or get vaccinated throughout our life, our body, with the help of the immune cells (such as T cells and B cells) builds up immune memory, a bit like a library of antibodies to previous infections. If a pathogen manages to get past the innate immune response, this adaptive or acquired immunity kicks in. It takes longer to spring into action but can target specific invaders.



CHAPTER

2 INFECTION-FIGHTING FUEL

Good nutrition is essential for immune health. Evidence from the HSIS research shows that the COVID-19 pandemic has influenced how people think about their health and diet. Some are now eating better than at the start of the pandemic.

Almost three quarters (73 per cent) say the pandemic has made them more aware of their health and wellbeing, with concerns about diet featuring highly. Despite over a third of survey respondents (34 per cent) admitting they've been eating more comfort foods and snacks during lockdown and 28 per cent eating more sweets and crisps, more than four in 10 (41 per cent) started cooking from scratch more, and almost four in 10 (38 per cent) used the lockdown period to stock up on fruit and vegetables.

BY THE TIME OF THE SURVEY IN MAY THIS YEAR, OVER HALF (51 PER CENT) HAD MADE CHANGES TO THEIR DIETS FOR THE BETTER SINCE THE START OF THE PANDEMIC:

80%
have increased their consumption of vegetables

77%
are eating more fruit

60%
are eating more fish

PLANT POWER

Respondents also showed an interest in improving their diets, with more than half (53 per cent) saying they ought to eat more fruit and vegetables, and almost one in ten (9 per cent) wanting to increase their intake of plant-based meals. Interestingly, older Brits (60 and over) are the group most likely to want to increase their intake of plant-based meals; 14 per cent of this age group compared with 7 per cent of those aged 18-29 and 30-44. One quarter said they'd like to cut back on sweets and chocolate, while 14 per cent want to try to eat less processed meat.

Advice on healthy eating is available in the government's Eatwell Guide, but worryingly, Britons do not take account of this easily-available nutrition advice.

- Only 27 per cent have heard of the Eatwell Guide, (29 per cent of women)
- 18-29 year olds are most likely to have heard of the Eatwell Guide (44 per cent)
- Almost half (48 per cent) say they have no idea what the Eatwell Guide advises
- Almost half (47 per cent) think their diet is nutritionally on target some of the time, while three in ten say it's on target most of the time.

This is despite the fact that more than a fifth (21 per cent) have been advised by a healthcare professional to change their diet to lose weight, while 12 per cent have been advised to lose weight due to a medical condition.

NUTRITIONAL GUIDANCE FALLING ON DEAF EARS

When it comes to food portions, three in five Britons (60 per cent) don't pay attention to recommended portion sizes or portion control, instead taking as much as they're hungry for. Less than half (41 per cent) of respondents guessed correctly that men should consume approximately 2,500 calories a day, while 50 per cent said women should consume 2,000 calories daily.

Half of respondents said they read the nutritional information on the back of food packs, but mainly to see the calories, sugar or fat content. Vitamins and minerals, essential nutrients for overall health, including immune health, weren't mentioned.

WHY VITAMINS AND MINERALS ARE ESSENTIAL FOR IMMUNE HEALTH

Optimal intakes of vitamins, minerals and other essential substances, such as essential fatty acids, provide the fuel for immune health, making it more likely that the immune system can respond to the challenges of harmful invaders.

However, poor intakes of nutrients may make it more challenging for the immune system to respond effectively. Almost three quarters (74 per cent) of respondents in the HSIS survey say a nutrient deficiency can affect the immune system, while 50 per cent strongly agree that good nutrition helps to support optimal immunity.

MOUNTING AN IMMUNE REACTION

When pathogens gain entry to the body, the immune system springs into action. This activity requires a lot of energy, which is produced by breaking down carbohydrate, fats, and proteins. Almost all vitamins and minerals are needed for these processes, to support the biochemical reactions and help to fuel the production of immune cells. To mount an immune response, the body also needs more DNA and RNA, essential fatty acids and proteins, for building immune cell membranes.

GP Dr Gill Jenkins explains that: "Part of the immune response is to create an inflammatory cascade, including the 'cytokine storm'. Although this is a normal reaction that's needed to fight off invaders, it puts stress on the body. Therefore, antioxidant vitamins and minerals, such as vitamins C and E and selenium, are needed to provide protection.

"A shortage of vitamins and minerals can compromise the immune response in several ways, including compromising energy forming biochemical reactions and the manufacture of immune cells. A diet low in vitamins and minerals, which is common in the UK, is often low in fruit and vegetables, wholegrains, and lean protein. Such a diet can be pro-inflammatory and is linked with a less healthy gut microbiome, which itself can increase inflammation and compromise immune function."

IMPORTANT ROLE

40%

of participants in the HSIS survey correctly said that the gut plays an important role in immune function.

> "ANTIOXIDANT VITAMINS AND MINERALS ARE NEEDED TO PROVIDE PROTECTION"

ESSENTIAL VITAMINS AND MINERALS FOR IMMUNE HEALTH

Most vitamins and minerals are essential for immune health, with some supporting the action of others and some working together to exert their effect.

"Vitamins A, C, D, E, and zinc are important in innate immunity to maintain the structure and function of the body's barriers to pathogens, including the skin, nose and throat and gastrointestinal tract. Both innate and adaptive immunity depend on a range of processes, including recognising and destroying pathogens, immune cell growth, producing antibodies, and regulating the inflammatory response (the cytokine storm).

"All of these activities require sufficient amounts of vitamins including vitamins A, B6, B12, folate, C, D, E, and minerals, including copper, iron, magnesium, selenium, and zinc[5,6]. Omega-3 fatty acids are also important in immune function, mainly by helping to reduce the inflammatory response,[7]" says public health nutritionist Dr Emma Derbyshire.

Vitamin A:

- Helps to maintain the integrity of the external barriers to pathogens[8]
- Essential for the production and growth of immune cells
- Helps to curb the inflammatory cytokine storm
- Contributes towards immune defence in the gut.

B group vitamins:

