UC Leuven Limburg
MOVING MINDS

IARC Monograph on red meat & processed meat – Materials and methods assessment

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List of abbreviations

AA	Arachidonic Acid
AI	Adequate Intake
ALA	Alpha Linolenic Acid
BMI	Body Mass Index
CLA	Conjugated Linoleic Acid
CVD	Cardiovascular disease
DHA	Docosahexaenoic Acid
DIAAS	Digestible Indispensable Amino Acid Score
DPA	Docosapentaenoic Acid
DRI	Dietary Reference Intake
EAA	Essential Amino Acid
EAR	Estimated Average Requirement
EFA	Essential Fatty Acid
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic Acid
EPIC	European Prospective Investigation into Cancer and Nutrition
EU	European Union
FAO	Food and Agriculture Organization
FAOSTAT	Food and Agriculture Organization of the United Nations Statistical Databases
HCA	Heterocyclic Amine
IARC	International Agency for Research on Cancer
LA	Linoleic Acid
MUFA	Monounsaturated Fatty Acid
NEAA	Non-Essential Amino Acid
NOC	N-Nitroso-Compounds
OECD	Organisation for Economic Co-operation and Development
PAH	Polycyclic Aromatic Hydrocarbon
PDCAAS	Protein Digestibility Corrected Amino Acid Score
PUFA	Polyunsaturated Fatty Acid
RDA	Recommended Dietary Allowances
RDI	Recommended Dietary Intake
SFA	Saturated Fatty Acid
WCRF	World Cancer Research Fund International
WHO	World Health Organization

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1. Introduction and objective

Meat provides an important source of energy, macro and micronutrients, all of which are essential for a good health.(1,2) The consumption of meat is highly variable depending on several factors, hence the impact on human health is also variable.(1)

The difference between red and white meat is that red meat has a higher content of myoglobin and haem iron, but the definition is not always clear.(1) It is usually considered that red and processed meats are derived from mammals, while white meat derives from poultry.(1)

Meat products are defined in Annex I of Regulation (EC) No 853/2004 as "processed products resulting from the processing of meat or from the further processing of such processed products, so that the cut surface shows that the product no longer has the characteristics of fresh meat".(3) Processed meat suffers one or more methods of preservation and it is made from red meats (mainly pork and beef), but can also include poultry, offal or meats by-products.(4–6) The processes of preservation enhance flavour and improve preservation, and can include salting, curing, fermentation and smoking.(6)

Currently many concerns have emerged related to the consumption of meat, particularly red and processed meat due to an increasing trend in associating its consumption with chronic diseases, including colorectal cancer, coronary heart disease and type 2 diabetes.(1) In parallel, growing environmental claims have been contributing in stigmatizing animal proteins.(1) In Western countries, red meat intake has been changing and its role in society is being influenced by several factors, such as economic, environmental, ethical and health issues.(1)

In 2015, the International Agency for Research on Cancer (IARC), a specialized cancer research agency of World Health Organization (WHO), spread a press release concerning the carcinogenicity of red and processed meat, classifying processed meat as "carcinogenic to humans" and red meat as "probably carcinogenic to humans" for colorectal cancer.(1, 8) On March of this year, the working group released the full monograph on the same subject, although no press released accompanied the Monograph publication this time.(7)

In result, the benefits and adverse health effects associated with the consumption of red and processed meat had been a controversial issue, many times with conflicting messages that contribute to the public's confusion.(2) However these meats, particularly red meat can be part of a balanced healthy diet.(1) It is worthy to note distinctions in health outcomes, dietary quality and recommended intakes between red meat and processed meat.(2)

Consequently, the aim of this paper is to report the actual knowledge on the relationship between red and processed meat consumption and health. The roles of red and processed meat will be discussed, although this paper will focus particularly on red meat.

Therefore, it was proposed to assess "Does the consumption of red meat and processed meat among population have beneficial health effects considering the IARC Monograph?"

2. Methodology and materials

This thesis had been realized with document analysis method. Scientific publications about the subject to investigate were analysed. To the research of publications related to the subject, scientific databases namely ScienceDirect®, PubMed®, MedlinePlus® and SciELO® were accessed. For more control of the scientific research, Boolean operators, including "and", "or" and "not", were used with the keywords. According to the topic in question, different keywords were employed. The table 1 shows the words used in each topic.

Table 1: Keywords used to search for publications

Topics	Keywords
Nutritional value of red meat	"red meat"; "processed meat"; "meat"; "nutritional composition"; "energy; "protein"; "nutrients"; "minerals"; "vitamins"; fatty acids"; "essential amino acids"; "omega-3"; "omega-6"; "iron"; "haem iron"; "iron deficiency"; "anaemia"; "vitamin D"; "B complex vitamins"
Disease prevention	"red meat"; "processed meat"; "meat"; "nutritional composition"; "anaemia"; "elderly"; "children"; "adolescents"; "pregnancy"; "sarcopenia"
IARC Monograph	"red meat"; "processed meat"; "meat"; "nutritional composition"; "IARC"; "cancer"; "colorectal cancer"; "carcinogenicity"

The organizations WHO and Food and Agriculture Organization (FAO) were accessed to supplement the research paper. The documents of IARC, particularly the press release, the Monograph and other relevant documents were reviewed, and they represent the scope of this paper.

For the analysis of meat consumption in several countries the databases European Food Safety Authority (EFSA), Food and Agriculture Organization of the United Nations Statistical

Databases (FAOSTAT) and Organisation for Economic Co-operation and Development (OECD), and the European Prospective Investigation into Cancer and Nutrition (EPIC) study were consulted. For the recommended meat intakes, several dietary guidelines organizations were accessed.

3. Nutritional value of red meat

Meat can contain a valuable source of high biological protein and several nutrients, including long chain n-3 fatty acids, iron, copper, zinc, potassium, selenium, phosphorus, iodine, manganese and vitamins, particularly B complex vitamins, such as niacin, vitamin B6 and B12(1, 4, 7), that are essential for optimal health in humans.(9) Meat provides these nutrients mostly in a better organic well-absorbable form, than in alternative plant sources.(1, 7) The table 6 reports the nutritional composition of different lean red meats (beef, veal, lamb and mutton).

3.1. Energy

Significant differences in nutritional content can be found in groups of the same food (cheese, beef, eggs and butter) raised differently, including levels of: conjugated linoleic acid (CLA), omega-3 fatty acids (Alpha Linolenic Acid (ALA), Docosahexaenoic Acid (DHA) and Eicosapentaenoic Acid (EPA)).(10)

Therefore, as the energetic profile is affected by several chemical compounds and it does not represent the main scope of this work, this paper will not give much relevance to this kind of investigation.(10)

3.2. Protein content

Proteins are vital to the organism.(11) Every cell in the body contains proteins.(11) They are essential for cell structure and function, and for several components of skin, tissues, muscles and organs.(11) Proteins can act as enzymes, hormones and antibodies in cellular functions of the organism.(11) They are required to build, maintain and repair body tissues, primarily lean mass, provide mechanical support and immune protection, generate movement, transmit nerve impulses and control growth and differentiation of cells.(11)

Consumption of an adequate amount of protein to meet the individual requirements is essential to achieve the goals of a balanced diet.(12) Infants, children, adolescents, pregnant women, elderly and athletes benefit from an optimal protein intake:(13,14)

- Due to periods of accelerated growth, proteins are essential to the tissue building of infants, children and adolescents.(13)
- Adequate protein intake during pregnancy is of great importance to ensure healthy fetal growth and development, and also fetal-support tissues such as, the placenta, amniotic fluid, uterus, breast and total blood volume.(15) Insufficient protein intake is associated with low birth weight infants.(15)
- Aging is accompanied by a progressive decline of lean mass and muscular strength.(16) Elderly should have an adequate protein intake to attenuate or reverse lean mass wasting, and also cognitive dysfunction.(17)
- Athletes benefit from an optimal protein intake, because it enhances the skeletal muscle adaptive response to training, improve lean mass recovery, increase training efficiency and maximize performance capacity.(14)

To synthesize proteins are necessary twenty different amino acids, the "building blocks" of proteins.(18) Amino acids can be classified as Essential Amino Acids (EAAs) or Non-Essential Amino Acids (NEAAs).(12) NEAAs can be synthetized by the human body, while EAAs cannot or aren't produced at a rate sufficient to meet nutritional requirements, and thus, they must be provided through diet.(12,19) Dietary proteins can be complete or incomplete based on their amino acid content.(11) Complete proteins have all the EAAs, that are lysine, threonine, methionine, phenylalanine, tryptophan, leucine, isoleucine and valine.(5,6,18) Incomplete proteins have low amounts, or one or more EAA is missing.(5,11,19) The EAAs lacking in certain foods are called limiting amino acids.(19) For instance, rice and wheat have lysine, and legumes have methionine, as limiting amino acids.(19) Only animal sources, such as meat, fish, poultry, eggs and cheese have complete proteins.(11)

The nutritional value of a protein can be determined by the quantity and quality of the amino acids content.(19) When choosing a dietary protein, the quality, density of the protein and the non-protein components present in the protein food source should be taken into account.(12) The quality of a protein is given by the content and profile of EAAs, by their true digestibility in the ileum and extent of bioavailability.(12) The density is determined by the total of calories ingested to achieve the intake of the daily requirements of EAAs.(12) Lastly, the non-protein components of protein food sources are considered the amount and nature of fat, carbohydrate, fiber and micronutrients present in the protein food source.(12)

Specific individual dietary amino acids have different metabolic effects in the organism and so, it is recommended that dietary amino acids should be treated as individual nutrients.(20)

Although the NEAAs can be produced by the body, studies suggest that the intake of NEAAs is necessary to ensure the adequate bioavailability of all the NEAAs.(12) Thus, the designation of NEAA is in a way a misnomer, as they are important for optimal protein nutrition.(12) High quality proteins have at least 50% of NEAAs.(12)

These factors take into account in the calculation of the Digestible Indispensable Amino Acid Score (DIAAS).(12,20) The DIAAS is a scoring system to quantify dietary protein quality, recommended by FAO, which replaces the Protein Digestibility Corrected Amino Acid Score (PDCAAS), the then recommended method by FAO/WHO since 1989.(20) The DIAAS is based on the content and profile of the EAAs in the test protein, in terms of their ability to supply the dietary requirements for EAAs, and the extent of their digestion in the terminal ileum.(12,20) DIAAS determines the percentage of the daily requirement of the most limiting EAA that would be provided if 0,66 g/kg/day (Estimated Average Requirement (EAR) for protein (21)) of the test protein was consumed.(12) The most limiting EAA is determined by the amount of each EAA in one gram of test protein, considering their respective daily requirement.(12) The EAR is one of the values that make up the Dietary Reference Intakes (DRIs).(22) The DRIs were developed in order to help individuals plan a healthy and nutritious diet.(22) The EAR is the average daily intake level of a specific nutrient estimated to meet the requirements of half of the healthy individuals in a group by age and gender.(22)

