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Markers of ultra-processing:
Market analyses and association with mortality and morbidity

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Nathalie Judith Neumann
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List of Abbreviations

CVD	Cardiovascular disease
FOPL	Front-of-package labelling
HR	Hazard Ratio
MBP	Meat-based products
MUP	Markers of ultra-processing
OR	Odds Ratio
PBMP	Plant-based meat products
T2DM	Type 2 diabetes mellitus
UK	United Kingdom
UPF	Ultra-processed foods
USA	United States of America

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1. Introduction

In recent years, interest in the health effects of ultra-processed foods (UPF) has increased tremendously(1).
The term "ultra-processed food" was first introduced by Carlos Monteiro in 2009(2). UPF are ready-to-eat or ready-to-heat products(3). They usually have a low nutrient density, a low fibre content, and are high in simple carbohydrates, saturated fats, as well as sodium(3). UPF are heavily advertised and packaged attractively(3).

A systematic review from 2021 assessed UPF consumption as a percentage of total energy intake in 21 countries around the world based on 99 individual studies(4). A wide range of UPF intake was found, with the United States of America (USA) and the United Kingdom (UK) having the highest percent energy intake from UPF, i.e., generally > 50 %, and Italy having the lowest UPF intake, i.e., about 10 %(4). Moreover, the UPF sales per capita in kg increased in the period from 2006 to 2019 throughout the world(5).

Since the introduction of the UPF concept, a variety of studies and meta-analyses have examined the association of UPF consumption with diverse health outcomes(6). In the last few years, the number of publications has increased tremendously(7). A self-conducted PubMed search for the term "ultra-processed" retrieved 204 papers for the period from 2009 to 2018 whereas 1667 papers were published between 2019 and July 2024.

There are several classification systems for categorising food items according to their degree of processing (Table 1)(8). The NOVA classification is the most commonly published classification system worldwide and a large number of publications use its definition of UPF(3,9). Therefore, the current doctoral thesis focuses exclusively on the NOVA classification (subchapter 1.1). Although there is good evidence for an association of UPF with diverse health outcomes (subchapter 1.2), an ongoing debate exists about the objectivity and the complexity of the NOVA classification (subchapter 1.3).

***Table 1:** Classification systems for categorising food items according to their degree of processing. Modified according to de Araújo et al., 2022*(8)

Classification System	Groups	Definition	Examples
IARC-EPIC International Agency for Research on Cancer-European Prospective Investigation into Cancer and Nutrition (Europe) Slimani et al., 2009(10)	Non-processed foods	Foods that can be consumed raw.	Crustaceans, fresh juice, fruits, molluscs, non-processed nuts, vegetables
	Moderately processed foods	Commercial foods that undergo modest processing and can be consumed without further preparation. Foods that are prepared at home by using raw or moderately processed foods.	Dried fruits, extra virgin olive oil, frozen basic foods, fruits and vegetables canned in water, brine or own juice, packaged salad Meat, fish and vegetables cooked from raw, fresh, vacuum-packed, frozen or canned ingredients
	Highly processed foods	Industrially prepared foods that need no or minimal preparation at home.	Bread, breakfast cereals, canned foods, cheese, commercial cakes, biscuits and sauces
IFIC International Food Information Council (USA) Eicher-Miller et al., 2012(11)	Minimally processed foods	Foods whose properties are largely unchanged.	Washed or packaged fruits and vegetables, roasted nuts
	Food processed for preservation	Food that is processed to preserve and enhance nutrients and freshness.	Canned tuna and beans, frozen vegetables and fruits
	Mixture of combined ingredients	Addition of sweeteners, spices, oils, colours, flavours, and preservatives to affect safety, taste, and appearance.	Cake mix, salad dressing, tomato sauce
	Ready-to-eat processed foods	Packaged ready-to-eat foods and ready-mixes.	Breakfast cereals, carbonated beverages, crackers, fruit drinks, ice cream, yoghurt
	Prepared food/meals	Packaged foods/meals that are easy to prepare.	Pizza, prepared meat dishes, pasta

IFPRI International Food Policy Research Institute (Guatemala) Asfaw, 2011(12)	Unprocessed foods	Not defined in the paper.	Beans, corn, dairy, eggs, fish, fruits, meat, roots, tubers, vegetables
	Primary processed foods	Not defined in the paper.	Bread, butter, corn products, dairy products, sugar, sweetener, vegetable oil
	Highly processed foods	Food in a readily edible form through secondary processing likely with a high proportion of added sugar, fat, and salt.	Breakfast cereals, cookies, crackers, ice cream, pasta products, prepared meals, prepared meat, sausages, soft drinks, sweets
NOVA (Brazil) Monteiro et al., 2019(13)	Unprocessed or minimally processed foods	Minimal processing is used to extend the shelf-life of unprocessed foods, to enable them to be stored, and to simplify their preparation.	Coffee, fresh, frozen or dried fruits and vegetables, fresh or chilled meat and fish, fresh or dried herbs, grains, juice, legumes, milk, tea
	Processed culinary ingredients	Ingredients obtained from NOVA group 1 foods or nature that are used in the preparation of NOVA group 1 foods.	Butter, honey, salt, starch, sugar, vegetable oil
	Processed foods	Products manufactured by adding NOVA group 2 ingredients to NOVA group 1 foods in order to improve their shelf-life or sensory properties.	Canned fish and vegetables, fresh bread and cheese, salted meat and fish, salted or sugared nuts and seeds
	Ultra-processed foods	Formulations of ingredients that are the result of a series of industrial processes to make the products more palatable. Products usually contain non-culinary ingredients or cosmetic additives.	Breakfast cereals, cakes, cookies, fruit yoghurt, ice cream, instant sauces, pre-prepared pasta and pizza dishes, soft drinks, sweet or savoury packaged snacks