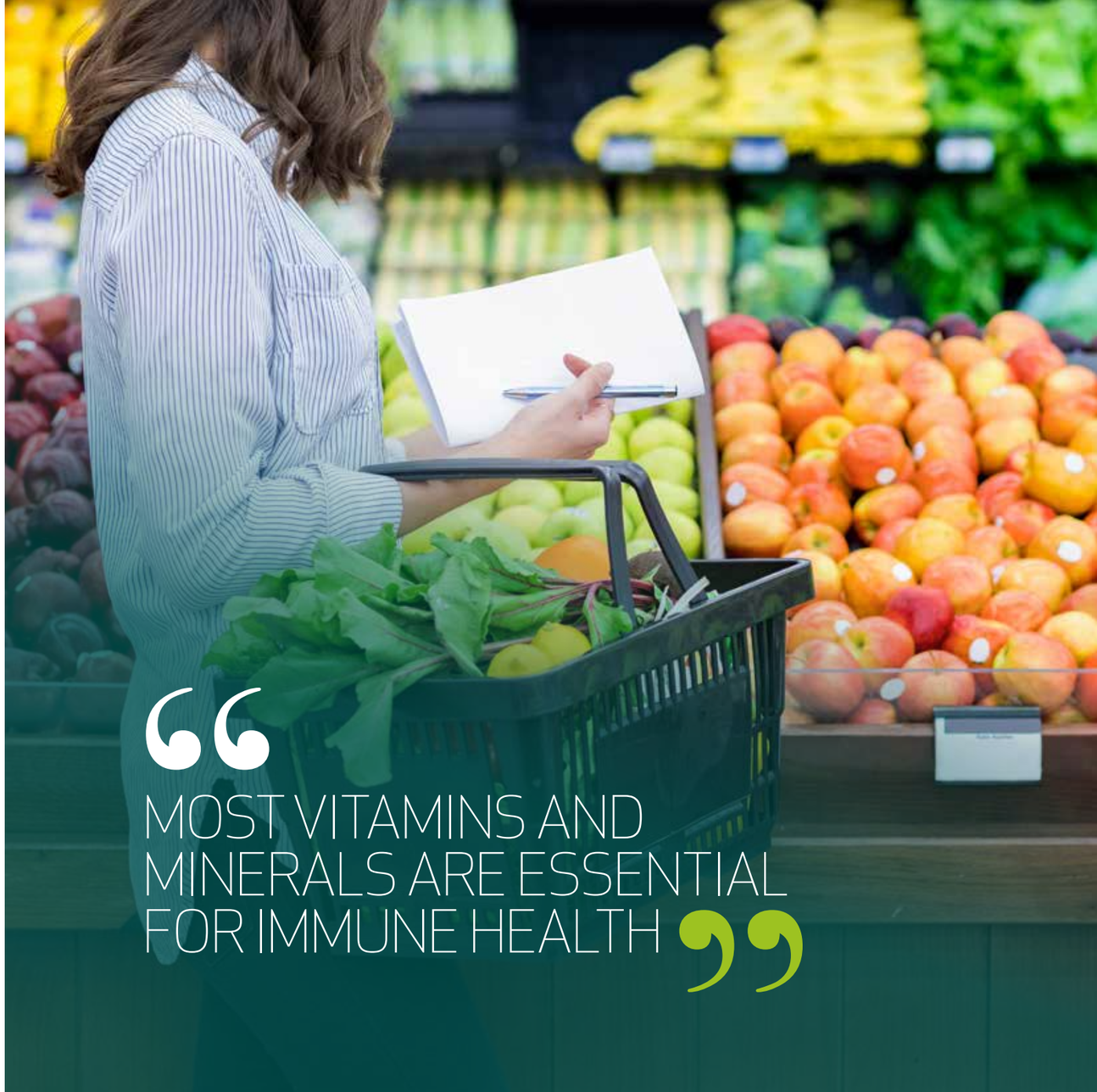
- Help enzymes (proteins that help speed up chemical reactions) to fuel energy production from food, which immune cells need for their metabolism[9]
- Vitamins B6, B12, and folate are involved in DNA and RNA synthesis in all cells, including immune cells
- Involved in gastrointestinal immune regulation, including the metabolic pathways of the gut microbes, helping to protect the gut barrier.

Vitamin C:

- One of the most important water-soluble antioxidant vitamins
- Important for the growth, movement, and overall function of immune cells[10]
- Protects immune cell membranes from inflammatory damage by free radicals.[11]

Vitamin D:

- Of special interest (particularly in the context of the COVID-19 pandemic) because of its involvement in the immune response
- The vitamin D receptor is found on the surface of most immune cells, including T and B lymphocytes The enzyme that converts vitamin D to its active form (calcitriol) is also present in these immune cells[12]
- Calcitriol protects the lungs and contributes to the healthy balance of bacteria in the gut, so helping to maintain the gut barrier and protect against the pro-inflammatory cytokine storm.[13]



Vitamin E:

- The main fat-soluble antioxidant vitamin
- Helps to protect immune cell membranes, amino acids and fatty acids from reactive oxygen species produced by pathogens during the cytokine storm[14]
- Contributes to the production of immune cells and antibodies.

Iron:

- Plays an important role in immune function
- Many pathogens need iron to function and grow but iron is regulated inside the body to limit pathogens getting access to it. Instead, iron is taken into immune cells[15]
- Promotes the growth of immune cells whilst iron deficiency alters their numbers, so reducing the ability of the immune system to destroy harmful organisms
- Regulates cytokine production and the inflammatory response in collaboration with other nutrients.[16]

Zinc:

- A cofactor (supporting nutrient) for at least 3,000 proteins and enzymes (catalysts for biochemical reactions), including making DNA
- Helps to maintain the structure and function of the skin and the gut barrier
- Needed for the function, growth, and balance in numbers of different immune cells.[17]

Selenium:

- Needed for several enzymes involved in biochemical reactions
- Helps to protect immune cells from damage caused by invading pathogens[18]
- Selenoprotein K is a key component of immune cells
- Important for maintaining T cell function, including antibody production.[19]

Copper:

- Plays an important role (which is yet to be fully understood) in immune function
- Supports the function of several immune cells, particularly in the production of anti-inflammatory substances that help to regulate the cytokine storm.[20]

Magnesium:

- Required for both innate and adaptive immune function[21]
- A cofactor of enzymes involved in making DNA and RNA and regulating immune cell function
- Magnesium deficiency is associated with altered levels of antibodies.

Omega-3 fatty acids:

- Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are long chain omega-3 fatty acids found mainly in fish oil and oily fish
- Help to curb inflammation in the immune response
- Regulate the fatty composition of cell membranes and inhibition of various proinflammatory factors.[22]

CHAPTER

3 EFFECTS OF POOR MICRONUTRIENT INTAKES ON IMMUNE FUNCTION

Clinical deficiencies of vitamins and minerals negatively affect the immune system and make us susceptible to infection. Less is known about the impact on immune health of poor intakes of micronutrients in the UK. However, the shortfalls in vitamin and mineral intakes evident in UK dietary surveys may compromise immune health, particularly if low intakes continue in the medium to long term.

Specific micronutrient shortfalls and their immune health consequences include:

Vitamin A:

- Can result in excessive inflammation, decrease the number and growth of T and B immune cells, and compromise antibody-production[23]
- Can increase the risk that pathogens will invade the eye, and the respiratory and gastrointestinal tracts (due to the role of vitamin A in maintaining the physical barriers within the body).[24]

B vitamins:

- Reduces the ability of the immune system to respond to pathogens
- Vitamin B6 deficiency reduces production of immune cells and antibodies whilst promoting inflammation[25]
- Deficiencies of both folate (folic acid) and vitamin B12 depress the antibody response and immune cell growth
- Folate deficiency suppresses RNA and DNA synthesis.[26]

Vitamin C:

- Increases the risk of oxidative and inflammatory damage in immune cells and throughout the body, which can predispose us to infection
- May increase the severity of pneumonia and other infections, mainly caused by increased oxidative damage and inflammation[27,28]
- Vitamin C supplementation restores impaired function of immune cells and reduces inflammation.[29]

Vitamin D:

- Associated with a range of features of poor immune function, including an unhealthy balance of the gut microbiota, fewer lymphocytes, reduced ability to kill pathogens, reduced maintenance of the respiratory and gastrointestinal barrier function, impaired T and B cell movements in the intestine, and overall impaired innate immunity[30]
- Increases the risk of respiratory tract infections[31,32]
- Associated with increased risk and severity of COVID-19[33]
- Linked with autoimmune diseases, such as type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus (SLE)
- Linked to increased risk of respiratory tract infection, including COVID-19 (see Appendix I).