Thus, if a test protein has a DIAAS of 100%, it denotes that the ingestion of 0,66 g/kg/day of that protein would supply 100% of the daily requirement of the most limiting amino acid in that protein and 100% or more of the daily requirements of the other EAA.(12)

The equation to calculate DIAAS is defined as:

- DIAAS (%) = 100 x [(mg of digestible dietary EAA in 1 g of the dietary test protein) / (mg of the same dietary EAA in 1 g of the reference protein)].(12,20)

DIAAS values lower than 100% mean that to supply the daily requirements for EAAs, only by the consumption of that specific protein, more protein is needed, than supplied by the protein source as indicated by the EAR for protein of 0,66 g/kg/day.(12) The DRIs state that the value of EAR is based on the consumption of high quality proteins, knowing that high quality proteins are defined as having a DIAAS greater than 100%.(12) High quality proteins are readily digestible and contain the dietary EAAs in sufficient amounts to supply daily requirements.(20)

It is worthy to note that the protein of a diet is not entirely ingested by the same source and different sources have different DIAAS, and it is possible to supply the requirements of all EAAs with the combination of foods of different groups.(12) However, animal foods have a higher protein quality than plant-based foods.(12) As demonstrated in figure 1 and table 2, with the exception of soy protein, only animal protein sources have DIAAS greater than 100%.(12) DIAAS values for plant-based proteins range from 50 to 70%, and for a plant-based diet is about 65%.(12) On average the plant sources have a DIAAS of 61,1% while the animal sources have 113,7%.(23) Beef, pork and lamb are the meats with the highest DIAAS, with values of 111,6%, 113,9% and 116,8%, respectively.(23)

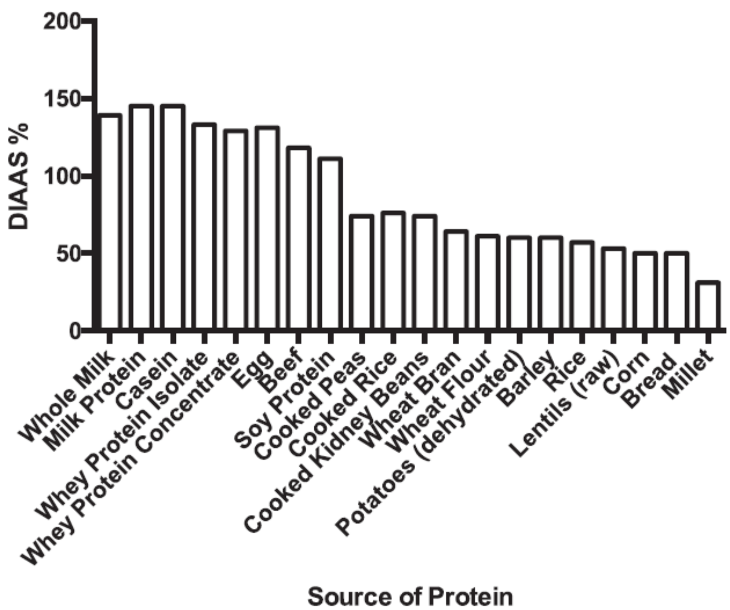

Figure 1: DIAAS (%) of several protein sources

Adapted from Wolfe R, 2018 (12)

Table 2: DIAAS (%) for several animal and plant sources

Protein Source	DIAAS (%)
Wheat	40,2
Corn grain	42,4
Average plant source	61,1
Peas	64,7
Soybeans	99,6
Chicken	108,2
Beef	111,6
Average animal source	113,7
Pork	113,9
Milk	115,9
Eggs	116,4
Lamb	116,8

Adapted from Ertl, 2016 (23)

Meat supplies high biological value proteins,(1) which are highly digestible.(19) About 94% of their protein is readily digested, while only 78% and 86% are digested in beans and whole wheat, respectively.(5) The table 3 shows the EAAs profile of different foods. The results are represented by mg of EAA per g of Nitrogen (N). Proteins are nitrogen-containing substances, and 1 g of Nitrogen is provided by 6,25 g of protein.(24) To correctly analyze the table is crucial to notice that the values of EAAs are reported by quantity of nitrogen and not protein. What this means is if the table was analyzed by grams of protein instead of nitrogen, the difference of EAAs between foods, would be even greater because animal foods, mainly red meat are the major protein sources.

Meat protein can vary significantly.(19) Their average content is 22%, but it can range from 12,3% (duck meat) to 34,5% (chicken breast).(19) The amino acid profile of muscle tissue of animals is relatively conserved in farm animals.(1) Raw red meat contains about 20-25 g of protein per 100 g of meat, while cooked meat contains about 28-36 g of protein.(5) During cooking the water content decreases and nutrients become more concentrated, which explains why cooked meat has a higher content of protein than raw meat.(5)

Table 3: EAA profile of different foods (mg/g N)

	Lysine	Threonine	Methionine	Phenylalanine	Tryptophan	Leucine	Isoleucine	Valine
Rice (mean) raw	227	219	129	301	82	487	246	374
Cheddar cheese	532	286	204	368	88	562	361	466
Butter bean (raw)	311	284	83	179	64	320	203	296
Beef (raw)	572	304	156	253	76	524	305	336
Lamb (raw)	577	294	147	249	84	499	286	319
Pork (raw)	573	304	156	248	73	506	306	336
Chicken (raw)	605	306	154	261	85	526	334	351
Turkey (raw)	505	324	179	284	79	493	340	318
Duck (raw)	514	341	174	275	79	518	348	339
Rabbit (raw)	491	332	175	288	76	474	335	329
Salmon (canned)	513	343	201	295	84	448	311	364
Spinach	334	281	93	285	90	465	248	330

Adapted from NUTTAB, 2010(25)

Inadequate intake of protein can lead to protein deficiency.(19) Although it is severe, is relatively rare in developed countries,(11) but, in many developing countries, in areas of famine, limited food supply and low levels of education, it occurs commonly.(26) This nutrient deficiency causes the Kwashiorkor disease, with symptoms like, large belly, edema, fatigue, irritability, lethargy, poor growth, apathy, decreased muscle mass, diarrhea, dermatitis, loss of skin pigmentation, changes in colour and texture of hair, infections, shock, coma and death.(26)

3.3. Essential fatty acid content

Dietary fats have several roles in the body.(27) They are necessary for the absorption, transport and function of the fat-soluble vitamins – ADEK.(27) Also, they are needed to produce cellular components, hormones and other essential compounds to the organism.(27)

The dietary fats divide in: Saturated (SFAs), Monounsaturated (MUFAs) and Polyunsaturated Fatty Acids (PUFAs).(28) The main classes of PUFAs divide in omega-3 fatty acids (also called ω-3 fatty acids or n-3 fatty acids) and omega-6 fatty acids (or ω-6 fatty acids or n-6 fatty acids).(28) Omega-3 fatty acids include EPA, DHA and ALA, while omega-6 fatty acids enclose Linoleic Acid (LA) and Arachidonic Acid (AA).(27)

The human body can synthetize in the liver almost all the fats, except the Essential Fatty Acids (EFAs), which are LA, from omega-6 group, and ALA, from omega-3 group.(27) ALA and LA are not produced by the organism and must be assured through dietary sources.(27,29) ALA can be utilized as a precursor to create EPA and DHA, and in the same way, LA can be used to be converted to AA.(27,29) The amount of conversion is determined by the quantity of their precursors on the human body.(29)

SFAs are negatively associated with cardiovascular and metabolic health.(19) Omega-6 is also associated with negative outcomes for humans, such as pro-inflammatory, pro-thrombotic and pro-arrhythmogenic effects.(30) Its overconsumption and an increased n-6:n-3 PUFAs ratio may increase the risk of health conditions such as cardiovascular diseases, metabolic or immune pathologies, rheumatoid arthritis, cancer and dementia.(27,28,30,31) On the other hand, omega-3 has a protective role in cardiovascular diseases and health in general.(19) This group of PUFAs stabilizes the development of atherosclerosis or arterial plaques, reduces the synthesis of triglycerides, reduces oxidative stress and increases the size of low-density lipoproteins reducing the likelihood of cardiovascular diseases.(27,29–32)

Over the years, the balance of fatty acids in the diet has been changing from n-3 fatty acids towards n-6 fatty acids.(27) This can be explained by the changing farming practices that have resulted in domesticated animal tissues with less n-3 fatty acids, the rising cost of oil-rich fish, developments in food technology, namely n-6 sunflower and soybean oil products and nutrition myths promoting the preference for n-6 fatty acids rather than n-3 fatty acids.(27) Apart from the negative factors associated with omega-6, this offers consequences to the organism because high levels of n-6 PUFAs result in inhibition of the elongation and desaturation of n-3 PUFAs, as they compete for the same enzymes.(28,29)

The major sources for PUFAs are found in fatty fish, however in many industrialized countries the main source of PUFAs is represented by meat and eggs.(1) In meat, the fatty acid composition of tissues vary significantly, but usually are considered high in saturated fat and low in PUFAs.(1) The table 4 reports the fatty acid profile of some lean meats, where it is observed that apart from the oily fish, the content of n-3 fatty acids, EPA and DHA are significant in lamb, beef and mutton. It is possible to enrich foods with omega-3, particularly red meat, with the inclusion of these fatty acids in the livestock’s feed.(32) Enriching foods with n-3 fatty acids may be an important alternative to naturally rich foods and supplements, to increase the dietary intake of PUFAs.(32,33) This method can be reached by adding flaxseed, fish oil, or fishmeal to livestock's feed.(32)

The dietary fatty acid content of animals' feed is the major factor determining the fatty acid composition of animals tissues.(1) Animals digestive process influences the deposit of fat in tissues.(1) Due to the intense lipolysis and biohydrogenation in the rumen, ruminant animals generally have a higher content of saturated fatty acids and lower in PUFAs compared to fats from monogastric animals.(1) In monogastric animals, fats do not suffer much transformation during digestion and absorption, therefore it is possible a reliable composition of the dietary fatty acids ingested.(1) It is worthy to note that culinary practices may influence significantly the fat content and fatty acid profile of the food, such as trimming the visible fat from meat and the use of culinary fats or oils.(1)

There is some disagreement about the optimal level of intake for n-3 fatty acids.(27) There are no Dietary Reference Intakes (DRIs) for EPA and DHA, but several sources recommend a typically range from 250 mg/d to 500 mg/d for EPA and DHA combined for general health.(34) Other recommendations range from 200 to 1000 mg/d, the most recent being 650 mg/d as an adequate intake for adults, of which at least 200 mg/d should be DHA.(32) This target is easily surpassed in countries with a high consumption of fish, however in countries where the consumption of fish is not so great, the average dietary intake of n-3 fatty acids fall of recommendations.(32)

Table 4: Fatty acid profile of raw lean meats (100 g edible portion)