Siga (France) Davidou et al., 2020(14)	Unprocessed or minimally processed foods including culinary ingredients	Similar to NOVA groups “Unprocessed or minimally processed foods” and “Processed culinary ingredients”.	
	Processed foods	Similar to NOVA group “Processed foods”, further distinguished by levels of salt, sugar, and fat.	
	Ultra-processed foods	Similar to NOVA group “Ultra-processed foods”, further distinguished by levels of salt, sugar, and fat, as well as number of markers of ultra-processing and hazardous additives.	
UNC University of North Carolina (USA) Poti et al., 2015(15)	Less processed foods	Unprocessed or minimally processed foods that consist of only one ingredient and that have not been altered or only slightly altered so that the properties of the food are retained.	Eggs, fresh, frozen or dried fruits, vegetables and legumes, milk, unseasoned meat, wholegrain cereal
		Processed basic ingredients obtained by extraction or purification. Minimally processed foods for the purpose of preservation or precooking.	Canned fruits, vegetables and legumes, canned meat, oil, pasta, plain yoghurt, salt, sugar, unsweetened fruit juice
	Moderately processed foods	Slightly processed foods with flavour additives to improve taste and moderately processed cereal products.	Cheese, chocolate milk, crackers, nuts with salt, seasoned, frozen or canned meat, sweetened or flavoured juice, tea and yoghurt
	Highly processed foods	Industrially produced mixtures of several ingredients whose original plant/animal source is no longer recognizable due to processing.	Alcoholic beverages, breaded meat, cakes, chocolate, frozen or canned pasta dishes, margarine, marinades, sauces, soda

1.1 NOVA classification

The NOVA classification has been developed by the Brazilian researcher Carlos Monteiro and his colleagues and was first introduced in a commentary in 2009(2) and a research article in 2010(16). In the following years, the classification was further developed into its current form(17). In the NOVA classification, food items are assigned to four groups depending on the nature, scope, and purpose of their industrial processing(3,13). Food processing includes all physical, biological, and chemical processes that are applied to the products during manufacturing(3,13).

NOVA group 1 contains unprocessed food items including edible parts of plants, i.e., seeds, fruits, leaves, stems, and roots, or of animals, i.e., muscle, offal, eggs, and milk, as well as mushrooms and water(3). Furthermore, minimally processed food items which have been modified by different processes such as drying, chopping, filtering, roasting, cooking, and pasteurising are also found in this group(3). No salt, sugar, oils, or fats are added to the food during processing(13). Processing aims to extend shelf-life, enables better storage of food, or makes it easier to prepare(13).

NOVA group 2 includes processed culinary ingredients that are derived from NOVA group 1 foods or directly from nature, e.g., salt, oil, sugar, and butter(3,13). These ingredients are obtained by processes such as pressing, refining, grinding, and milling to produce long-life items that are used for cooking(3,13). They are not intended to be eaten on their own(3).

NOVA group 3 contains processed foods such as canned vegetables, canned fish, fruit in syrup, cheese, and freshly baked bread(3,13). They are produced by adding salt, oil, sugar, or other ingredients of NOVA group 2 to NOVA group 1 foods to increase their shelf-life or sensory properties(3,13).

NOVA group 4 corresponds to UPF(3,13). UPF are compositions of ingredients that are mostly used on an industrial scale and are the result of industrial processes, hence "ultra-processed"(13). They contain sources of energy and nutrients that are of no or rare culinary use, so-called non-culinary ingredients such as varieties of sugar, modified oils, and protein sources, the latter including casein, hydrolysed proteins, gluten, and whey(13). In addition, UPF contain special classes of additives that are used to mimic or enhance the sensory properties of food, so-called cosmetic additives such as colouring agents, flavours, flavour enhancers, sweeteners, and processing aids(3,13). Non-culinary ingredients and cosmetic additives are together referred to as markers of ultra-processing (MUP)(14). These MUP are exclusively found in UPF(3,13). The aim of ultra-processing is to create long-life, ready-to-eat, hyper-palatable, and highly profitable foods that are usually attractively packaged and intensively marketed(3).

Monteiro and his colleagues state five reasons, why the NOVA classification was developed and why it is necessary to focus on UPF(3).

(1) Conventional food group systems classify food items concerning their botanical or animal origin, e.g., whole grains are often in the same group as sugar-sweetened cereals and fresh chicken is grouped together with chicken nuggets(3). This grouping is not reasonable concerning the different health effects of the various foods(3).
(2) The association between food processing and health consequences is becoming increasingly evident(3).
(3) There is a transition in food systems and the food supply that changes consumers purchasing and consumption behaviour, e.g., there is a decrease in home-cooking whereas pre-packaged products are available often around the clock(3).
(4) The increase in processed food supply is driven by transnational corporations(3). This has changed the food supply in middle and low-income countries(3).
(5) Additional to (4), it is increasingly recognised that transnational food corporations have enormous resources to produce, market, and promote their products(3). They often calculate a 10 % or more increase in annual sales in middle- and low-income countries(3).

Based on this reasoning, it is important to identify UPF(3). However, the food industry does not label UPF and it is not obliged to declare the processes used in food production(13). Therefore, it is difficult for consumers, health experts, policy makers, and even for researchers to identify UPF(13). The only way to identify them is to check whether the ingredient lists contain either a non-culinary ingredient or a cosmetic additive, i.e., whether they contain any of the MUP(13).

1.2 Consumption of ultra-processed foods and health

There is a strong link between UPF consumption and health that has been analysed in several studies(18–26). Recently, a systematic umbrella review of existing meta-analyses was published by Lane and colleagues and included 14 meta-analyses of observational epidemiological studies in the time period from 2009 to 2023 with 45 separate pooled analyses(18). The average number of original research articles in the pooled analyses per outcome was four and varied between two and nine(18). In total, 9,888,373 participants were included(18). UPF consumption was assessed as dose-response, i.e., continuous exposure (e.g., with each additional portion per day), and/or non-dose-response, i.e., categorical exposure (e.g., high compared to low daily consumption)(18).