Vitamin E:

- May impair B and T cell function which can compromise adaptive immunity[34,35]
- Reduces T cell development
- May reduce resistance to infection.[36]

Iron:

- Associated with alterations in T lymphocyte numbers, a reduced antibody response, and impaired killing of pathogens[37,38]
- Associated with more frequent and longer lasting respiratory tract infections in children.[39]

Zinc:

- Alters cytokine production, and impairs T cell function and antibody production[40,41]
- Increases susceptibility to infection (bacteria, viral, fungal) of the respiratory and gastrointestinal tracts.[42]

Copper:

- Associated with reduced T cell growth and impaired ability to kill pathogens, even in marginal deficiency[43]
- Associated with poor overall immune defence to infection.[44]

Selenium:

- May impair the antibody response to vaccination[45]
- Linked with respiratory tract infection in young children[46]
- Associated with greater risk of COVID-19.[47]

Magnesium:

- Reduces immune cell activity
- Increases levels of cytokines
- Increases inflammation
- Has been shown to reduce resistance to bacterial, viral, and fungal infections.[48]

Omega-3 Fatty Acids:

- Can result in delayed or inadequate resolution of inflammation,[49] which can impair the immune response.

CHAPTER

4 THE UK IMMUNE HEALTH MICRONUTRIENT EMERGENCY

Increased susceptibility to infections (including respiratory tract infections) and poorer outcomes have been seen in cases of low and inadequate vitamin and mineral intakes.[50] And unfortunately, poor intake and low circulating levels of many important immune health vitamins and minerals and omega-3 are common.

Nutritionist, Dr Pam Mason reminds us that: "While nutrition overall quite rightly has a high profile in health, the importance of micronutrients is not always considered, including their importance for immune health. The UK NDNS data shows shortfalls in micronutrients, including those involved in immune function, over many years, reminding us not to forget these essential substances."

APPROVED BY EFSA

The European Food Safety Authority (EFSA) recognises the importance of vitamins and minerals for immune function, authorising health claims on product labels for several micronutrients. These include vitamins A (including beta-carotene), B6, folate, B12, C and D, and the minerals zinc, selenium, iron, and copper.

> "THE IMPORTANCE OF MICRONUTRIENTS IS NOT ALWAYS CONSIDERED"

WHAT THE NATIONAL DIET AND NUTRITION SURVEY REVEALS

The UK National Diet and Nutrition Survey (NDNS) measures intakes and status of several nutrients of importance in immune function. The most recent data from the NDNS Rolling Programme (NDNS-RP)[51] indicates that intakes across the UK population of most micronutrients measured are close to the Reference Nutrient Intake (RNI; the amount of a nutrient considered sufficient for 95 per cent of the population).

However, a significant proportion of the population still doesn't meet the Lower Reference Nutrient Intake (LRNI; the amount of a nutrient considered sufficient for only a small number of people with low needs) for several micronutrients, including those contributing to immune function.

DECLINING NUTRIENT INTAKES SINCE 2008/9

According to NDNS-RP time trend data, since 2008/9 there has been a decline in the intakes of some of these micronutrients, such as vitamin A, vitamin D, B vitamins (riboflavin and folate) and iron, in some age groups.

Dr Carrie Ruxton warns that: "Vegetarian and vegan diets, which are increasing in popularity, can also be low in nutrients of importance in immune function, such as vitamin B12, vitamin D, iodine, iron, selenium, and zinc, as well as the marine omega-3 fatty acids, DHA and EPA.[52] In addition, emerging data suggest that recommended intakes of micronutrients may not be high enough to support optimal immune function."[53]

Population groups under pressure according to the HSIS research includes:

TEENAGERS AND YOUNG ADULTS (11-18s)

IRON: Almost one third (30 per cent) fail to achieve the LRNI for iron – a six per cent increase in the proportions of youngsters not achieving even that low intake from 2008/9.

VITAMIN A: Just under a fifth (18 per cent) did not achieve the LRNI for vitamin A compared with 13 per cent in 2008/9

FOLATE: Nearly one in 10 (9 per cent) didn't achieve the LRNI for folate compared with four per cent in 2008/9.

ZINC: Despite a small improvement, more than one in six in this age group still fail to achieve the LRNI for zinc (18 vs. 16 per cent).

TEENAGE GIRLS AND YOUNG WOMEN (11-18s)

IRON: 43 per cent failed to achieve the LRNI for iron in 2008/9, and this has only increased since, ranging from 48 to 54 per cent over the 10-year survey period from 2008/9 to 2018/19.

VITAMIN A: Similarly in 2008/9, 14 per cent didn't achieve the LRNI for vitamin A, a figure that has increased to as high as 24 per cent in recent years.

VITAMIN B2: Figures for riboflavin (vitamin B2) were 18 per cent in 2008/9, increasing to as high as 26 per cent in recent years.

FOLATE: For folate the figure was 6 per cent in 2008/9, increasing to 10 per cent in the most recent data, with a peak of 15 per cent during the NDNS-RP period.

WOMEN OF CHILDBEARING AGE (16-49s)

FOLATE: The proportion not achieving the LRNI has increased from 3 to 7 per cent.

VITAMIN A: The proportion not achieving the LRNI has increased from 5 to 8 per cent, with a peak of 10 per cent during the course of the survey.

IRON: The proportion not achieving the LRNI has increased from 21 to 25 per cent respectively with a peak of 27 per cent.

SENIORS (OVER 65s)

There have been increases in the proportions of people over 65 not meeting the LRNI for vitamin A, iron, magnesium, and zinc since 2008/9.

OLDER WOMEN (OVER 65)

IRON: The proportion not achieving the LRNI has increased from 1 per cent to 5 per cent, with a peak of 10 per cent over the survey period.

ZINC: The proportion not achieving the LRNI has increased from 1 per cent to 4 per cent.

Vitamin A

The most recent NDNS-RP report showed that mean intake of vitamin A was above or close to the RNI in all age/sex groups. However, a significant proportion of the population is hidden by this statistic.

Below LRNI intakes of vitamin A occur in:

- 8 per cent of adults of 65 and over
- 10 per cent of adults aged 19-64
- 18 per cent of 11–18-year-olds
- 11 per cent of 4–10-year-olds
- 9 per cent of children aged 18 months to 3 years.

Vitamin A intake overall has fallen since 2008/9 by 21 and 23 per cent in children and teenage age groups respectively, by 13 per cent in adult groups, and by 29 per cent in people aged 65 and over.

B Vitamins

Folate

The most recent NDNS-RP report[54] found that 10 per cent of 11–18-year-old girls and 7 per cent of 19–64-year-old women had below LRNI intakes for folate. Blood folate concentrations have also decreased considerably since 2008/9 for most population groups, and there has been an increase in the proportion of participants with folate concentrations indicating risk of anaemia.

RISK TO HEALTHY PREGNANCY

In women of childbearing age (16 to 49 years),[55] red blood cell folate decreased by 20 per cent over the survey period. Analysis of the proportion of women of childbearing age with a red blood cell folate concentration below the threshold for increased risk of pregnancies affected by a neural tube defect (748nmol/L) increased from approximately two thirds to almost 90 per cent over the course of the NDNS survey.[56]

Vitamin B12

Since 2008/9, overall intakes of vitamin B12 have continued to meet recommendations. However, this micronutrient is found in animal foods such as meat and dairy (and in some fortified plant-based foods such as some breakfast cereals). Therefore, vegans are at particular risk from low vitamin B12 intakes as they consume no animal foods, and the growing population of vegetarians and those following plant-based diets could also be at risk if they fail to carefully plan their food intake.