	Beef	**Veal**	**Lamb**	**Mutton**	**Lean pork**	**Chicken**	**White fish**	**Oily fish**
Total Saturated (g)	1,149	0,409	1,730	1,464	0,500	0,400	0,300	3,320
Total Monounsaturated (g)	1,205	0,399	2,066	1,413	0,700	0,430	0,200	5,390
EPA (g)	0,031	0,028	0,028	0,044	0,005	0,000	0,048	0,913
DHA (g)	0,006	0,003	0,013	0,020	0,009	0,004	0,111	1,118
Total n-3 (g)	0,136	0,086	0,157	0,224	0,033	0,020	0,180	2,355
Total n-6 (g)	0,300	0,244	0,424	0,449	0,258	0,148	0,050	0,250
Total Polyunsaturated (g)	0,448	0,259	0,603	0,673	0,300	0,200	0,200	2,655
n-6:n-3 ratio (g)	2,206	2,837	2,700	2,004	7,818	7,400	0,278	0,106

Adapted from Williams P, 2007 (5)

3.4. Trace element composition

3.4.1. Iron

Iron is a trace element involved in many body functions including, respiration, oxygen transport and storage, DNA synthesis, energy production, cell proliferation(35) and normal development of the central nervous system.(36)

Iron deficiency is a global public health problem. It is the most common disorder widespread in the world, affecting developing and developed countries. Iron deficiency occurs when there is a negative balance between iron requirements, intake, absorption and losses.(37) The most significant consequence of iron deficiency is anaemia(36) and over 30% of world's population is estimated to be anaemic.(38) Anaemia will be discussed in more detail in chapter 4.1. Increase dietary iron intake is a known effective approach in both preventing and treating iron deficiency and anaemia.(39) Iron deficiency can result in symptoms such as fatigue, weakness, lethargy, breathlessness, headaches, irritability, dizziness, weight loss, deficits in learning and concentration, difficulty maintaining body temperature, reduced immunity, exercise intolerance, constipation, menstrual irregularity, muscle fasciculation, tingling and numbness in the extremities, tinnitus, heart palpitations, pallor, glossitis, growth retardation, reduced school achievement, impaired motor and cognitive development in children.(40)

Iron can be obtained in two different forms: haem iron and non-haem iron.(41) Haem iron is only found in animal sources, and is derived mainly from haemoglobin and myoglobin in animal tissues.(37,42) Non-haem iron is found in plant foods.(37) Haemoglobin is only present in the blood of living beings.(40) As haem iron bounds with the haemoglobin molecule, haem iron foods come exclusively from animal origin, including meat, poultry and fish.(40)

The major source of haem iron in the human diet is red meat.(41,43) The myoglobin content in animal tissues can be influenced by their breed, age and muscle activity.(36) Beef is the major source of myoglobin per gram of meat (15 mg) followed by mutton (10 mg), pork (5 mg), poultry and rabbit meat (≤ 5 mg).(36) The table 5 shows the content of iron and haem iron in raw and cooked meats. Cooking procedures cause an increase of non-haem iron content in meat and a decrease of haem iron.(44) In fact, the haem:non-haem iron ratio decreases after cooking.(44) However, the table 5 reports higher values for haem iron in meat after cooked. As it was said before, during processing of the meat, the water content decreases and nutrients become more concentrated(5), whence the higher values of haem-iron in cooked meat.

Non-haem iron is found in foods such as milk products, fortified cereals, bread, pasta, rice, beans, lentils, chickpeas and green leafy vegetables, particularly spinach.(12, 15, 16)

However, haem iron is more readily bioavailable than non-haem iron.(36) About 10 and 25% of non-haem and haem iron, respectively, are absorbed by the organism.(41) The presence of enhancers and inhibitors consumed during the same meal as iron sources, as well as the individual iron status, also have a significant impact on the absorption of non-haem iron.(45) The bioavailability of haem iron is much less affected by enhancers and inhibitors, which contributes significantly to the absorption of iron.(37,41–43) In fact, the form (haem or non-haem iron) has more influence to the iron status of individuals than the amount of dietary iron ingested.(42) Tannins, phytates, calcium, polyphenols, soya protein and dietary fibre (vegetable fraction of the diet) are known inhibitors of iron absorption.(43) Minerals such as, zinc, calcium, copper and manganese can also inhibit the iron absorption, because they compete for the same carrier in enterocytes.(36) On the other hand, ascorbic acid, citric acid and some amino acids enhance the absorption of iron.(19, 20) As result, meat eaters have a better iron status than vegetarians and vegans.(42) Studies have shown that eating red meat has a beneficial effect on iron status and reducing its consumption may lead to a negative impact on the iron status, which can lead to anaemia.(42) Consuming red meat is an effective approach in the prevention of iron deficiency, since is the major source of haem iron and it is easily absorbed.(36)

Table 5: Iron content in different animal sources (100g)

	Raw			**Cooked**		
	Total Fe (mg)	**Haem Fe (mg)**	**% Haem Fe**	**Total Fe (mg)**	**Haem Fe (mg)**	**% Haem Fe**
Chicken	0,59	0,22	38	1,01	0,28	28
Turkey	0,79	0,35	42	1,25	0,45	35
Beef	2,09	1,82	87	3,39	2,63	78
Veal	0,85	0,71	84	1,58	1,33	83
Lamb	2,23	1,68	75	3,20	2,25	70
Horse	2,21	1,75	79	3,03	2,16	71
Ostrich	2,43	1,76	72	3,78	2,85	75
Rabbit	0,45	0,25	56	0,60	0,31	52
Pork	0,42	0,26	62	0,64	0,39	61

Adapted from Lombardi-Boccia, 2002 (44)

3.4.2. Zinc

Zinc is an essential micronutrient of great importance considering its functional roles in enzymatic systems, cell division and growth, gene expression, immune, antioxidant and reproductive functions.(9, 19)

Zinc deficiency could lead to significant adverse health effects. Manifestations of its deficiency include increased risk and severity of infections, hypogonadism in males, skin lesions, loss of hair, impaired wound healing, impaired taste, poor appetite, oxidative stress, genetic damage, diarrhoea, growth retardation in children and adolescents and affects specific outcomes in pregnancy.(9, 20, 21) Zinc deficiency is known to be a significant malnutrition problem worldwide.(49) It is estimated that zinc deficiency affects 31% of population, ranging from 4% to 73% across subregions(49), being more prevalent in zones of high cereal and low animal food ingestion.(50) Although severe zinc deficiency is rare, mild-to-moderate zinc deficiency is quite common.(49)

Dietary sources include meat, poultry, seafood, wholegrain cereals, pulses and dairy foods, although, zinc adequacy also depends on its bioavailability.(51) As it happens with iron, zinc absorption is greater in animal sources than in plant sources, and the requirements for zinc may be 50% higher in vegetarians.(5) The bioavailability of zinc is strongly influenced by the animal-to-plant ratio of the diet.(51) Bioavailability is affected by personal factors such as age, sex, nutritional status and health status, but also by dietary factors (chemical structure of the nutrient and inhibitors and enhancers present in the diet and cooking methods.(51)

Meat is the major source of zinc and red meat contains more zinc than white meat.(2) Higher red meat consumption is associated with lower prevalence of inadequacy of zinc.(2) Around 40% of zinc intake from meat is absorbed, while the absorption part from plant sources are between 17 and 38%.(52) The absorption of water soluble zinc salt is between 50 – 60%.(52)

3.5. Vitamins composition

3.5.1. Vitamin B12 and other B Complex vitamins

Animal foods are the only source of vitamin B12, as it is entirely absent from plant foods.(1, 4) It is assumed that vitamin B12 absorption is 50%.(19) Red meat is an important source of vitamin B12 and other B complex vitamins such as vitamin B6, niacin, thiamine, pantothenic acid and riboflavin.(2, 5, 14, 32) In fact, beef, lamb, pork and veal are qualified for "high in" claim, providing at least 30% per 100g of meat, for these vitamins.(2) Older animals have higher B complex vitamins concentrations in their meat.(5)

Studies have demonstrated that medium meat consumers supply the daily requirements for vitamin B12.(19) Red meat provides more than two-thirds of the daily requirements for vitamin B12, in a 100 g portion of meat.(5) Low dietary intake of vitamin B12 is very susceptible to happen in vegetarians and particularly vegans.(19) It can also be due to absorption impairments caused by gastric atrophy and malabsorption from food, frequent in elderly.(19)

Severe B12 deficiency can result in unusual fatigue, tingling in fingers or toes, poor cognition, poor digestion and failure to thrive in young children.(53) Vitamin B12 deficiency may lead to megaloblastic anaemia, high levels of blood homocysteine, which are a cardiovascular disease risk factor, clinical depression and neurological impairment.(19) When the deficiency is long term there is higher risk for stroke, dementia and poor bone health which is associated with osteoporosis.(53)

3.5.2. Vitamin D

Vitamin D status is dependent on sunlight exposure, which is the main factor for an optimal intake of vitamin D.(8,53) The extent of its production, after exposure to the sun is highly variable and dependent on several factors such as, time of the day, season, latitude, air pollution, skin pigmentation, sunscreen use, amount of skin exposed to the sun and age.(53)

There are not many dietary sources of vitamin D, but meat is an important one.(8) Other sources include oily fish, which is the major source, although it is low consumed among population, eggs and fortified products such as margarine and some breakfast cereals.(8) Studies have reported that 100 g of cooked beef and lamb could provide more than 12 and 25%, respectively, for Adequate Intake (AI) for 51-70 years old individuals (reference values for Australia and New Zealand), making red meat an important source of this nutrient.(5) The AI is another reference value of the DRIs and is based on observed or experimentally approximations of nutrient intake by a group.(22)

Vitamin D has a role in the development and maintenance of bones,(8) cognitive functions,(54) preservation of lean mass, strength and physical function, and so it is important in the prevention and treatment of sarcopenia.(53) Investigations have also documented that vitamin D may have a protective role against colorectal cancer.(55) Studies suggest that vitamin D has an effect in reducing the risk of colorectal cancer, by inhibiting cell proliferation and angiogenesis and stimulating apoptosis.(55) Although, further revisions are needed to identify this association.(55)

There is a high prevalence of vitamin D deficiency in Europe, particularly in winter.(2) This vitamin is a nutrient of public health concern due to the high prevalence of inadequacy of intake and/or status in the population.(2) Studies have reported that vitamin D deficiency may be associated with Cardiovascular diseases (CVD), autoimmune disease and cancer.