All results of the umbrella review were categorised as convincing ("Class I"), highly suggestive ("Class II"), suggestive ("Class III"), weak ("Class IV"), or no evidence ("Class V") according to pre-specified evidence classification criteria(18). There was convincing evidence for the non-dose-response associations of UPF consumption with **cardiovascular disease (CVD)-related mortality, anxiety outcomes, common mental disorder outcomes** and a convincing dose-response association **for type 2 diabetes mellitus (T2DM)** (Table 2)(18). Highly suggestive evidence was described for the non-dose-response associations with **all-cause mortality, heart disease-related mortality, adverse sleep-related outcomes, depressive outcomes, wheezing, obesity**, and **T2DM** (Table 2)(18). There was suggestive evidence for the non-dose-response associations of UPF consumption with **overall cancer, colorectal cancer, CVD events combined, CVD morbidity, hypertension, abdominal obesity, overweight**, and a suggestive dose-response associations for **all-cause mortality, CVD events combined, CVD morbidity, abdominal obesity, obesity**, and **overweight** (Table 2)(18). Weak evidence was seen for the non-dose-response associations with **low high-density lipoprotein cholesterol, Crohn's disease, metabolic syndrome, non-alcoholic fatty liver disease, overweight and obesity**, and for the dose-response associations with **CVD-related mortality, colorectal cancer**, and **overweight and obesity** (Table 2)(18). All further pooled analyses were graded as no evidence(18).

Two further recently published umbrella reviews have obtained broadly similar results that are also depicted in Table 2 under "Further analyses"(19,20). Besides the outcomes shown in Table 2, some additional endpoints were analysed: In the umbrella review conducted by Dai et al., UPF consumption was significantly associated with **renal function decline** (Odds Ratio (OR); 95 % Confidence Interval (CI): 1.25; 1.18-1.33), **colon cancer** (1.18; 1.05-1.33), **inflammatory bowel disease** (1.32; 1.11-1.57), and **hyperuricaemia** (1.09; 1.00-1.20)(19).

Barbaresko et al. showed significant associations with **colon cancer** (Summary Risk Ratio; 95 % CI: 1.25; 1.14-1.36) and **CVD incidence** (1.04; 1.02-1.06)(20). There were no significant non-dose-response associations for premenopausal breast cancer(19,20), postmenopausal breast cancer(19,20), rectal cancer(19,20), low-grade prostate cancer(20), high-grade prostate cancer(20), colorectal adenomas(20), adverse maternal and neonatal outcomes(19), high low-density lipoprotein cholesterol(19), and frailty(19).

Apart from the findings in these systematic umbrella reviews, there has been additional evidence for other outcomes in recently published meta-analyses and cohort studies: In a meta-analysis of ten observational studies, high versus low intake of UPF was associated with an increased risk of **dementia** (Risk Ratio; 95 % CI: 1.44; 1.09-1.90)(21). Another meta-analysis showed an association of UPF-rich diet with **preeclampsia** (OR; 95 % CI: 1.28; 1.15-1.42) but not with hypertension during pregnancy, preterm birth and low birth weight(22). Moreover, UPF intake was associated with **dental caries** in children and adolescents (OR; 95 % CI: 1.55; 1.37-1.75)(23). In two further cohort studies, more detailed examinations of adverse liver and brain outcomes were carried out. Here, higher UPF consumption was associated with **severe liver disease** (Hazard Ratio (HR); 95 % CI: 1.50; 1.19-1.90) but not with liver cancer(24). Moreover, a 10 % increase in relative UPF consumption was associated with a higher risk of **cognitive impairment** (HR; 95 % CI: 1.16; 1.09-1.24) and **stroke** (1.08; 1.02-1.14)(25).

Besides this strong epidemiological evidence linking UPF consumption with adverse health outcomes, the causal role of UPF on energy intake and body weight gain was examined in a randomised controlled trial comparing an ultra-processed with an unprocessed diet(26). Ten male and ten female participants were assigned to either the ultra-processed or unprocessed diet for 14 days followed by the other diet for a further 14 day period(26). Each diet included three meals per day and free access to snacks and water, and participants were allowed to eat as much as desired(26). The two diets were well-matched for energy density, as well as contents of carbohydrates, fat, protein, fibre, sugar, and sodium(26). During the ultra-processed diet, the energy intake was significantly higher compared to the unprocessed diet by a mean (standard deviation) of 508 (106) kcal/day(26). Moreover, body weight increased during the ultra-processed diet by 0.9 (0.3) kg whereas it decreased by 0.9 (0.3) kg during the unprocessed diet(26). These results suggest that UPF are not only associated with adverse health outcomes in epidemiological studies but that they directly induce overeating and body weight gain.

Table 2: *Association of UPF consumption with adverse health outcomes. Modified according to Lane et al., 2024*(18)

Outcome	**Equivalent OR**	**95 % CI**	**k**	**Credibility**	**Further analyses**
Non-dose-response relations					
Mortality					
All-cause mortality	**1.21**	1.15 to 1.27	7	II	**a**
Cancer-related mortality	1.00	0.81 to 1.24	2	V	a, b
CVD-related mortality	**1.50**	1.37 to 1.63	4	I	**a**
Heart disease-related mortality	**1.66**	1.51 to 1.84	2	II	a
Cancer					
Breast cancer	1.15	0.99 to 1.34	6	V	a
Overall cancer	**1.12**	1.06 to 1.19	7	III	a
Central nervous system tumours	1.20	0.87 to 1.65	2	V	b
Chronic lymphocytic leukaemia	1.08	0.80 to 1.45	2	V	b
Colorectal cancer	**1.23**	1.10 to 1.38	7	III	**a**
Pancreatic cancer	1.24	0.85 to 1.79	2	V	a, b
Prostate cancer	1.02	0.93 to 1.12	4	V	a
Mental health					
Adverse sleep-related outcomes	**1.41**	1.24 to 1.61	2	II	
Anxiety outcomes	**1.48**	1.37 to 1.59	4	I	**a, b**
Common mental disorder outcomes	**1.53**	1.43 to 1.63	6	I	**a, b**
Depressive outcomes	**1.22**	1.16 to 1.28	2	II	**a, b**
Respiratory Health					
Asthma	1.20	0.99 to 1.46	2	V	**a**
Wheezing	**1.40**	1.27 to 1.55	2	II	**a**