Vitamin C

Vitamin C intake and status is not analysed in the recent NDNS. However, earlier NDNS reports and other UK studies indicate that having too little vitamin C in the diet is not uncommon in the UK.[57] The Norfolk arm of the European EPIC study evaluated more than 22,400 people (aged 40–79 years) and found that 1.4 per cent were vitamin C deficient (2.2 per cent for men and 0.8 per cent for women) with 12 per cent of participants (17 per cent of men and 8 per cent of women) having low vitamin C.[58]

Data from the 1994/1995 NDNS for more than 1,300 older people (aged ≥65 years) showed that 14 per cent were deficient in vitamin C,[59] whilst in the third MONICA study, carried out in Glasgow in 1992 in over 1,200 adults, 20 per cent of the group (26 per cent of men and 14 per cent of women) were deficient in vitamin C, whilst 44 per cent (52 per cent of men and 36 per cent of women) had low vitamin C.[60]

Vitamin D

Poor vitamin D status is common in the UK. The most recent NDNS (UK Government, 2020) shows that 16 per cent of adults aged 19-64 years (18 per cent of women and 15 per cent of men) have 25-OH D plasma levels below 25nmol/litre (the UK threshold indicating deficiency).[61] Amongst young people, 2 per cent of 4-10-year-olds (1 per cent of boys and 3 per cent of girls) and 19 per cent of 11-18-year olds (21 per cent of boys and 17 per cent of girls) also have low blood levels of vitamin D.

A study in UK primary care found that amongst 210,502 patients who had a vitamin D test, one third were deficient (with deficiency identified as a blood level below 30nmol/litre). Deficiency among minority groups ranged from 43 per cent among those of mixed ethnicity to 66 per cent of Asian people.[62] Encouragingly, the HSIS poll shows that over a third of Britons (35 per cent) are now taking a Vitamin D supplement most days of the week. This includes 46 per cent of respondents aged 60 and over.

> “THE HSIS POLL SHOWS THAT OVER A THIRD OF BRITONS ARE NOW TAKING A VITAMIN D SUPPLEMENT”

Iron

During the past 10 years, there has been a five per cent reduction in iron intakes. Average intakes of iron were below the RNI in some groups and below the LRNI in others. Nearly half (49 per cent) of girls aged 11-18 years and a quarter (25 per cent) of women aged 19-64 have intakes of iron below the LRNI, a level which is associated with risk of iron deficiency anaemia.[63]

Zinc

The most recent NDNS-RP report[64] showed that average zinc intake was above or close to the RNI in all population groups except children, with nearly one in five (18 per cent) 11–18-year-olds and 11 per cent of 4–10-year-olds not meeting the LRNI.

Selenium

Selenium intakes have changed little over the NDNS-RP survey period. However, in the 2020 NNDS-RP[66] 32 per cent of 11–18-year-olds, 36 per cent of 19–64-year-olds, and 47 per cent of those aged 65 and over had selenium intakes below the LRNI. Amongst women, the figures were 41 per cent, 46 per cent, and 59 per cent, respectively.

Magnesium

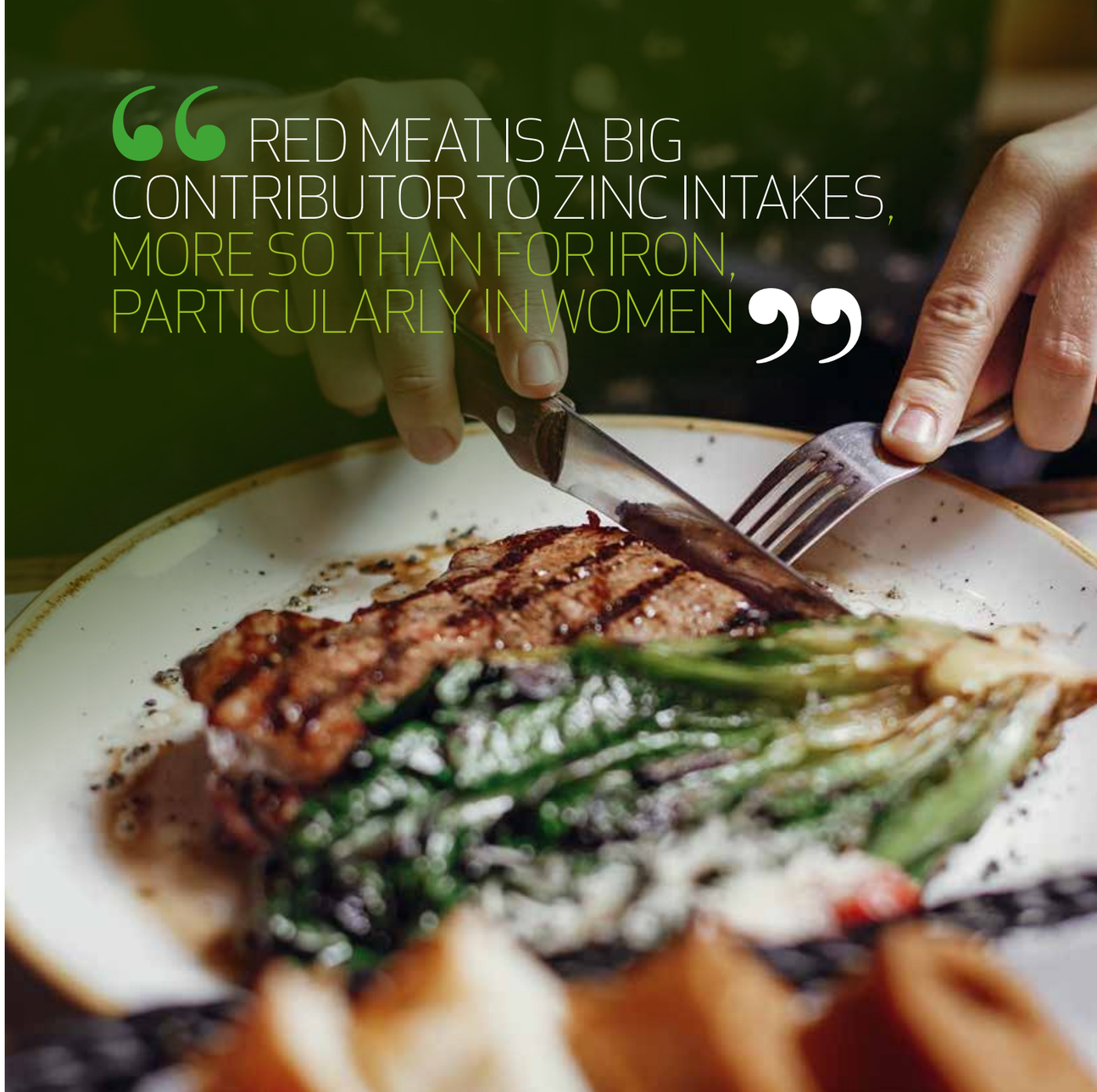
In the latest NDNS-RP report,[67] 40 per cent of 11–18-year-olds, 12 per cent of 19–64-year-olds, and 13 per cent of those aged 65 and over had magnesium intakes below the LRNI. For women across these age ranges the figures were 47 per cent, 11 per cent, and 11 per cent, respectively.

Omega-3 fatty acids

Omega-3 fatty acid intake reflects oily fish intake, the main source of the long chain omega-3s EPA and DHA. Amongst 11-18-year-olds, weekly intake of oily fish is 21g, and just 56g amongst adults – intakes which fall far below the recommended 140g a week.

PLANT-BASED PREDICAMENT

Red meat is a big contributor to zinc intakes, more so than for iron, particularly in women. Falling meat intake amongst those with lower intakes of zinc as well as those with lower iron intakes could increase the risk of deficiency of these essential minerals.[65]



CHAPTER

5 SCIENCE-BACKED SUPPLEMENTS: WHAT THE RESEARCH REVEALS

Good immune health depends on people having at least recommended intakes of all essential vitamins, minerals, and fatty acids – particularly omega-3s.