Enhancing red meat with vitamin D is possible, using a biofortification approach, where equivalents of vitamin D are added to the livestock feeds.(2) This approach has the potential to increase the intake of vitamin D among population, and so may have a significant impact on public health nutrition.(2) Also, studies have suggested that components of meat protein may enhance the absorption of vitamin D in humans, especially where sunlight exposure is limited.(8)

Table 6: Nutritional composition of beef, veal, lamb and mutton cooked meats (100g)

	Beef	**Veal**	**Lamb**	**Mutton**
Energy (kcal)	119,0	114,0	130,5	122,8
Protein (g)	23,2	24,8	21,9	21,5
Fat (g)	2,8	1,5	4,7	4,0
Cholesterol (mg)	50	51	66	66
Thiamin (mg)	0,04	0,06	0,12	0,16
Riboflavin (mg)	0,18	0,20	0,23	0,25
Niacin (mg)	5,0	16,0	5,2	8,0
Vitamin B6 (mg)	0,52	0,8	0,10	0,8
Vitamin B12 (µg)	2,5	1,6	0,96	2,8
Pantothenic acid (mg)	0,35	1,50	0,74	1,33
Vitamin A (µg)	‹5	‹5	8,6	7,8
Beta-carotene (µg)	10	‹5	‹5	‹5
Alpha-tocopherol (mg)	0,63	0,50	0,44	0,20
Sodium (mg)	51	51	69	71
Potassium (mg)	363	362	344	365
Calcium (mg)	4,5	6,5	7,2	6,6
Iron (mg)	1,8	1,1	2,0	3,3
Zinc (mg)	4,6	4,2	4,5	3,9
Magnesium (mg)	25	26	28	28
Phosphorus (mg)	215	260	194	290
Copper (mg)	0,12	0,08	0,12	0,22
Selenium (µg)	17	‹10	14	‹10

Adapted from Williams P, 2007 (5)

4. Disease prevention

4.1. Anaemia

Anaemia is a global health problem affecting developing and developed countries.(35) It is estimated that affects more than 30% of the population worldwide.(38)

Anaemia is diagnosed when the haemoglobin (Hb) concentration in the blood is lower than the established cut-off values, leading to a compromised transport of oxygen to tissues by the blood, resulting in symptoms such as weakness, fatigue, irritability, hair loss, poor concentration and poor school/work performance.(35,38)

The intake of certain nutrients is essential in the prevention of anaemia, due to their roles in the production of haemoglobin and erythrocytes.(38) Iron deficiency is the most common cause of anaemia, although other micronutrients deficiencies, such as vitamin A, B12, B6, B2, C, D, E, folate and copper may also lead to anaemia.(35,38)

Genetic haemoglobin disorders, such as sickle cell trait or thalassaemias, are also one of the major causes of anaemia globally.(38) If left untreated, these disorders may result in death in the first years of life, thus they affect more low-income countries.(38)

The most vulnerable groups to anaemia are children under 5 years old, particularly young children under 2 years old, adolescents, women of reproductive age, pregnant women(38) and vegetarians.(45)

Infants and children under 5 years of age are a group at risk of developing anaemia due to the high requirements of iron needed for their rapid growth and development, especially in the two first years of life.(38) Furthermore, complementary foods fed to children usually are low in iron content (in quantity and quality) and have high contents of iron inhibitors.(38) Anaemia in young children is associated with poor cognitive and motor development outcomes.(38) In the same way, the period of growth and development distinct of adolescents, makes them a vulnerable group to anaemia.(38)

Women of reproductive age and pregnant women are a group at risk of developing anaemia for several reasons.(38) Regular blood losses during menstruation increases iron losses, about 1 mg of iron per day(35), and thus higher requirements of iron.(38) Increased iron requirements are needed to support the growth and development of the fetus, placenta and expanded maternal blood volume in pregnant women.(38) During childbirth, women may have significant iron losses from bleeding, and frequently women have diets with low bioavailability of iron.(38) Anaemia in pregnancy is associated with low birth weight and prematurity, and maternal and perinatal mortality.(38)

The table 7 reports the Recommended Dietary Allowances (RDA) of iron for different groups of age and stage. RDA are another reference value of the DRIs.(22) The RDA is the mean daily intake of a specific nutrient estimated to meet the requirements of nearly all healthy individuals of a group by age and gender.(22) Children, particularly in the first year of life, have high iron requirements, as well as adolescents, and pregnant and lactating women. Women of reproductive age have higher needs of iron than men.

Table 7: RDA for iron (mg/d) of groups

Group	**Iron (mg/d)**
6 – 12 months (M/F)	11
1 – 3 years (M/F)	7
4 – 8 years (M/F)	10
9 – 13 years (M/F)	8
14 – 18 years	
Males	11
Females	15
19 – 50 years	
Males	8
Females	18
≥51 years (M/F)	8
Pregnancy	27
Lactation	
14 – 18 years	10
19 – 50 years	9

Adapted from USDA, 2011 (56)

Vegetarians and vegans are also at risk of developing anaemia because of the low intake of iron and vitamin B12 frequent in non-meat diets.(57)

Elderly may be a group at risk of developing anaemia, because of the increasing size of the old population globally and increasing lifespans.(38) The major causes of anaemia in elderly are nutrition deficiencies, particularly iron, folate and vitamin B12, and chronic inflammations and diseases.(38)

4.2. Sarcopenia

Ageing is related with a progressive decline of muscle mass and physical function, however when it is in higher rates is known as sarcopenia.(58,59) Sarcopenia is associated with physical disability, poor quality of life and increased mortality in the elderly.(59) Rates of decline of muscle mass vary in the population, which means modifiable behavioral factors may influence the development of sarcopenia.(59) Inadequate protein intake and physical inactivity are the main behavioral factors influencing the development of this condition.(58)

Nutrition intervention, especially protein intake, plays a role in both prevention and treatment of sarcopenia.(58) An increased dietary protein intake enhances muscle mass, stimulates body protein synthesis and improves physical performance.(58)

4.3. Prevention of deficiency of protein and other essential nutrients

Red meat is one of the major dietary sources of high quality protein.(9) Optimal protein intake is essential for growth and development of children and to help adults age well.(9)

For those who do not consume enough oily fish, red meat intake makes an important contribution for PUFAs.(9)

Moreover, red meat is an important source of micronutrients such as iron, zinc, selenium, potassium and B complex vitamins, including niacin, riboflavin, thiamin, vitamin B6 and B12, and vitamin D.(9) Iron and zinc are more bioavailable in red meat than in other food sources, and red meat enhances their absorption.(9) Iron is particularly important in children and pregnant women, as has been said before, and its deficiency can lead to symptoms including fatigue, weakness, impaired cognitive and physical development, and impaired immune system.(9) Zinc plays an important role in the immune system, wound healing and normal growth and development of children.(9) Iron and zinc are nutrients of concern due to the prevalence of inadequate intakes, even in developed countries.(9) Children, adolescents, women of reproductive age, pregnant women, elderly, as well as vegetarians, are at risk of low iron and zinc intakes.(5,38,45,60)

Other important minerals found in significant amounts in red meat are selenium and potassium.(9) Selenium act as an antioxidant and it is essential to the immune system, and potassium has functions in blood pressure regulation.(9) The B complex vitamins have an important role in the functioning of the nervous system and in releasing energy from foods.(9)

5. IARC Monographs evaluate consumption of red meat and processed meat

5.1. Overview on the IARC and on the WHO activities

The IARC is constituted by a group of independent international experts that identify and evaluate environmental causes of cancer in humans, including chemicals, complex mixtures, occupational exposures, physical and biological agents and personal habits.(61) The working group assesses available scientific evidence of the carcinogenicity of a specific agent.(61) Scientific evidence is critically reviewed according to strict criteria, to determine the strength of evidence of the available data.(6) The working group analysis situations where people are exposed to the agent, epidemiological studies on the development of cancer in humans exposed to the agent, experimental studies on cancer in laboratory animals exposed to the agent and studies about the development of cancer in response to the agent.(61)

Each agent is classified in one of the five different categories:

- **Group 1:** *The agent is carcinogenic to humans*.
  Agents are classified in this category when there is sufficient evidence, usually based in epidemiological studies, of carcinogenicity in exposed humans. Or, also, when there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in humans.(61)

- **Group 2:**
  - **Group 2A:** *The agent is probably carcinogenic to humans*;

  When there is limited evidence of carcinogenicity in humans, which means that a positive association between exposure to the agent and cancer is present, but other explanations for the association could not be excluded; and there is sufficient evidence in experimental animals.(61)

  - **Group 2B:** *The agent is possibly carcinogenic to humans*;

  When there is limited evidence of carcinogenicity in humans and less than sufficient evidence in experimental animals; or when there is inadequate evidence of carcinogenicity in humans, which means there is not possible to reach a conclusion, but there is sufficient evidence in experimental animals.(61)

- **Group 3:** *The agent is not classifiable as to its carcinogenicity to humans*;
  When there is inadequate evidence of carcinogenicity in humans and inadequate or limited evidence in experimental animals. Limited evidence in experimental animals suggests a carcinogenic effect however not conclusive.(61)

- **Group 4:** *The agent is probably not carcinogenic to humans*.
  When the evidence suggests lack of carcinogenicity in humans and in experimental animals.(61)

It is worthy to note this classification indicates the strength of evidence that an agent is carcinogenic or not (hazard), but does not measure the risk of cancer associated with exposition to the agent.(61) The likelihood that cancer will occur associated with agents classified in the same group may vary significantly according to factors such as, strength of the effect of the agent and type and extent of exposure to the agent, thus, different agents classified in the same group should not be compared.(61) This means that "the IARC Monographs Programme evaluates cancer hazards but not the risks associated with exposure".(61) A cancer hazard is an agent capable of causing cancer under some circumstances, while the risk is the probability that cancer will occur depending on the level of exposition to the agent.(61) The IARC does not analyze the risk assessment of an agent nor it is intended to make dietary recommendations.(6)

5.2. Evaluation on the carcinogenicity of red meat and processed meat

IARC Monograph classified red meat as probably carcinogenic to humans (Group 2A), based on limited evidence.(7) This classification was based on epidemiological studies that showed a positive association between red meat consumption and development of cancer.(61) The association was observed mainly for colorectal cancer, but other associations for pancreatic and prostate cancer were also observed.(7) However, the evidence is limited which means that a positive association has been observed between exposure to red meat and cancer but other explanations for the associations (chance, bias and confounding) could not be excluded.(61) Bias is the effect of factors in a study design or execution that can lead to a stronger or weaker association between the agent and disease.(6) Confounding is a form of bias, that occurs when an association between the studying agent and another factor that is associated with it, increases or decreases the incidence of the disease.(6) Chance is the biological variability and the influence of sample size on the precision of estimation of the effect.(6)

On the other hand, processed meat was classified as carcinogenic to humans (Group 1), based on sufficient evidence of the association between consumption of processed meat and development of colorectal cancer.(7)

The Working Group evaluated the association between consumption of red meat or processed meat and the risk of cancer of several sites, including cancer of the colorectum, stomach, pancreas, prostate, breast, lung, oesophagus and other cancers: non-Hodgkin lymphoma, cancer of the liver (hepatocellular carcinoma), cancer of the gallbladder and biliary tract, cancer of the testis, kidney, bladder, ovary, endometrium, brain and leukemia.(6)

Only positive associations were observed between consumption of red meat and cancers of the colorectum, pancreas and prostate.(6) On the other hand, there is sufficient evidence between consuming processed meat and development of cancer of the colorectum.(6) Despite that, positive associations were only found between cancer of the stomach and processed meat.(6)