Cardiovascular health					
CVD events combined	**1.35**	1.18 to 1.54	6	III	**a**
CVD morbidity	**1.20**	1.09 to 1.33	2	III	
Hypertension	**1.23**	1.11 to 1.37	9	III	**a, b**
Hypertriacylglycerolaemia	0.95	0.60 to 1.50	2	V	**a, b**
Low HDL cholesterol	**2.02**	1.27 to 3.21	2	IV	**a, b**
Gastrointestinal health					
Crohn’s disease	**1.71**	1.37 to 2.14	4	IV	**a, b**
Ulcerative colitis	1.17	0.86 to 1.61	4	V	a, b
Metabolic health					
Abdominal obesity	**1.41**	1.18 to 1.68	4	III	**a**
Hyperglycaemia	1.10	0.34 to 3.52	2	V	a, b
Metabolic syndrome	**1.25**	1.09 to 1.42	9	IV	**a,** b
Non-alcoholic fatty liver disease	**1.23**	1.03 to 1.46	4	IV	a, b
Obesity	**1.55**	1.36 to 1.77	7	II	**a**
Overweight	**1.36**	1.14 to 1.63	4	III	**a**
Overweight and obesity	**1.29**	1.05 to 1.58	2	IV	**b**
T2DM	**1.40**	1.23 to 1.59	7	II	**a**
Dose-response relations					
Mortality					
All-cause mortality	**1.02**	1.01 to 1.03	9	III	**b**
CVD-related mortality	**1.05**	1.02 to 1.08	5	IV	**b**
Heart disease-related mortality	1.18	0.95 to 1.47	2	V	b
Cancer					
Breast cancer	1.03	0.98 to 1.09	3	V	b
Colorectal cancer	**1.04**	1.01 to 1.07	5	IV	**b**
Prostate cancer	0.99	0.97 to 1.02	3	V	b

Cardiovascular health					
CVD events combined	**1.04**	1.02 to 1.06	8	III	**b**
CVD morbidity	**1.04**	1.02 to 1.06	2	III	**b**
Metabolic health					
Abdominal obesity	**1.05**	1.02 to 1.07	6	III	**b**
Obesity	**1.07**	1.03 to 1.11	7	III	**b**
Overweight	**1.06**	1.03 to 1.10	2	III	**b**
Overweight and obesity	**1.03**	1.01 to 1.06	3	IV	
T2DM	**1.12**	1.11 to 1.13	7	I	**b**

CI, Confidence Interval; CVD, Cardiovascular disease; HDL, High-density lipoprotein; OR, Odds Ratio; T2DM, Type 2 diabetes mellitus; UPF, ultra-processed foods; CVD events combined include morbidity and mortality; k indicates the number of original research articles; Further analyses include a(19) and b (Summary Risk Ratio)(20); If a or b are not indicated, this outcome was not studied in the respective analysis; All significant results are presented in **bold.**

1.3 Limitations of the NOVA classification

Although the NOVA classification is the most widely published classification to categorise foods according to their degree of processing, it has several limitations(9). Critics point out that the NOVA classification is too inconsistent and is based on broad and ambiguous definitions that are not supported by scientific evidence(9,27,28). A lack of accurate definition of the NOVA groups can lead to misclassifications(29). Even nutrition experts(30) and researchers(31,32) have disagreements when classifying foods according to their degree of processing. When comparing different publications that use the Oxford WebQ as a 24-hour dietary assessment tool, food items are assigned to NOVA groups in different ways(33–37). Furthermore, tools such as food frequency questionnaires or 24-hour recalls are not validated for recording UPF(4,38).

Another point of criticism is that several food additives defined as MUP, e.g., added flavours, which are to be avoided in NOVA, are extensively tested and declared as safe by regulatory authorities, e.g., the European Food Safety Authority, before approval(39,40). Moreover, results of epidemiological studies analysing the association of UPF and health can be biased due to the nutrient content of UPF being mostly higher in energy, fats, and sugar, and lower in fibre(4). Therefore, it is not possible to separate the influence of nutritional composition or the overall diet quality from the influence of processing(4). However, in an analysis of nutrient intake across quintiles of UPF consumption, the lower quintile differed little from the upper quintile in terms of fat, saturated fat, and sodium intake, while differences were seen for sugar and fibre(28).

It is also criticised that there are food items considered as UPF that have a favourable nutrient composition, e.g., whole-grain packaged bread or unsweetened breakfast cereals(41). The Siga classification, an extension of the NOVA classification, addresses these criticisms by considering both the degree of processing and nutrients(14). It adds information on processing effects on the food matrix, the contents of salt, sugar, and fat, as well as the number of MUP and hazardous additives(14). This leads to a last point of limitations: There are several classification systems and each system differs from the others in various ways (Table 1). Thus, comparability of study results using NOVA with studies using another classification system is not guaranteed(8). Therefore, a universally accepted definition for UPF remains a research priority(7,8).

Nevertheless, it must be mentioned that several of these publications(9,27,28,30,32,40) show a close link to the food industry and, therefore, have potential conflicts of interest(42).

1.4 Research gaps

Taking into account the studies summarised above, there are **three main research gaps** in the field of UPF that were analysed in the present work.