THE EUROPEAN FOOD SAFETY AUTHORITY

The European Food Safety Authority has authorised immune health claims for several micronutrients, including:

- Vitamin A (including beta-carotene)
- Vitamin B6
- Folate
- Vitamin B12
- Vitamin C
- Vitamin D
- Zinc
- Selenium
- Iron
- Copper[68]

With the UK NDNS data showing that a significant proportion of the population aren't meeting the recommended intakes for several essential micronutrients, many people may be compromising their overall health including their immune health.

BOLSTER YOUR DEFENCES

Dr Nisa Aslam says: "It makes sense to take a multivitamin and multimineral supplement containing recommended intakes of a wide range of micronutrients to help prevent deficiency and support all aspects of health. Micronutrient supplementation has been shown to improve several specific aspects of immune health, particularly where deficiencies exist."

OPTIMISE YOUR IMMUNITY

It is also possible that intakes of vitamins and minerals above recommended intakes may be needed for optimal immune function. This applies in particular to vitamin C,[69] where the NRV is 80mg daily (the amount quoted on supplement labels), but doses as high as 200mg may be required to benefit immune health and reduce the risk of infection. However, no definitive agreement on micronutrient doses beyond the recommended levels has so far been reached. Until that happens, it's sensible to stick with a supplement containing the NRV.

SPOTLIGHT ON IMMUNE HEALTH MICRONUTRIENTS

Most of the research on specific micronutrients and their benefits to immune function has been carried out for vitamins C, D, E, zinc, selenium, and multivitamins.

Vitamin C

High doses of vitamin C have been shown to stimulate the activity of immune cells and reduce the risk of damage from the inflammatory cascade.[70] A recent meta-analysis study reported a significantly lower risk of pneumonia amongst people supplementing with vitamin C, particularly in those with low dietary intakes.[71] In older people, severity of pneumonia and risk of death were reduced with vitamin C use, particularly when vitamin C blood levels were low.

Vitamin C supplementation has also been shown to reduce the duration and severity of the common cold. Additional vitamin C may reduce the risk of infection in people under physical stress.[72] In terms of dose, at least 200 mg/day maximises vitamin C concentrations in the blood,[73] and has been shown to reduce the risk, duration, and severity of upper and lower respiratory tract infections.[74] The body needs more vitamin C when fighting infection.

Vitamin D

When given as a supplement, the active form of vitamin D (calcitriol) helps to restore optimal immune cell function.[75] A 2017 review of 25 clinical trials involving 11,321 participants aged 0 to 95 years found that the risk of acute respiratory tract infection was reduced by 12 per cent with vitamin D supplementation.

The researchers found a 19 per cent reduction in infections amongst those receiving daily or weekly vitamin D. Protective effects were stronger in those who were deficient (25-OH D levels of less than 25 nmol/L) at the start, compared with those with 25-OH D levels of 25 nmol/L or above.[76]

A 2020 analysis of 45 clinical trials (involving 73,384 participants),[77] and a 2021 update of the same study including 46 clinical trials (involving 75,541 participants),[78] found that a significantly lower proportion of participants supplementing with vitamin D had one or more acute respiratory tract infections. Protective effects of vitamin D supplementation were seen in trials in which vitamin D was given at a dose of 400-1,000 IU (10-25 micrograms) daily for 12 months or less.[79] Initial vitamin D blood concentration did not affect the findings.

Vitamin E

Vitamin E supplementation may also have a positive role in immune function, particularly in older people.[80] Vitamin E supplementation improves antibody response to vaccines in healthy older people (over 65 years)[81] and has been shown to improve immune cell activity, bringing it closer to that of younger adults.[82] Supplementation with 200 IU of vitamin E a day for 12 months reduced the risk of upper respiratory tract infections in a nursing home study involving 617 residents.[83]

Selenium

Selenium supplementation has shown variable effects on immunity. In a 12-week study in healthy adults with marginal selenium status, supplementation after an influenza vaccine had positive effects on some aspects of immune cell function and negative effects on others.[84] Additionally, a small trial in 22 UK adults found that those with marginal selenium status had suboptimal immune status. When receiving the polio vaccination, those with poor selenium status displayed impaired handling of the virus, while supplementation with selenium improved part of the immune response.[85]

COVERING ALL BASES

Several peer-reviewed papers have evaluated the effect of multivitamins and other multiple nutrient supplements on immune function. A 12-week clinical trial in 42 older adults (over 65 years) found that multivitamin and multimineral supplementation reduced the duration of minor illness, and improved vitamin C and zinc status.[86]

In a study using data from adult participants (over 19 years old) in the NDNS-RP (2008-2016), increasing intake of vitamin A and E (from diet and supplements) was shown to reduce the risk of respiratory problems. For vitamin D, intake from supplements, but not diet, reduced respiratory complaints. However, no association between vitamin C and respiratory complaints was found.[87]

Another clinical trial involving 477 healthy adults (with an average age of 36 years) showed a 13.6 per cent reduction in the incidence of viral respiratory infections in the group taking a multivitamin/mineral with a probiotic supplement compared with the placebo group. Symptoms of common cold and flu were reduced in the supplement group.[88]

Most recently, a study from King's College London[89] looked at dietary supplement use amongst 445,840 subscribers to a COVID-19 app collecting self-reported health data. In 372,720 UK participants, 175,652 of whom said they took supplements and 197,068 of whom didn't, there was a 14 per cent lower risk of SARS-CoV-2 infection amongst those taking probiotics, omega-3 fatty acids, multivitamins, or vitamin D.

LAST WORD

It almost goes without saying that our overall health depends on a healthy immune function. But until recently, we may not have given much thought to this vital aspect of health. The good news is that more than three quarters of us (76 per cent) do at least now think about our immune health and wellness. Thinking about it isn't enough, though. As we have seen with the pandemic, infection travels fast, so we need to be prepared.

Good nutrition, made up of a healthy diet including recommended intakes of vitamins and minerals and omega-3 fatty acids, is a vital tool in our immune health toolbox. Micronutrients have a significant impact on immune health as they play a role in the development and function of immune cells and protecting the structure of the external barriers, such as the skin, gut, and respiratory tract, from virus and bacteria attacks.

However, data from the NDNS-RP show that the UK population does not achieve the recommended intakes. We can see below even LRNI intakes across the board, particularly in younger adults and particularly for trace minerals, and the problem has grown worse over time.

In theory, recommended intakes of vitamins and minerals could be achieved by following a healthy diet, but for a whole host of reasons many people do not manage this. Lack of time and motivation to buy, prepare and eat healthy food, the ease of access to food high in sugar, fat, and salt and low in micronutrients and fibre, and the desire to try various diets can adversely affect vitamin and mineral intakes. Even following the pandemic, only half (51 per cent) of participants in the HSIS survey are trying to increase their fruit and vegetable intake.

> "ONLY HALF OF PARTICIPANTS IN THE HSIS SURVEY ARE TRYING TO INCREASE THEIR FRUIT AND VEGETABLE INTAKE"

People pursuing 'healthy plant-based diets' are not immune to poor micronutrient intakes either. A report commissioned by HSIS in 2020 demonstrated the popularity of plant-based diets in the UK and found they may be connected with worrying shortfalls of vitamin B12, vitamin D, iron, zinc, selenium, and iodine. This was largely because people shifting to plant-based eating didn't research or plan their new diets and had no idea that their diets could lack micronutrients. This worrying dietary gap should be bridged with a vitamin and mineral supplement, plus an omega-3 fatty acid supplement, to help meet recommended intakes and maintain immune health.