For the evaluation by IARC, retrospective case-control studies and prospective cohort studies were considered.(6) Retrospective studies are more cheaper and people are asked about their past diet.(62) Then the answers of cancer patients are compared with the answers of the non-cancer individuals.(62) The problem is that the estimation of food consumption years before is not accurate, which biases case-control comparisons.(62) On the other hand, prospective studies are longer and more expensive, but avoid this limitations.(62) During the study that takes about ten to twenty years, heathy people are asked about their current diet and lifestyle and the occurrence of diseases is registered.(62) Then, the association between current diseases and dietary and lifestyle habits are searched for.(62)

During the evaluation, the IARC Group gave greatest emphasis on the studies with separate data for unprocessed meat and processed meat, less weight to the studies that defined total red meat including processed meat and least weight to the ones that reported red meat, unclear if processed meat was included.(6)

It was excluded studies including poultry, fish and seafood for processed meat, studies of dietary patterns and results of reported ratios of red to white meat.(6) Studies with unspecified meat intake, studies that reported combined results for red and white meat or just for white meat were excluded for most cancers, or were given less weight.(6) Also, studies that only reported on estimated carcinogens derived from meat, but not on red meat or processed meat variables were excluded.(6) Only studies with a sample size of at least 100 cases were considered for the evaluation.(6)

5.2.1. Cancer of the colorectum

In evaluating the evidence for cancer of the colorectum and the consumption of red meat or processed meat, several cohort and case-control studies in countries from Europe, North America, South America, Asia and Australia were examined.(6) It was given more weight to the cohort studies in the general population with quantitative data of the consumption of red or processed meat, and to complete the evaluation, it was used information from some case-control studies.(6)

There was found heterogeneity in the studies designs and instruments used to assess meat intake, including different definitions of red meat and processed meat, and studies combining or not processed meat with red meat.(6)

Approximately 20 cohort studies and 150 case-control studies were reviewed.(6) In seven cohort studies, positive associations between high consumption of red meat and cancer of the colorectum were observed.(6) Only about 10% of the reviewed case-control studies were considered informative.(6) Seven of the studies, about half of those judged informative, showed positive associations between cancer of the colorectum and consumption of red meat.(6) However, in many case-control studies, no association with red meat was found, but with other factors including cooking practices and doneness of the meat.(6)

For processed meat, 18 cohort studies were reviewed, in which 12 showed positive associations for cancer of the colorectum. Six of the nine case case-control studies considered informative, also showed positive associations.(6)

The majority of the cohort and case-control studies that combined together red meat with processed meat reported positive associations for cancer of the colorectum.(6) A meta-analysis including 10 cohort studies showed a positive association for red meat and/or processed meat and cancer of the colorectum, in which the relative risk was 1,17 for an increase of 100 g/day of red meat and 1,18 for an increase of 50 g/d of processed meat.(6)

An association between consumption of red meat and processed meat and cancer of the colorectum was observed.(6) However, in several of the larger studies no association was observed for red meat, which means that chance, bias or confounding factors could not be ruled out of the studies.(6) Also, the available evidence suggested that some cooking methods used in the preparation of red meat may had contributed for the positive associations in some studies.(6)

5.2.2. Cancer of the stomach

For the evaluation of the association between cancer of the stomach and consumption of red meat, cohort studies from Europe, USA and China were reviewed, where a positive association was observed in two studies.(6) Evidence was also available in 2 population-based case-control studies from USA and Canada, but the results were inconsistent.(6)

Four of seven cohort studies demonstrated positive associations between processed meat and cancer of the stomach.(6) The other three studies did not find any associations.(6) Statistically significant associations were found in the majority of case-control studies from Canada, USA and Mexico.(6) How it was a modest number of studies and some of them did not find any association, it was suggested that chance, bias and confounding could not be ruled out.(6)

5.2.3. Cancer of the pancreas

The association between cancer of the pancreas and consumption of red meat was found in three of nine cohort studies.(6) The other six studies showed no association.(6) Two case-control studies from USA, Canada, Italy and China showed that one of the studies demonstrated a positive significant association and the other one a null result.(6) As it occurred in the studies for cancer of the stomach, the modest number of studies and the lack of positive association in some of them suggest that chance, bias and confounding could not be excluded.(6)

Concerning the association between processed meat and cancer of the pancreas, three of eight cohort studies showed a positive association, but only one of them was statistically significant.(6) The other five studies reported null results.(6)

5.2.4. Cancer of the prostate

The association of cancer of the prostate with red meat or processed meat was evaluated in more than 20 cohort studies.(6) A pooled analysis of 15 cohort studies showed positive associations between red meat intake and cancer of the prostate, with an increase of 19% in the highest category.(6) Weaker associations were found for processed meat in the same pooled analysis.(6)

A third of the cohort studies showed statistically significant associations, usually between the degree of doneness of the meat and advanced cancer of the prostate.(6) The association for red or processed meat irrespective of cooking method was null or weak.(6)

The same results happened for the case-control studies from USA and New Zealand, where the positive associations for advanced clinical stages of cancer of the prostate were almost exclusively linked to the degree of doneness of the red meat.(6)

5.2.5. Cancer of the breast

About 10 cohort studies and a consortium of eight prospective cohort studies in North America and Europe reported a positive association between cancer of the breast and red meat intake, which may or may not have included processed meat.(6) On the other hand, case-control studies from USA, South America, Europe and Asia showed inconsistent evidence.(6) The results of the studies did not permit to determine whether the association between meat and cancer of the breast is influenced by menopausal status.(6)

5.2.6. Cancer of the lung

Six cohort studies were informative for the evaluation of the association between cancer of the lung and consumption of red meat and processed meat.(6) There were found positive associations for the red meat intake, however confounding from tobacco smoking could not be ruled out, given the strong association between smoking and lung cancer.(6)

A meta-analysis showed an increased risk for cancer of the lung with red meat intakes, but not with processed meat.(6)

5.2.7. Cancer of the oesophagus

A limited number of studies investigated the association between red meat and processed meat intake and cancer of the oesophagus, in which they showed inconsistent results.(6)

5.2.8. Other cancers

The same occurred in the evaluation of other cancers, including non-Hodgkin lymphoma, leukemia, cancer of the liver, gallbladder, testis, kidney, bladder, ovary, endometrium and brain, in which resulted no conclusions.(6)

5.2.9. Studies in experimental animals

Studies in experimental animals with mice and rats reported inadequate evidence for the carcinogenicity of red meat, processed meat and haem iron.(6)

5.3. A balanced diet to minimize risks

The IARC process may be considered outmoded.(63) It assesses the carcinogenicity of agents based on hazard-identification.(63) It is based on a model developed in the 70s, that identified chemicals in carcinogens or non-carcinogens.(63) This type of categorization puts together in the same category chemicals and agents with different potencies and modes of action.(63) At the time, the intention of this method was to detect chemicals of potential concern and replace them with non-carcinogens.(63) However, the separation of agents in carcinogens and non-carcinogens is overly simplistic, since the hazard is not characterized in terms of potency, severity, dose response, mode of action and extent of human exposure.(63)

The IARC classification is about the evidence that there is some increase in risk, but not on how much the risk increases.(6) IARC evaluates cancer hazards, even when the cancer risk is very low at current exposure levels.(6) Agents classified in group 1 (Carcinogenic to humans) are capable of causing cancer, but the risk may increase a lot or a little, according to the different agents.(6) This means there is sufficient evidence to support that processed meat is carcinogenic, but does not mean, for example, that the consumption of processed meat is as bad as smoking, as the risk for cancer is much higher in tobacco than in the consumption of processed meat.(64) In the same way, processed meat and sulfur mustard gas are classified in the same category, which leads to confusion in terms of how to treat processed meat or sulfur mustard gas.(63) If both were treated in the same way, than exposure to processed meat should be reduced to zero.(63) On the contrary, if sulfur mustard gas was treated equally as processed meat, then it could be part of a healthy lifestyle if exposed to humans in moderation.(63)

The IARC classification in the groups "carcinogenic to humans", "probably carcinogenic to humans" or "possibly carcinogenic to humans" can lead to negative publicity, contradictory, confusing and unnecessary actions(63), for instance the recommendation to reduce red meat intake in developed countries, even when its consumption is within nutritional guidelines.(9) This results in an anxiety and behavior change of the population in detrimental to achieving the desirable public health goals.(63) If the potential risk is not considered, even when it is very low, that may lead to unnecessary restrictions on marketing and use or emendations in recommended exposures, even when risk-assessments show that there is reasonable certainly no harm will result.(63) Several organizations have had to explain to public how IARC works in efforts to try to alleviate unnecessary concern and anxiety.(63)

There is limited evidence that red meat causes cancer.(6) Cancer has multifactorial etiology and it is not caused by one single factor.(65) Nearly half of cancer deaths are due to preventable causes, particularly by unhealthy behaviors such as, smoking, drinking alcohol and obesity.(66) In addition, meat consumption is not the only food item or agent that contributes to the exposure to some of the carcinogenic compounds.(1) The association between red meat with cancer may be linked with the presence of different carcinogenic compounds, acting on multiple stages of cancer development, such as haem iron.(1)

High consumption of red meat and processed meat are often associated with unhealthy lifestyles, that can also be correlated with cancer incidence, such as total energy/caloric intake, high body mass index (BMI), low physical activity, alcohol drinking and tobacco smoking.(6) Studies reported that the consumption of processed meat was associated with consumption of foods such as French fries, sweets, cakes, desserts, snacks and alcoholic drinks.(4) High glycemic index diets and alcohol drinking may be correlated with cancer incidence, including colorectal cancer.(4) A significant number of studies reported no association between consumption of red meat or processed meat and cancer incidence.(6) A study found out that the link between colorectal cancer and red meat intake is very low in those who have a diet plenty of vegetable fibers.(55) The consumption of red meat was associated with increased risk of colorectum and colon cancers, although with rectal cancer the link was not significant.(6) In the same way, consumption of processed meat was related with the risk of colorectum and colon cancers, but not with rectal cancer.(67) However, some studies have reported no associations between the consumption of red meat and the incidence of colon cancer.(68)

In several studies the increased risk of cancer is related to high consumption of red meat and processed meat.(6) In most countries, the consumption of red meat or processed meat is around 50-100g/day, and high consumption is more than 200g/day.(6) The World Cancer Research Fund International (WCRF) recommends limiting the consumption of red meat to 71 g/day (cooked weight) and avoiding the consumption of processed meat.(69) "The risk increase of colon cancer was 37% for every 100 g/day increase in red and processed meats, and the risk increase of colorectal cancer was 29% for every 100 g/day increase in red meat, and 21% for every 50 g/day increase in processed meat."(67) It is expected that about 4 or 5% of people will develop cancer of the colorectum in their lifetime.(70) If people increased consumption of processed meat by 50 g per day, it would be expected for further 18% people to develop cancer of the colorectum(6), which means that would be a rise from 4 or 5 people in 100 to 5 or 6 people in 100. Average intakes of red and processed meat across Europe are below the excessive levels highlighted by IARC.(9)

Red meat offers high biological proteins and essential micronutrients, including vitamins and minerals.(1) Red meat provides all the essential amino acids, being a complete protein.(1) It contains about 30 g of protein per 100 g of meat.(5) Red meat is rich in B complex vitamins, such as B12 that is only found in food derived from animal products.(5) 100g of lean beef meat provides about 2,5g of vitamin B12 corresponding to 79% of its RDAs.(6) Red meat is an important source of iron, zinc, potassium, phosphorus and selenium, and has a higher nutrient bioavailability than plant foods.(6) Many international dietary guidelines recognise the role of red and processed meat in a balanced diet; nevertheless, there are no consensus over the optimal quantity of meat intake, although all agree that lean meat should be the preferred choice when including red meat in the diet.(2) The table 8 provides examples of dietary recommendations on red meat from International guidelines.