Research gap 1: Which underlying mechanisms can explain the effects of UPF on overeating and body weight gain?

The current literature shows an adverse effect of UPF on health outcomes including body weight(18–26). Therefore, it is important to clarify underlying mechanisms. Since added flavours are one of the most frequent MUP(43), their role in eating behaviour and body weight control should be elucidated.

Research gap 2: How can UPF be detected more objectively?

The NOVA classification is often criticised for being too complex and unclear in its application(9,27,28). Even professionals have difficulties in applying it(30–32). Since consumers should avoid UPF, an approach is needed to detect UPF more objectively and more easily.

Research gap 3: Can the MUP concept be adapted to the German food market?

The original MUP terms for UPF were defined as English terms by Monteiro et al.(3,13) and most UPF studies are published in English. To apply these MUP terms to the German food market, they need to be translated into adequate German search terms. Since plant-based meat products (PBMP) are a growing market segment(44), they are ideal to apply the MUP concept to the German food market and to compare them with their meat-based counterparts concerning ultra-processing.

2. Publications

Within this doctoral thesis, three publications have addressed the research gaps summarised in subchapter 1.4 and are presented within the next subchapters.

Research gap 1: Which underlying mechanisms can explain the effects of UPF on overeating and body weight gain?

(1) **Neumann, Nathalie Judith;** Fasshauer, Mathias (2022) Added flavors: potential contributors to body weight gain and obesity? *BMC Medicine 20(1):417*. DOI: 10.1186/s12916-022-02619-3.

Research gap 2: How can UPF be detected more objectively?

(2) **Neumann, Nathalie Judith;** Eichner, Gerrit; Fasshauer, Mathias (2023) Flavour, emulsifiers, and colour are the most frequent markers to detect food ultra-processing in a UK food market analysis. *Public Health Nutrition 26(12): 3303-3310.* DOI: 10.1017/S1368980023002185.

Research gap 3: Can the MUP concept be adapted to the German food market?

(3) Metz, Kemja-Maria[1]; **Neumann, Nathalie Judith[1];** Fasshauer, Mathias (2023) Ultra-processing markers are more prevalent in plant-based meat products as compared to their meat-based counterparts in a German food market analysis. *Public Health Nutrition 26(12): 2728-2737.* DOI: 10.1017/S1368980023002458.

[1] KMM and **NJN** contributed equally to this work and are joint first authors.

2.1 Publication 1: Added flavors: potential contributors to body weight gain and obesity?

Author information

Nathalie Judith Neumann[1] and Mathias Fasshauer[1,2,*]
[1]Institute of Nutritional Science, Justus Liebig University Giessen, 35390 Giessen, Germany
[2]Department of Internal Medicine (Endocrinology, Nephrology, and Rheumatology),
University of Leipzig, 04103 Leipzig, Germany.
*Correspondence: mathias.fasshauer@uni-giessen.de

Authors' contributions

NJN and MF conceived the research and wrote the article. The authors read and approved the final manuscript. MF is the guarantor of the manuscript and accepts full responsibility for the work, had access to the data, and controlled the decision to publish. He attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Summary

Research gap 1 was addressed in the publication “Added flavors: potential contributors to body weight gain and obesity?”(45).

Within this publication, animal and human data elucidating the impact of added flavours on the regulation of food intake and body weight gain were assessed. A comprehensive literature search was done.

The article defined three aspects on the association of added flavours and obesity.

(1) Mechanistic studies suggest two independent mechanisms how added flavours induce overeating and body weight gain. The first mechanism describes that added flavours might promote hedonic eating by increasing the rewarding characteristics of a food item(2,3,46–48). Thus, the hedonic system overrides homeostatic control of food intake, which aims to maintain current body weight through metabolic regulation of food intake and energy expenditure(47–49). Hedonic overeating leads to body weight gain and obesity in the long term(48). The second mechanism states that added flavours disrupt flavour-nutrient learning: In the process of flavour-nutrient learning, flavour-nutrient associations are developed through repeated orosensory experiences of a food and its postingestive consequences(50,51). Added flavours might lead to inconsistency between orosensory experiences and associated nutrients which impairs the ability to predict nutrients in food items causing overeating and subsequent body weight gain(51).

(2) Added flavours increase feed intake and body weight as compared to non-flavoured control diets in a broad range of animal studies(52–66). Moreover, added flavours have been used in the production of animal feed for more than 40 years(67) and are actively promoted by feed additive manufacturers as useful tools to improve palatability, feed intake, and performance parameters(68).

(3) The use of added flavours in human nutrition is extensively tested concerning toxicity(69–72); however, no data exist concerning their impact on food intake and body weight. In the second half of the twentieth century, the worldwide flavour and fragrance industry expanded tremendously(73–86). In parallel to its growth, there was an increase in obesity prevalence in the USA(87). This parallel increase is no proof for the weight-inducing effects of added flavours, but it provides a further argument that added flavours might be contributors to the obesity epidemic.

In conclusion, the article shows two potential mechanisms by which added flavours might induce overeating and body weight gain and presents the current evidence considering animal and human data. Since there are no studies examining the link between added flavours and obesity in humans, the role of added flavours in human nutrition needs to be assessed in future studies, e.g., in double-blind controlled trials, randomised controlled trials, or epidemiological cohorts.

The published manuscript is attached.

Neumann and Fasshauer *BMC Medicine* (2022) 20:417
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BMC Medicine

OPINION

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Added flavors: potential contributors to body weight gain and obesity?

Nathalie Judith Neumann[1] and Mathias Fasshauer[1,2*]

Abstract

Background: Added flavors are a marker for ultra-processing of food and a strong link exists between the intake of ultra-processed food and the development of obesity. The objective of the present article is to assess animal and human data elucidating the impact of added flavors on the regulation of food intake and body weight gain, as well as to define areas for future research.