Some scientists have advised higher-than-recommended intakes of micronutrients for immune function.[90] For example, Professor Philip Calder's Colleagues from Southampton University recommend at least 200mg of vitamin C, 50 micrograms of vitamin D and 8-11mg of zinc in addition to a healthy diet and general multivitamin and multimineral supplement. Also, a daily supplement of at least 250 mg EPA/DHA is advised, although this is below the UK's recommendation of 450 mg EPA/DHA from the overall diet. As a result, for the future, our focus should be on improving the poor nutrient intakes and nutrient status evident in the UK population, by encouraging use of multivitamin and multimineral supplements in recommended amounts plus an omega-3 supplement each day.

ABOUT HSIS

HSIS (the Health and Food Supplements Information Service) is a communication service providing accurate and balanced information on vitamins, minerals and other food supplements to the media and to health professionals working in the field of diet and nutrition. Find out more at **www.hsis.org**

For further information or to arrange an interview with an HSIS spokesperson, please contact the HSIS press office **HSIS@junglecatsolutions.com** or call **020 3600 0228**. Out of hours please call **07867 513 361.**

HSIS
THE HEALTH AND FOOD SUPPLEMENTS INFORMATION SERVICE

APPENDIX I

Low vitamin D levels linked to respiratory tract infections, including COVID-19: what the research reveals

Cross-sectional data from 6,789 participants in the nationwide 1958 British birth cohort who had measurements of serum 25-OHD, lung function and respiratory infection data available from the age of 45 years indicated that the prevalence of respiratory infections reduced when 25-OH D concentrations increased. Each 10 nmol/l increase in 25-OHD was associated with a 7 per cent reduced risk of respiratory infection (95 per cent CI 3, 11 per cent) combined with improved lung function.[91] A 2019 systematic review of epidemiological studies also found an increased risk of upper and lower respiratory tract infections when serum vitamin D levels were low.[92]

During 2020 a number of studies examined the possible association between vitamin D status and risk of COVID-19. Two studies found inverse associations between national estimates of vitamin D status and COVID-19 incidence and mortality in European countries.[93,94] Lower circulating 25-OH D concentrations have also been associated with susceptibility to SARS-CoV-2 infection[95] and COVID-19 severity.[96]

An Israeli study found associations between low pre-pandemic 25-OH D levels and later incidence and severity of COVID-19.[97] However, a recent UK Biobank Cohort study did not suggest a link between vitamin D concentrations and risk of COVID-19 infection.[98] Of note is that both of these studies employed historic 25-OHD measurements which might not have reflected vitamin D concentrations at the time of exposure to SARS-CoV-2.

Small studies in patients hospitalised with COVID-19 have found more chronic disease in those with low vitamin D levels. One small Irish observational study involving 33 men admitted to hospital for pneumonia associated with COVID-19 found lower vitamin D levels in those admitted to the intensive care unit (ICU). Low vitamin D levels were also linked with a greater likelihood of needing to be put on a ventilator.[99]

An analysis of patients in hospital with COVID-19 in Spain compared vitamin D levels in these patients with those of a control group of healthy patients matched for age. Overall, vitamin D deficiency was recorded in 82 per cent of patients with COVID-19 compared to 47 per cent of the healthy controls. Compared to those who were vitamin D deficient, vitamin D replete patients had a reduced need for the antiviral medication tocilizumab, fewer intensive care admissions and a slightly shorter hospital stay (12 vs 8 days).[100]

Studies in people of South Asian origin find low intakes of vitamin D and also 25-OH D levels below 25nmol/litre throughout the year even in summer. Low vitamin D status may contribute to the higher observed rates of COVID-19 in black and minority ethnic people. In the UK Biobank cohort, 55 per cent of the 6,433 South Asians with a 25-OHD measurement had a 25-OH D < 25 nmol/litre (severe deficiency) and 92 per cent had a 25-OH D < 50 nmol/litre (insufficiency). One fifth (20 per cent) of those with a measurement had a 25-OH D concentration <15 nmol/litre (very severe deficiency).[101] When 824 additional participants with undetectable (<10 nmol/litre) 25-OH D measurements were included, 29 per cent had 25-OHD < 15 nmol/litre, 60 per cent had 25-OH D < 25 nmol/litre and 93 per cent had 25-OH D < 50 nmol/litre. However, low vitamin D levels in the UK Biobank Study did not explain the pattern of COVID-19 related to ethnic origin. This suggests that factors underlying ethnic differences in COVID-19 are complex and different avenues of research need to be pursued.