Table 8: International dietary recommendations for optimal intake of red meat

Dietary guideline	**Year published**	**Number of protein servings**	**Meat serving size**
Canada (Eating well with Canada's food guide)(71)	2011	Females: 2 servings/day; Males: 3 servings/day	75 g of cooked meat
Ireland (Healthy food for life – healthy eating guidelines and food pyramid)(72)	2016	2 servings/day	50 – 75g of cooked lean beef, lamb, pork, mince or poultry
UK (Eatwell guide)(73)	2016	No protein food group serving recommendation	70 g/day of red meat or processed meat
Australia (Australian dietary guidelines)(74)	2013	Females: 2 – 2,5 servings/day; Males: 2,5 – 3 servings/day	65g of cooked lean red meats (beef, lamb, pork, venison or kangaroo) **or** 130g of cooked red meat on every second day
WCRF(69)	2018	3 portions per week of red meat	500 g of lean red meat per week **or** 71 g per day
USA (Dietary guidelines for Americans 2015-2020, 8th edition)(75)	2015	≈155 g/day from protein foods	No specific reference to meat serving size

Adapted from Cashman and Hayes, 2017 (2)

It is possible to improve the content of nutrients in meat.(1) Meat contains in its composition SFAs, MUFAs and PUFAs.(5) However, generally red meat and processed meat are high in saturated fatty acids and low in polyunsaturated fatty acids.(66) The fatty acids composition of meat is susceptible to manipulation.(1) The animal's feed influences PUFAs levels in meat, therefore it is possible to enrich meat with fatty acids.(66) Studies have shown that this increase can reduce the total cholesterol of meat.(68)

Meat can be part of a healthy diet and its intake has several health benefits(9), due to its nutritional composition, such as:

- Helps muscle growth and maintenance;(13,14)
- Helps the maintenance of normal bones and prevents hair loss;(48)
- Children's normal growth and development;(13)
- Can prevent the development of anaemia and supports the formation of red blood cells and contributes to oxygen transport.(39)

5.4. Cooking methods recommendations

Cooking methods may include braising, stewing, broiling/frying, grilling/barbecuing and roasting/baking.(76) Cooking meat has the benefits of changing flavour, taste, colour and texture, and can inactivate pathogens present in the food.(76) However, cooking at high temperatures may cause the formation of carcinogenic compounds.(76) When meat is exposed at high temperatures during cooking, hazardous compounds such as heterocyclic amines (HCAs), polycyclic aromatic hydrocarbons (PAHs)(76), and N-nitroso compounds (NOC) may be originated.(1,4) The cooking methods that promote the most carcinogenic compounds formation are barbecuing, grilling and pan-frying(76), where the meat is exposed directly to a hot surface or flame.(66) Baking and roasting expose meat to high temperatures (up to 200°C), but the contact with a direct hot surface is limited and so the formation of carcinogenic compounds is low.(66) Steaming, boiling, or stewing are much safer cooking methods, because it is used a lower temperature, around 100°C, thus the carcinogenic compound formation is also much lower.(66) The choice of cooking method has an impact in health outcomes(76), as the formation of HAAs, PAHs and NOC can be prevented according to the chosen method.(1) Studies suggest that haem iron, present in red meat, is carcinogenic because is cytotoxic in the gut, mediates the formation of NOC in the colon, and stimulates the formation of lipid oxidation products.(1,4)

6. Discussion

Since the publication of the IARC evaluation on the carcinogenicity of red meat and processed meat, the role of meat in human health has been controversial.(2) Conflicting messages have leaded to the confusion of the public, whether red meat consumption plays a role in a healthy diet.(2)

In the first place, it is important to distinguish between unprocessed red meats, such as beef, veal, pork and lamb, and processed meats such as bacon, sausages, ham and salami,(9) in associations with health outcomes.(2) Processed meat have normally higher contents of sodium and saturated fat than red meat(19), furthermore several non-meat substances and compounds, that may be carcinogenic, are added to processed meat to reduce the microbial contamination, to create attractive products and to reduce waste and reconstitute the muscle meat scraps or offal.(6) These substances include salt, for the taste, impact on meat protein and shelf-life; nitrates and nitrites for curing, color, flavor and shelf-life; ascorbic acid, phosphates and chemical preservatives.(6) Additionally, processed meat suffers cooking methods for preservation.(6) Several studies did not distinguish between red meat and processed meat or were unclear whether processed meat was included with red meat, thus their results are limited.(9) Challenges need to be faced for improvement of the flavor perception and safety of sodium-reduced processed meat products.(77) New technological treatments, such as hydrostatic pressure and ultrasound technology, seem to be promising to ensure microbiological safety in low-sodium meat products.(77)

Recommendations have been made to limit the consumption of red meat and avoid processed meat in many developed countries(62), although red meat intakes appear to be within current guidelines.(9) For Europe, the EFSA collected data from national food consumption surveys of member states of the European Union (EU).(6) The mean meat consumption for adults was about 35 g/d, ranging from 10 g/day in Sweden to 110 g/day in Austria.(6) In the 95th percentile, meat consumption ranged from 20 g/d in 21% of the Swedish consumers to 237 g/day in 88% of the Austrian consumers.(6) In the EPIC study, a computerized 24-hour dietary recall method was used to calibrate dietary measurements across countries.(6) It was noted that the red meat consumption ranged from 24 to 57 g/day in women and from 40 to 121 g/day in men.(6) The table 9 and table 10 report the mean meat consumption per capita for some regions in EU countries, for women and men respectively.

In the USA, the mean consumption of red meat was 86 g/day, and at the 95th percentile, the red meat intake was 242 g/day (72% of consumers).(6) The mean consumption per capita of beef, mutton, goat and pig meat was 30, 60, 130, 140 and 200 g/day, respectively for Africa, Asia, America, Europe and Oceania, according to FAOSTAT in 2011.(6)

The annex I, II and III show the intake of beef and veal, pork and sheep, respectively, starting 1990 to 2026, according to OECD. In the 3 charts is notable a relatively decrease over the years.(78) The latest data is from 2013, which means that starting that year the values are a trend.(78) The values of meat consumption are expressed in tones of carcass weight(78), which means, that the results may be overestimated, because this includes the weight of bones, visible fat and also because raw meat is heavier than cooked meat. The annex IV compares the consumption of beef and veal, pork, poultry and sheep. For beef, the mean consumption per capita in the World is very low, followed by the European Union, while the United States have the highest intake of beef.(78) On the other hand, the European Union has the highest intake of pork.(78)

Table 9: Mean daily intake (g/day) of total meat, red meat and total processed meat in women from European countries participating in the EPIC study

Country		Total meat [a]	Red meat	Total processed meat
Greece		47,1	25,1	5,8
Spain				
	Granada	72,1	24,2	26,5
	Murcia	82,6	25,8	24,7
	Navarra	107,5	36,5	35,7
	San Sebastian	123,7	56,5	30,6
	Asturias	110,1	46,0	30,4
Italy				
	Ragusa	90,3	32,5	17,2
	Naples	68,0	36,2	15,2
	Florence	92,4	40,7	18,9
	Turin	90,5	39,8	19,6
	Varese	89,5	34,7	27,0
France				
	South Coast	104,2	39,8	28,7
	South	103,4	46,2	28,5
	North-west	108,4	43,2	33,3
	North-east	107,9	48,4	29,7

Table 9 (continued): Mean daily intake (g/day) of total meat, red meat and total processed meat in women from European countries participating in the EPIC study

Country	Total meat [a] (g/day)	Red meat (g/day)	Total processed meat (g/day)
Germany			
Heidelberg	85,7	28,3	41,0
Potsdam	82,9	28,8	40,7
The Netherlands			
Bilthoven	92,3	40,8	38,5
Utrecht	93,0	41,2	37,2
United Kingdom			
General population	72,3	24,6	22,3
'Health-conscious'	15,1	2,4	4,9
Denmark			
Copenhagen	88,4	44,7	25,6
Aarhus	88,1	43,5	25,0
Sweden			
Malmö	94,7	39,5	42,9
Umea	89,0	31,0	43,6
Norway			
South & East	89,8	27,3	44,4
North & East	87,3	29,6	48,4

Adapted from EPIC, 2002 (79)

(a) Total meat – red meat + offal + horse + goat + game + rabbit + poultry + processed meat

Table 10: Mean daily intake (g/day) of total meat, red meat and total processed meat in men from European countries participating in the EPIC study

Country	Total meat [a] (g/day)	Red meat (g/day)	Total processed meat (g/day)
Greece	78,8	45,3	10,0
Spain			
Granada	131,4	44,4	50,8
Murcia	131,1	44,7	45,8
Navarra	173,9	78,0	55,3
San Sebastian	233,7	120,7	52,1
Asturias	182,0	82,1	60,1

Table 10 (continued): Mean daily intake (g/day) of total meat, red meat and total processed meat in men from European countries participating in the EPIC study

Country	Total meat [a] (g/day)	Red meat (g/day)	Total processed meat (g/day)
Italy			
Ragusa	138,9	62,6	23,9
Florence	132,1	56,8	28,7
Turin	125,7	48,0	32,1
Varese	163,5	63,9	49,2
Germany			
Heidelberg	156,2	56,6	79,1
Potsdam	153,0	47,7	87,3
The Netherlands			
Bilthoven	155,6	63,8	72,4
United Kingdom			
General population	108,1	40	38,4
'Health-conscious'	20,6	7,9	6,8
Denmark			
Copenhagen	145,6	72,1	52,5
Aarhus	136,5	67,1	51,3
Sweden			
Malmö	142,6	64,5	63,5
Umea	135,0	49,0	68,1

Adapted from EPIC, 2002 (79)

(a) Total meat – red meat + offal + horse + goat + game + rabbit + poultry + processed meat

Many organizations recommend replacing animal foods with plant foods, such as the substitution for plant proteins.(12) The problem that comes with that is that recommendations do not take into account the quality and sources of protein and what is considered animal protein alternatives, many times have different amounts of proteins, EAAs and energy.(12) Usually these guidelines focus on the caloric value of different food groups rather than the nutritional composition.(12) The figure 2 shows the association between energy and EAAs intake.(12) To supply 100% of the most limiting EAA of some protein sources represented, a much higher intake of calories is consumed in plant sources rather than animal proteins.(12)