Main text: Mechanistic studies suggest that added flavors induce overeating and body weight gain by two independent mechanisms: Added flavors promote hedonic eating and override homeostatic control of food intake, as well as disrupt flavor-nutrient learning and impair the ability to predict nutrients in food items. Supporting these potential mechanisms, added flavors increase feed intake and body weight as compared to non-flavored control diets in a broad range of animal studies. They are actively promoted by feed additive manufacturers as useful tools to improve palatability, feed intake, and performance parameters. In humans, added flavors are extensively tested concerning toxicity; however, no data exist concerning their impact on food intake and body weight.

Conclusions: Added flavors are potential contributors to the obesity epidemic and further studies focusing on their role in humans are urgently required. These studies include obesity interventions specifically targeting food items with added flavors and cohort studies on independent associations between added flavor intake and metabolic, as well as cardiovascular, morbidity, and mortality.

Keywords: Added flavors, Body weight, Flavor-nutrient learning, Food intake, Hedonic eating, Metabolic syndrome, Obesity, Ultra-processed food

Background

Food additives are substances added intentionally to food to preserve flavor, as well as to enhance taste, appearance, or other sensory qualities [1]. Examples for food additives are flavors, flavor enhancers, sweeteners, colors, emulsifiers, stabilizers, gelling agents, thickeners, and preservatives [1]. Added flavors, also called flavorings, are defined as products "not intended to be consumed as such, which are added to food in order to impart or modify odour and/or taste" [2]. The European food law distinguishes different categories of which added flavors can consist, such as flavor preparations which are obtained from different natural sources and flavor substances which are single chemical compounds [2]. Flavor substances can be called natural if they are "obtained by appropriate physical, enzymatic or microbiological processes from material of vegetable, animal or microbiological origin […] [and if they] correspond to substances that are naturally present and have been identified in nature" [2]. In the United States of America (US), artificial flavors are defined as substances not obtained from spices, fruits, vegetables, meat, or other natural sources, while natural flavors are essential oils, oleoresins, extractives, and other products derived from natural sources [3].

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*Correspondence: mathias.fasshauer@uni-giessen.de

[1] Institute of Nutritional Science, Justus-Liebig-University of Giessen, 35390 Giessen, Germany
Full list of author information is available at the end of the article

Added flavors are used in food for different reasons. Within the last decades, industrial processing of food has led to flavor losses which were compensated by added flavors [4, 5]. They save costs; improve, change, enhance, or complement the taste of products; and mask undesirable flavor characteristics [5, 6]. Added flavors equalize the taste of products with less sugar, fat, and salt whose demand is rising [7]. They are able to maintain the typical taste of products and, thus, meet consumer expectations even if there are variations in the raw materials [6, 7]. In the past, added flavors also masked spoilage and enabled the consumption of food that would otherwise have been thrown away [5]. Despite their frequent use in food, limited data are available on how added flavors influence excessive calorie intake and body weight.

In the present opinion article, arguments are presented that added flavors contribute to the obesity epidemic in recent decades. Thus, mechanistic studies suggest that added flavors induce overeating and body weight gain by two independent mechanisms: Added flavors promote hedonic eating and override homeostatic control of food intake, as well as disrupt flavor-nutrient learning and impair the ability to predict nutrients in food items. Supporting these potential mechanisms, added flavors increase feed intake, as well as body weight, in animals and are actively promoted by feed additive manufacturers. In humans, added flavors are extensively tested concerning toxicity; however, no data exist concerning their impact on food intake and body weight.

These arguments are based on the literature search summarized in Additional file 1 [8–13] and explored in more detail within the next chapters.

Main text

Potential mechanisms for flavor-induced weight gain

There are two potential mechanisms by which added flavors might induce food intake and body weight gain:

- Added flavors promote hedonic eating
- Added flavors disrupt flavor-nutrient learning

Promotion of hedonic eating

Added flavors might induce overeating and weight gain by promoting hedonic eating and overriding homeostatic control of food intake (Fig. 1). Food intake and body weight are controlled by the homeostatic and the hedonic systems [14, 15]. The homeostatic control aims to maintain current body weight through metabolic regulation of food intake and energy expenditure, i.e., its primary goal is eating for survival [14, 15]. Hedonic eating, in contrast, is driven by the reward system and independent of energy balance, i.e., its primary aim is eating for pleasure [14, 15]. Food intake due to hedonic mechanisms may involve extra calories which would not have been consumed under homeostatic control [16]. In situations of energy deficiency, both systems work together to induce food intake and cover energy needs; however, they might collide in food-rich environments [16]. Processing increases rewarding properties and hedonic value of products compared to unprocessed food items [17, 18]. The availability of these palatable, energy-dense foods in the modern environment promotes hedonic pathways [14, 19, 20]. In response to those rewarding food items, the hedonic system is able to override homeostatic control despite energetically unbalanced conditions [14, 15, 20]. This "eating in the absence of hunger" (EAH) was convincingly shown in adolescents who ate highly palatable snacks even after a meal that exceeded energy requirements [21]. EAH has also been linked to weight gain, food overconsumption, and loss of control over eating in adults [22–24]. Permanent hedonic overeating can cause weight gain in the long term [14]. Added flavors and other so-called cosmetic additives make products palatable or even hyperpalatable [25, 26]. Therefore, added flavors might increase rewarding characteristics of food, promote hedonic eating, and override homeostatic control of food intake, leading to obesity in the long term. This potential mechanism is illustrated in Fig. 1. Scenario a depicts balanced regulation of food intake by the homeostatic and hedonic systems when exposed to non-processed food, e.g., fresh strawberries, as a physiological reward. Here, food is consumed according to energy requirements (Fig. 1a). In scenario b, the hedonic system overrides homeostatic control of food intake when exposed to ultra-processed, hyperpalatable food with added flavors as a supra-physiological reward, e.g., strawberry-flavored food items. Here, food is consumed for pleasure independent of energy requirements (Fig. 1b). It is interesting to note in this context that several additives including flavors, flavor enhancers, sweeteners, colors, and emulsifiers are markers for food ultra-processing according to the NOVA system which classifies products based on "nature, extent and purpose of the industrial processing they undergo" [25, 26]. A strong link exists between the intake of ultra-processed food and the development of obesity [27–30]. There is considerable data suggesting that processing techniques applied in the manufacture of ultra-processed food such as the deconstruction of the original food matrix structure, as well as the use of high amounts of sugar, salt, and fat enhance orosensory properties and energy density [25, 26]. As a consequence, eating rate is increased and endogenous satiety