REFERENCES

1. Perspectus Global. Survey 1110 respondents; Autumn 2021
2. Perspectus Global. Survey 1110 respondents; Autumn 2021
3. Brodin P. Immune determinants of COVID-19 disease presentation and severity https://www.nature.com/articles/s41591-020-01202-8
4. Anderson, H. L., Brodsky, I. E., & Mangalmurti, N. S. (2018). The Evolving Erythrocyte: Red Blood Cells as Modulators of Innate Immunity. Journal of immunology (Baltimore, Md.: 1950), 201(5), 1343–1351. https://doi.org/10.4049/jimmunol.1800565
5. Calder PC, Carr AC, Gombart AF & Eggersdorfer M (2020) Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. Nutrients 12(4).
6. Gombart AF, Pierre A & Maggini S (2020) A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Nutrients 2020, 12(1).
7. Calder PC (2017) Omega-3 fatty acids and inflammatory processes: from molecules to man. Biochem Soc Trans 45(5):1105-15.
8. Maggini S, Wintergerst ES, Beveridge S & Hornig DH (2007) Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. Br J Nutr 98 Suppl 1: S29-35.
9. Yoshii K, Hosomi K, Sawane K & Kunisawa J (2019) Metabolism of dietary and microbial Vitamin B family in the regulation of host immunity. Front Nutr 6 (48).
10. Carr AC & Maggini S (2017) Vitamin C and immune function. Nutrients 9(11).
11. Ibid
12. Wu D, Lewis ED, Pae M & Meydani S (2018) Nutritional modulation of immune function: analysis of evidence, mechanisms, and clinical relevance. Front Immunol 9:3160.
13. Clark A & Mach N (2016) Role of Vitamin D in the hygiene hypothesis: The interplay between Vitamin D, Vitamin D receptors, gut microbiota, and immune response. Front Immunol 7: 627.
14. Maggini S, Wintergerst ES, Beveridge S & Hornig DH (2007) Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. Br J Nutr 98 Suppl 1: S29-35.
15. Maggini S, Beveridge S, Sorbara PJP & Senatore G (2009) Feeding the immune system: the role of micronutrients in restoring resistance to infection. CAB Review DOI: 101079/PAVSNNR20083098. 2009.
16. Agoro R, Taleb M, Quesniaux VFJ & Mura C (2018) Cell iron status influences macrophage polarization. PLoS One, 1 3(5), e0196921
17. Bonaventura P, Benedetti G Albarède F & Miossec P (2015) Zinc and its role in immunity and inflammation. Autoimmun Rev 14(4): 277-285.
18. Huang Z, Rose AH & Hoffmann PR (2012) The role of selenium in inflammation and immunity: from molecular mechanisms to therapeutic opportunities. Antiox Redox Signal16(7): 705-743.
19. Calder PC (2020) Nutrition, immunity, and COVID-19. BMJ Nutr, Prev Health 3(1): 74-92.
20. Ibid
21. Ibid
22. Calder PC (2017) Omega-3 fatty acids and inflammatory processes: from molecules to man. Biochem Soc Trans 45(5):1105-15.
23. Maggini S, Beveridge S, Sorbara PJP & Senatore G (2009) Feeding the immune system: the role of micronutrients in restoring resistance to infection. CAB Review DOI: 101079/PAVSNNR20083098. 2009.
24. Micronutrient Information Center. Immunity in Depth. Linus Pauling Institute. 2016. Available online: http://lpi.oregonstate.edu/mic/health-disease/immunity. Accessed April 18, 2021.
25. Ibid
26. Ibid
27. Carr AC & Maggini S (2017) Vitamin C and immune function. Nutrients 9(11).
28. Hemila C (2017) Vitamin C and infections. Nutrients 9(4): 339. https://doiorg/103390/nu9040339. 2013.
29. Carr AC & Maggini S (2017) Vitamin C and immune function. Nutrients 9(11).
30. Gombart AF, Pierre A & Maggini S (2020) A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Nutrients 2020, 12(1).
31. Jolliffe DA, Camargo CA, Jr., Sluyter JD, Aglipay M, Aloia JF, Ganmaa D et al (2021) Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials. Lancet Diabetes Endocrinol, https://www.thelancet.com/pdfs/journals/landia/PIIS2213-8587(21)00051-6.pdf.
32. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al (2017) Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data.BMJ i6583.
33. Mandal AKJ, Baktash V, Hosack T, Van den Abbeele K & Missouris CG (2021) Vitamin D status may indeed be a prognosticator for morbidity and mortality in patients with COVID-19. J Med Virol 93(3):1225.
34. Micronutrient Information Center. Immunity in Depth. Linus Pauling Institute. 2016. Available online: http://lpi.oregonstate.edu/mic/health-disease/immunity. Accessed April 18, 2021.
35. Saeed F, Nadeem M, Ahmed R, Nadeem MT, Arshad M & Ullah A (2016) Studying the impact of nutritional immunology underlying the modulation of immune responses by nutritional compounds – a review, Food and Agricultural Immunology 27:2, 205-229, DOI: 101080/095401052015179600. 2016.
36. Ibid
37. Gombart AF, Pierre A & Maggini S (2020) A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Nutrients 2020, 12(1).
38. Micronutrient Information Center. Immunity in Depth. Linus Pauling Institute. 2016. Available online: http://lpi.oregonstate.edu/mic/health-disease/immunity. Accessed April 18, 2021.
39. Ross A, Caballero B, Cousins R, Tucker K & Ziegler T (2012) Modern Nutrition in Health and Disease,11th ed.; Wolters Kluwer Health Adis (ESP): Philadelphia, PA, USA, 2012.
40. Bonaventura P, Benedetti G Albarède F & Miossec P (2015) Zinc and its role in immunity and inflammation. Autoimmun Rev 14(4): 277-285.
41. Micronutrient Information Center. Immunity in Depth. Linus Pauling Institute. 2016. Available online: http://lpi.oregonstate.edu/mic/health-disease/immunity. Accessed April 18, 2021.
42. Savino W & Dardenne M (2010) Nutritional imbalances and infections affect the thymus: Consequences on T-cell-mediated immune responses. Proc Nutr Soc 69: 4:636-43. doi:10.1017/S0029665110002545.