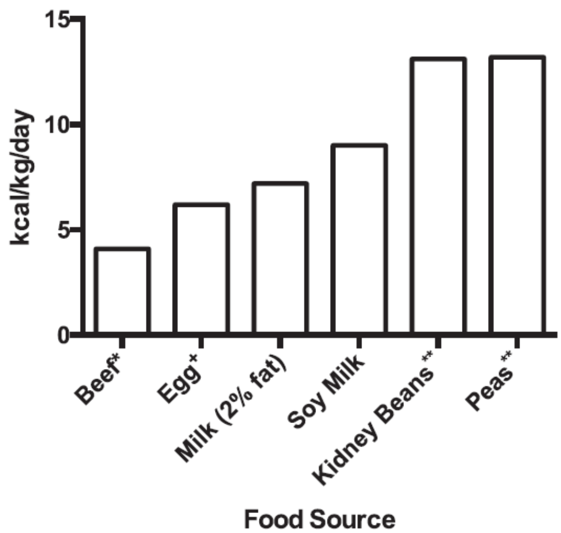

Figure 2: Energy intake to meet the most limiting EAA requirements of different foods
Adapted from Wolfe R, 2018 (12)
(+ hard boiled; ** cooked)

A small amount of non-protein calories is consumed in animal proteins to meet the daily requirements of EAAs.(12) If compared to plant sources, a much greater proportion of non-protein calories is consumed to supply the same requirements for EAAs, because the major non-protein nutrient in plant foods is carbohydrates.(12)

The limited evidence that red meat is carcinogenic is based on the statistical relationship between the quantity of red meat consumed and the cancer incidence.(12) However, confounding factors are difficult to eliminate, and usually a variety of unhealthy behaviors are linked to individuals that ignore warnings about health risks on certain behaviors.(12) These include smoking, drinking alcohol, physical inactivity and obesity.(12) It is impossible to adequately control all of these confounding during an assessment of studies.(12)

Besides, the evidence of some association between two variables does not imply a cause-effect relationship.(12) In other words, some studies had reported a link between red meat intake and some cancers, while others had showed no association at all.(12) A recent systematic quantitative assessment of the epidemiologic literature concluded that the link between red meat intake and colon cancer is weak, heterogenic, is not possible to distinguish effects from confounding, such as smoking or obesity, and has a lack of clear dose-response effect.(12)

7. Conclusions

Red meat offers high biological nutrients in a well-absorbable form, such as protein, iron, zinc, n-3 fatty acids, B complex vitamins, vitamin D and antioxidants(1,3,7), essential for a healthy life.(9) Due to its nutritional composition, red meat provides several health benefits in lifecycles.(2) Red meat helps the normal growth and development of children and adolescents(9), supports the fetal growth and development during pregnancy(15), and helps the maintenance of healthy bones and muscles in the elderly.(16) It is also essential for the immune and nervous systems, and for blood pressure regulation.(9)

Red meat consumption is effective in preventing and treating a burden of diseases, such as anaemia, sarcopenia and micronutrients deficiencies.(9,39) In fact, reducing the consumption of red and processed meat may have a potential negative impact on iron intake and status.(42)

The IARC, a specialized cancer research agency of WHO, recently classified red meat as probably carcinogenic to humans (Group 2A) and processed meat as carcinogenic to humans (Group 1).(6) It is worthy to note the IARC identifies the causes 'hazards' of human cancer, but does not do risk assessments nor dietary recommendations.(6)

Red meat was classified as probably carcinogenic to humans, based on limited evidence of an association between red meat and cancer.(6) The limited evidence was linked for colorectal cancer, but there was also evidence of links with cancer of the pancreas and the prostate.(61) Positive associations may be influenced by chance, bias and confounding.(6) Cancer has multifactorial etiology(65) and high consumption of processed meat and red meat are frequently associated with risk factors such as smoking, sedentary lifestyle and alcohol drinking.(6) Processed meat was classified as a cause for colorectal cancer and an association with cancer of the stomach was observed, although not conclusive.(61) Processed meat was classified in group 1 for colorectal cancer, but the IARC did not evaluated on how much the risk increases.(6)

In the evaluation by IARC, several studies analyzed by the team did not distinguish between processed meat and red meat or were based on raw carcass weights, where bones and visible fat are included.(6) In fact, a lot of studies found by IARC were not conclusive or had null results.(6)

Studies and databases showed that in most cases the consumption of meat is within the recommended dietary guidelines, and thus the current concern in eating meat is excessive.(9) Also, the cooking methods chosen may influence significantly the formation of carcinogenic compounds such as HCAs, PAHs and NOC, particularly in barbecuing, grilling and pan-frying.(76)

8. Summary

The consumption of meat, particularly red meat has been facing a decrease in the last decades, as is frequently associated with poor outcomes, such as the development of cancer and cardiovascular diseases. Recently, a working group of WHO, the IARC, evaluated the carcinogenicity of red meat and processed meat. They classified red meat as probably carcinogenic to humans (group 2A) and processed meat as carcinogenic to humans (group 1). The release of the press headline, before in 2015 led to an anxiety and concern from part of the population, that believed an effective way to prevent cancer was stopping eating meat. However, red meat has a rich nutritional composition, providing essential nutrients throughout the life cycle, in a well absorbable form, such as protein, iron, zinc, B complex vitamins and vitamin D.

The scope of this paper is to point the impact of red meat in the diet, as a nutritious food with several health benefits and explain the different variables that should be taken into account for a robust dietary assessment.

The carcinogenicity of red meat classified by IARC was based on limited evidence, thus other explanations such as smoking, drinking alcohol, sedentary lifestyle or not eating vegetables and fruit could had be associated with the development of the cancers reported. Similarly, associations between red meat and cancer were reported in relatively high consumptions (compared to the recommended dietary intakes found in several relevant worldwide dietary guidelines organizations). Finally, according with the recommended dietary intake range and bearing in mind always the individual characteristics of each person, this work recommends to pay attention to certain cooking methods and to certain ingredients, added to cooking preparations, both being able to influence in a significant way red meat and processed meat nutritional and hazardousness profiles.

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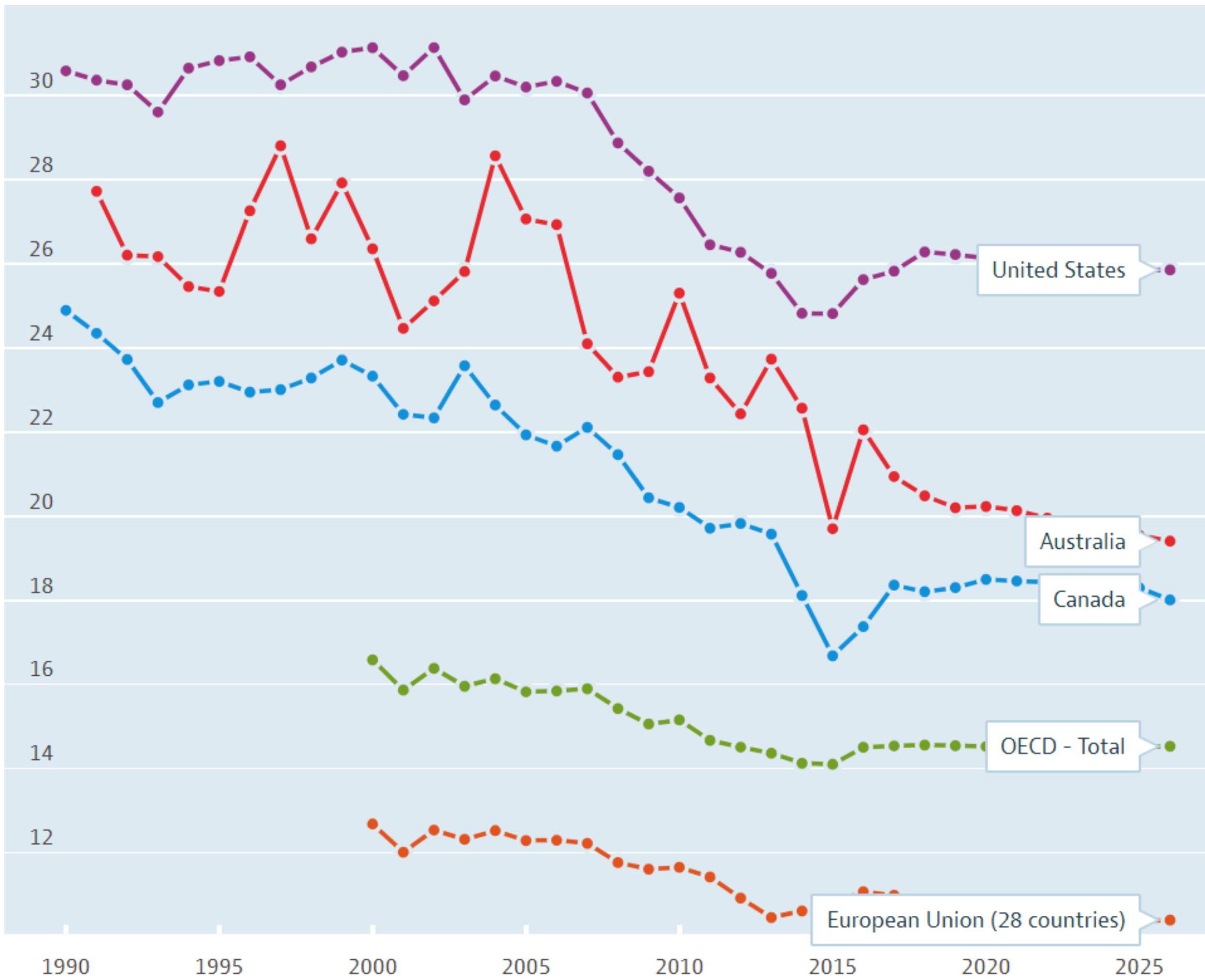
10. Annexes