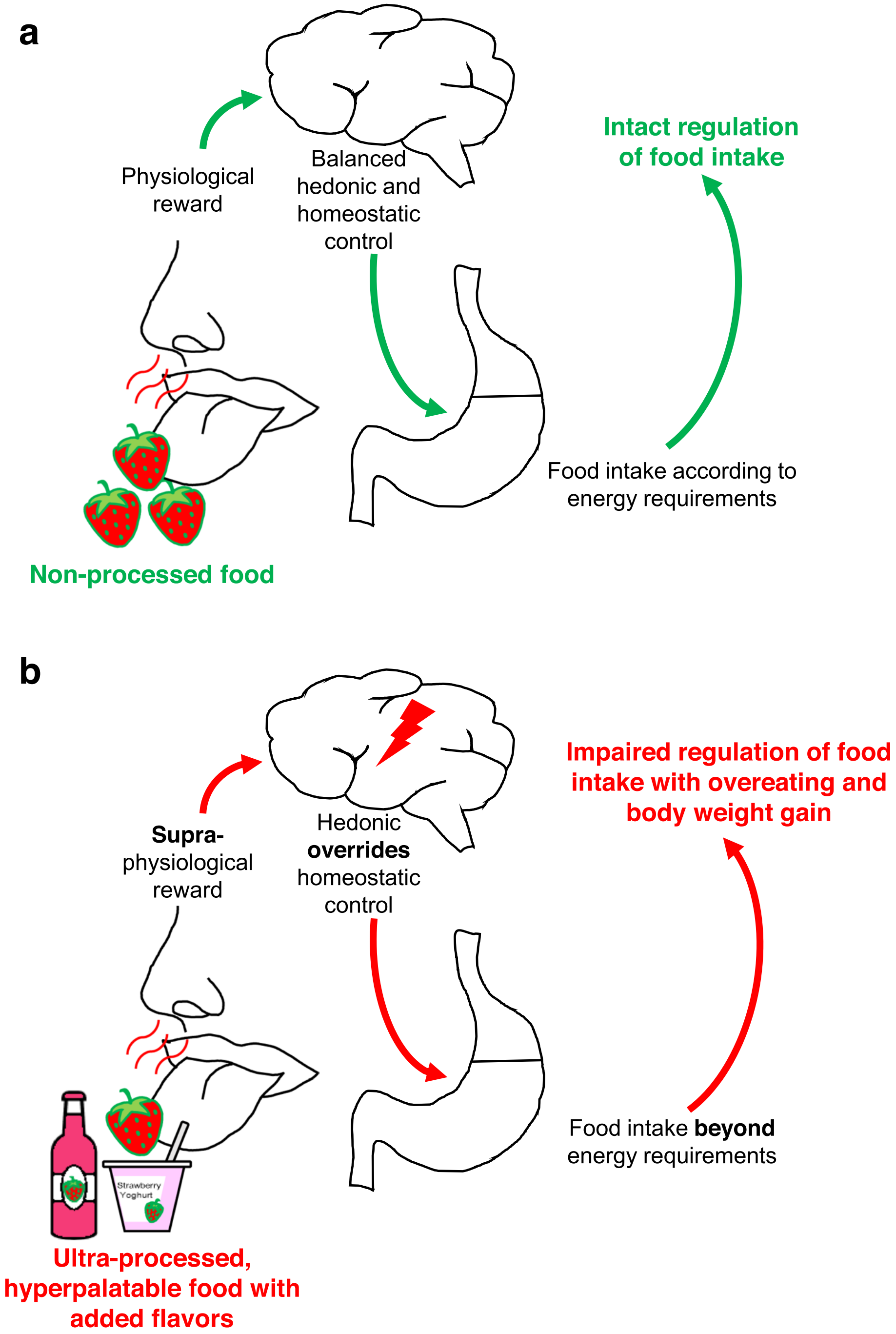

Fig. 1 Promotion of hedonic eating. Simplified presentation of hedonic eating **a** being balanced with homeostatic control (example: fresh strawberries) and **b** overriding homeostatic control (example: strawberry-flavored food items)

overridden, thereby, resulting in greater overall food intake [25, 26]. However, no study so far has analyzed the potential contribution of added flavors to excessive calorie intake and body weight gain in humans.

Disruption of flavor-nutrient learning

Added flavors might induce overeating and weight gain by disrupting flavor-nutrient learning and impairing the ability to predict nutrients in food items (Fig. 2). Flavor-nutrient learning describes the process of developing