43. Percival SS (1998) Copper and immunity. Am J Clin Nutr 67(5 Suppl): 1064s-1068s
44. Maggini S, Beveridge S, Sorbara PJP & Senatore G (2009) Feeding the immune system: the role of micronutrients in restoring resistance to infection. CAB Review DOI: 101079/PAVSNNR20083098. 2009.
45. Ibid
46. Gombart AF, Pierre A & Maggini S (2020) A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. Nutrients 2020, 12(1).
47. Im JH, Je YS, Baek J, Chung MH, Kwon HY & Lee JS (2020) Nutritional status of patients with COVID-19. International J Infect Dis 100:390-393.
48. Johnson S (2001) The multifaceted and widespread pathology of magnesium deficiency. Med Hypotheses 56(2): 163-70.
49. Calder PC (2017) Omega-3 fatty acids and inflammatory processes: from molecules to man. Biochem Soc Trans 45(5):1105-15.
50. Calder PC (2020) Nutrition, immunity, and COVID-19. BMJ Nutr, Prev Health 3(1): 74-92.
51. NatCen Social Research (2020) National Diet and Nutrition Survey. Rolling programme Years 9 to 11 (2016/2017 to 2018/2019). A survey carried out on behalf of Public Health England and the Food Standards Agency, 2020
52. Petti A, Palmieri B, Vadala M & Laurino C (2017) Vegetarianism and veganism: not only benefits but also gaps. Progress in Nutrition 19: 229–242.
53. Calder PC (2020) Nutrition, immunity, and COVID-19. BMJ Nutr, Prev Health 3(1): 74-92.
54. NatCen Social Research (2020) National Diet and Nutrition Survey. Rolling programme Years 9 to 11 (2016/2017 to 2018/2019). A survey carried out on behalf of Public Health England and the Food Standards Agency, 2020
55. ibid
56. ibid
57. Rowe S & Carr AC (2020) Global Vitamin C status and prevalence of deficiency: a cause for concern? Nutrients 12(7).
58. Canoy D, Wareham N, Welch A, Bingham S, Luben R, Day N, et al (2005) Plasma ascorbic acid concentrations and fat distribution in 19,068 British men and women in the European Prospective Investigation into Cancer and Nutrition Norfolk cohort study. Am J Clin Nutr 82(6): 1203-1209.
59. Bates CJ, Prentice A, Cole TJ, van der Pols JC, Doyle W, Finch S, et al (1999) Micronutrients: highlights and research challenges from the 1994-5 National Diet and Nutrition Survey of people aged 65 years and over. Br J Nutr 82(1):7-15.
60. Wrieden WL, Hannah MK, Bolton-Smith C, Tavendale R, Morrison C & Tunstall-Pedoe H (2000) Plasma vitamin C and food choice in the third Glasgow MONICA population survey. J Epidemiol Community Health, 54(5):355-360.
61. NatCen Social Research (2020) National Diet and Nutrition Survey. Rolling programme Years 9 to 11 (2016/2017 to 2018/2019). A survey carried out on behalf of Public Health England and the Food Standards Agency, 2020
62. Crowe, F. L., Jolly, K., MacArthur, C., Manaseki-Holland, S., Gittoes, N., Hewison, M., Scragg, R., & Niranthara kumar, K. (2019). Trends in the incidence of testing for vitamin D deficiency in primary care in the UK: a retrospective analysis of The Health Improvement Network (THIN), 2005-2015. BMJ open, 9(6), e028355. https://doi.org/10.1136/bmjopen-2018-028355
63. NatCen Social Research (2020) National Diet and Nutrition Survey. Rolling programme Years 9 to 11 (2016/2017 to 2018/2019). A survey carried out on behalf of Public Health England and the Food Standards Agency, 2020
64. ibid
65. Derbyshire E (2017) associations between red meat intakes and the micronutrient intake and status of uk females: A secondary analysis of the UK National Diet and Nutrition Survey. Nutrients 9(7):768.
66. NatCen Social Research (2020) National Diet and Nutrition Survey. Rolling programme Years 9 to 11 (2016/2017 to 2018/2019). A survey carried out on behalf of Public Health England and the Food Standards Agency, 2020
67. Ibid
68. European Commission of the European Union (2020) EU register of nutrition and health claims made on foods. https://ec.europa.eu/food/safety/labelling_nutrition/claims/register/public/?event=register.home (accessed April 20, 2021). 2020.
69. Calder PC, Carr AC, Gombart AF & Eggersdorfer M (2020) Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. Nutrients 12(4).
70. Maggini S, Beveridge S, Sorbara PJP & Senatore G (2009) Feeding the immune system: the role of micronutrients in restoring resistance to infection. CAB Review DOI: 101079/PAVSNNR20083098. 2009.
71. Hemilä H & Louhiala P (2103) Vitamin C for preventing and treating pneumonia. Cochrane Database Syst Rev. 2013(8): Cd005532
72. Hemilä H & Chalker E (2013) Vitamin C for preventing and treating the common cold. Cochrane Database Syst Rev. 2013(1): Cd000980.
73. Levine M, Conry-Cantilena C, Wang Y, Welch RW, Washko PW, Dhariwal KR, et al (1996) Vitamin C pharmacokinetics in healthy volunteers: evidence for a recommended dietary allowance. Proceedings of the National Academy of Sciences of the USA, 93(8):3704-3709.
74. Hunt C, Chakravorty NK, Annan G, Habibzadeh N & Schorah CJ (1994) The clinical effects of vitamin C supplementation in elderly hospitalised patients with acute respiratory infections. Int J Vitamin Nutr Res 64(3):212-219.
75. Fleming DM & Elliot AJ (2007) Epidemic influenza and vitamin D. Epidemiol Infect 135(7): 1091-1092.
76. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al (2017) Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data.BMJ i6583.
77. Jolliffe DA, Camargo CA, Jr., Sluyter JD, Aglipay M, Aloia JF, Ganmaa D, et al (2020) Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of aggregate data from randomised controlled trials. MedRxiv. 2020.
78. Ibid
79. Jolliffe DA, Camargo CA, Jr., Sluyter JD, Aglipay M, Aloia JF, Ganmaa D, et al (2020) Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of aggregate data from randomised controlled trials. MedRxiv. 2020.
80. Wu D & Meydani SN (2014) Age-associated changes in immune function: impact of vitamin E intervention and the underlying mechanisms. Endocr Metab Immune Disord Drug Targets 14(4):283-289.
81. Meydani SN, Meydani M, Blumberg JB, Leka LS, Siber G, Loszewski R, et al (1997) Vitamin E supplementation and in vivo immune response in healthy elderly subjects. A randomized controlled trial JAMA 277(17):1380-1386
82. De la Fuente M, Hernanz A, Guayerbas N, Victor VM & Arnalich F (2008) Vitamin E ingestion improves several immune functions in elderly men and women. Free Radic Res 42(3):272-280.
83. Meydani SN, Leka LS, Fine BC, Dallal GE, Keusch GT, Singh MF, et al (2004) Vitamin E and respiratory tract infections in elderly nursing home residents: a randomized controlled trial. JAMA 292(7): 828-836.
84. Ivory K, Prieto E, Spinks C, Armah CN, Goldson AJ, Dainty JR, et al (2017) Selenium supplementation has beneficial and detrimental effects on immunity to influenza vaccine in older adults. Clin Nutr 36(2):407-415.
85. Broome CS, McArdle F, Kyle JA, Andrews F, Lowe NM, Hart CA, et al (2004) An increase in selenium intake improves immune function and poliovirus handling in adults with marginal selenium status. Am J Clin Nutr 80(1):154-162.
86. Fantacone ML, Lowry MB, Uesugi SL, Michels AJ, Choi J, Leonard SW, et al (2020) The effect of a multivitamin and mineral supplement on immune function in healthy older adults: a double-blind, randomized, controlled trial. Nutrients 12(8).
87. Almoosawi S & Palla L (2020) Association between vitamin intake and respiratory complaints in adults from the UK National Diet and Nutrition Survey years 1-8. BMJ Nutr Prev Health 3(2):403-408.
88. Winkler P, de Vrese M, Laue C & Schrezenmeir J (2005) Effect of a dietary supplement containing probiotic bacteria plus vitamins and minerals on common cold infections and cellular immune parameters. Int J Clin Pharmacol Ther 43(7):318-326.
89. Louca P, Murray B, Klaser K, Graham MS, Mazidi M, Leeming ER, et al (2021) Modest effects of dietary supplements during the COVID-19 pandemic: insights from 445 850 users of the COVID-19 Symptom Study app). BMJ Nutrition, Prevention & Health. 2021: bmjnph-2021-000250
90. Calder PC, Carr AC, Gombart AF & Eggersdorfer M (2020) Optimal nutritional status for a well-functioning immune system is an important factor to protect against viral infections. Nutrients 12(4).
91. Berry DJ, Hesketh K, Power C & Hyppönen E (2011) Vitamin D status has a linear association with seasonal infections and lung function in British adults. Br J Nutr 106(9): 1433-40.
92. Zisi D, Challa A & Makis A (2019) The association between vitamin D status and infectious diseases of the respiratory system in infancy and childhood. Hormones (Athens) 18(4): 353-363.
93. Laird E, Rhodes J & Kenny R (2020) Vitamin D and inflammation: potential implications for severity of Covid-19. Irish Med J May 7 113(5): 81. PMID: 32603576.
94. Ilie PC, Stefanescu S & Smith L (2020) The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. Aging Clin Exp Res 32(7): 1195-1198.
95. D'Avolio A, Avataneo V, Manca A, Cusato J, De Nicolò A, Lucchini R, et al (2020) 25-Hydroxyvitamin D concentrations are lower in patients with positive PCR for SARS-CoV-2. Nutrients 12(5).
96. Panagiotou G, Tee SA, Ihsan Y, Athar W, Marchitelli G, Kelly D, et al (2020) Low serum 25-hydroxyvitamin D (25[OH]D) levels in patients hospitalized with COVID-19 are associated with greater disease severity. Clin Endocrinol (Oxf) 93(4): 508-511.
97. Merzon E, Tworowski D, Gorohovski A, Vinker S, Golan Cohen A, Green I, et al (2020) Low plasma 25(OH) vitamin D level is associated with increased risk of COVID-19 infection: an Israeli population-based study. FEBS Journal 287(17): 3693-3702.
98. Hastie CE, Pell JP & Sattar N (2021) Vitamin D and COVID-19 infection and mortality in UK Biobank. Eur J Nutr 60(1: 545-548.
99. Faul JL, Kerley CP, Love B, O'Neill E, Cody C, Tormey W, et al (2020) Vitamin D deficiency and ARDS after SARS-CoV-2 infection. Irish Med J, 113(5):84.
100. Hernández JL, Nan D, Fernandez-Ayala M, García-Unzueta M, Hernández-Hernández MA, López-Hoyos M, et al (2021) Vitamin D status in hospitalized patients with SARS-CoV-2 infection. J Clin Endocrinol Metab 106(3): e1343-e53.
101. Darling AL (2020) Vitamin D deficiency in western dwelling South Asian populations: an unrecognised epidemic. Proc Nutr Soc 79(3): 259-271.

hsis.org | **@HealthSuppsInfo**

Published Winter ©2021

The Health and Food Supplements Information Service is funded by PAGB, the consumer healthcare association, which represents manufacturers of branded OTC medicines, self care medical devices and food supplements in the UK.

HSIS
THE HEALTH AND FOOD SUPPLEMENTS INFORMATION SERVICE