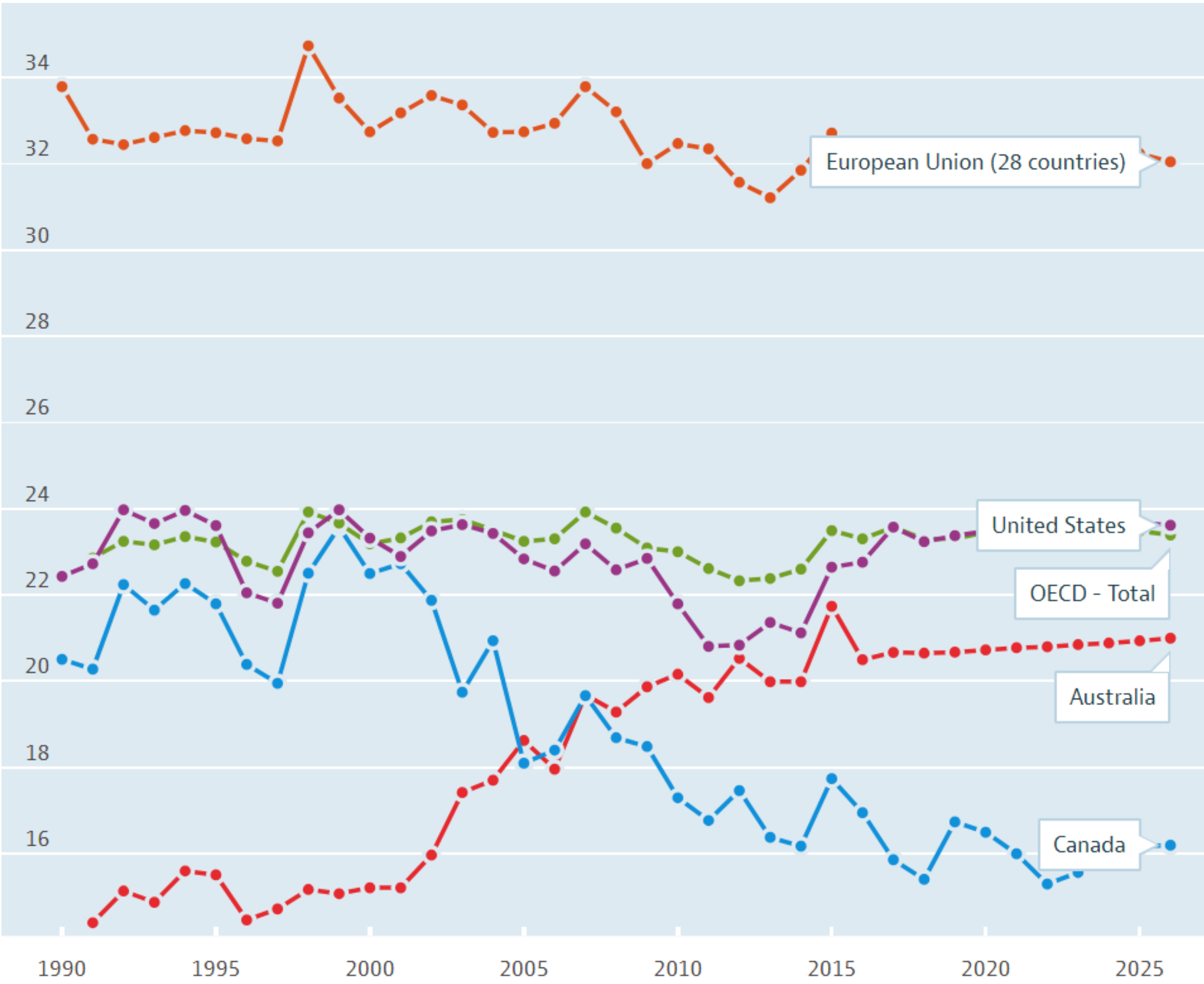
Annex I – Beef and veal, kilograms/capita, 1990 – 2026



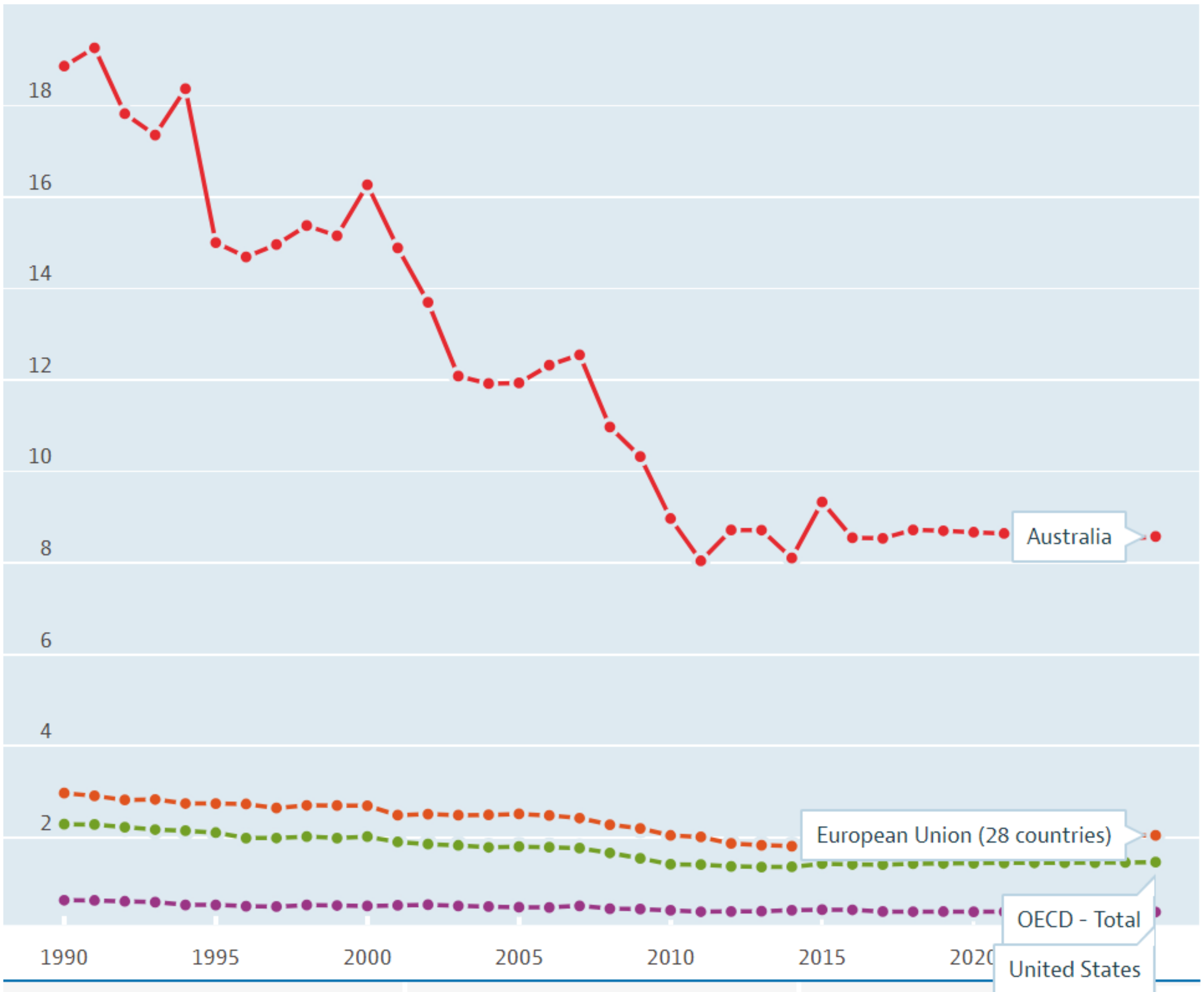
Adapted from OECD (78)

Annex II – Pork meat, kilograms/capita, 1990 – 2026

Adapted from OECD (78)

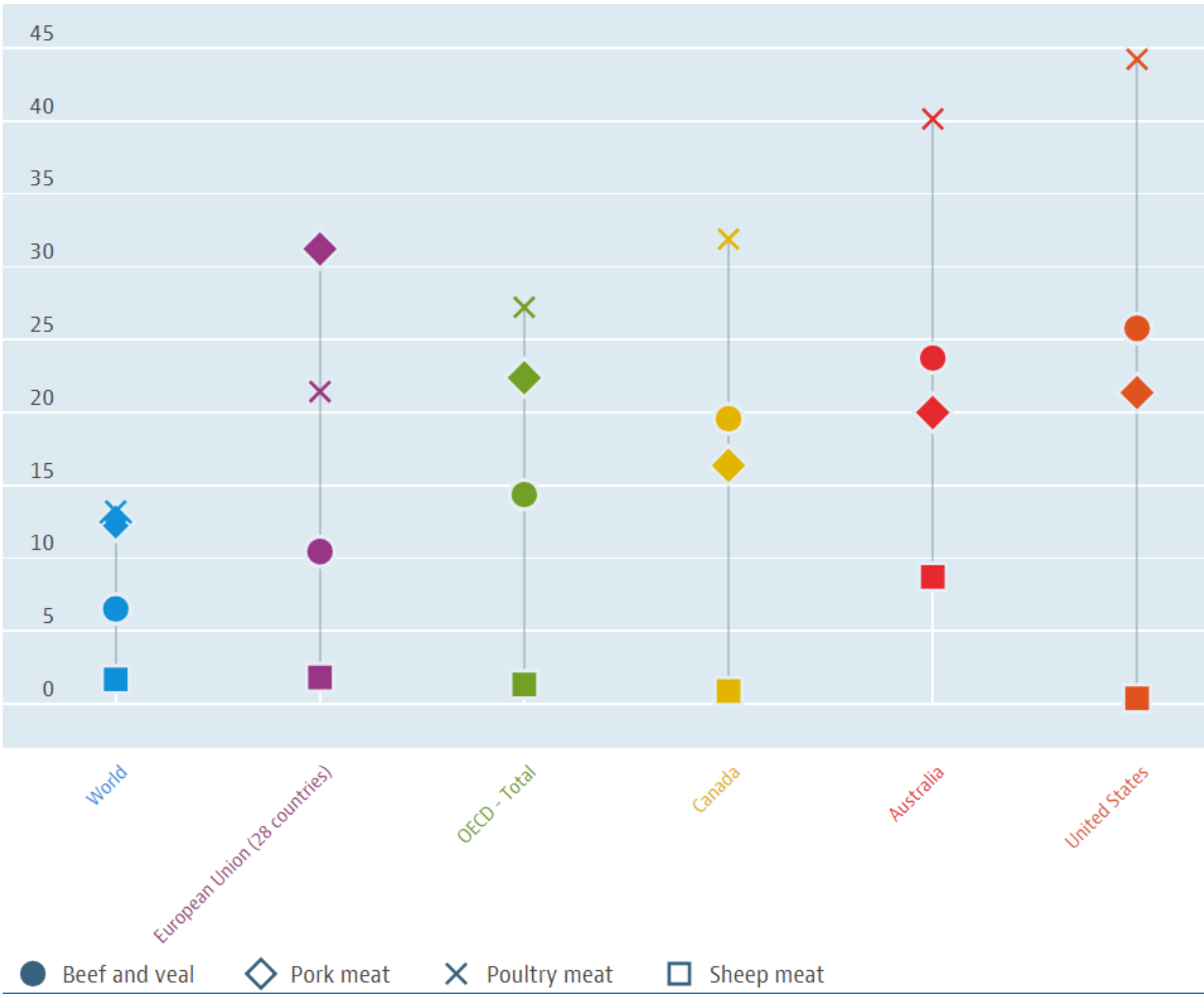


Annex III – sheep meat, kilograms/capita, 1990 – 2026



Adapted from OECD (78)

Annex IV – Beef and veal/pork meat/poultry meat/sheep meat, kilograms/capita, 2013



Adapted from OECD (78)