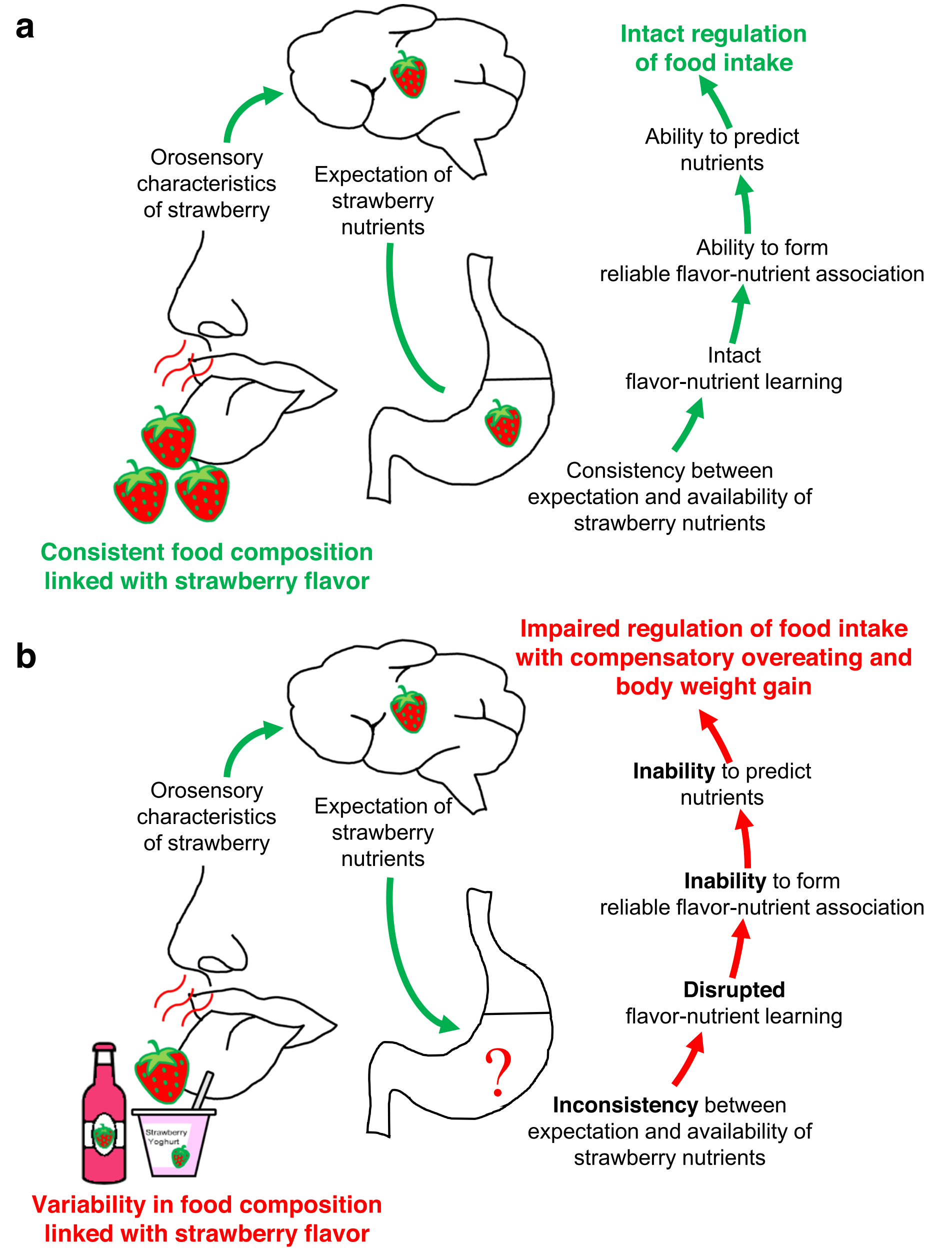

Fig. 2 Disruption of flavor-nutrient learning. Simplified presentation of (**a**) intact flavor-nutrient learning (example: fresh strawberries) and (**b**) disrupted flavor-nutrient learning (example: strawberry-flavored food items)

flavor-nutrient associations through repeated experiences with the orosensory characteristics of a food and the subsequent physiological impacts and postingestive consequences [31, 32]. Due to these learned associations, food intake can be matched to nutritional needs (Fig. 2a) [33, 34]. Figure 2a provides a simplified overview of intact flavor-nutrient learning using the example of fresh strawberries. Their orosensory characteristics are always linked with nutrients of real strawberries (Fig. 2a). This consistency between expected and available nutrients promotes an intact flavor-nutrient learning which allows the formation of reliable flavor-nutrient associations and correct predictions of nutrients in the future with subsequent intact regulation of food intake (Fig. 2a).

Added flavors potentially cause inconsistency between orosensory characteristics of a meal and associated nutrients. Products might taste similar despite differences in their nutritional composition which causes a higher variability in food composition linked with a specific flavor. Convincing evidence suggests that variability leads to disruption of flavor-nutrient learning which subsequently impairs both formation of reliable flavor-nutrient associations and proper regulation of food intake causing overeating and subsequent body weight gain [32].

Figure 2b provides a simplified overview of disrupted flavor-nutrient learning using the example of strawberry-flavored food items besides fresh strawberries. These products have a similar taste despite differences in energy and nutrient content inducing inconsistency between expected and available strawberry nutrients which causes disruption of flavor-nutrient learning (Fig. 2b). As a consequence, the inability to correctly predict nutrients leads to compensatory overeating and body weight gain (Fig. 2b). It is interesting to note in this context that rats exposed to inconsistent flavor-calorie pairings gained about 7% more weight than control rats exposed to a consistent flavor-calorie relationship [33]. Similarly, humans familiar with a wide variability of pizzas with different energy content have a lower expected satiation of a pizza and a decreased ability to compensate calories of eaten pizza in a subsequent test meal [35].

Added flavors in animal feed

Added flavors have been used in the production of animal feed for more than 40 years [36]. In pigs, they are applied in the weaning period in combination with synthetic sweeteners [37]. Palatant additives like added flavors are also included in a wide range of ruminant feed, e.g., milk replacers, mineral premix, compound, and concentrated feed [38]. The use of added flavors in calves is approved and recognized as absolutely necessary [37]. Although there is evidence that the feed intake can also be increased in cattle, the higher costs for flavored feed might make the use of added flavors unattractive to farmers [37]. Added flavors are also common additives for reward items in horses [37].

Added flavors are actively promoted by feed additive manufacturers. One manufacturer states that its flavors "are used by some of the biggest feed companies in the world" [39]. The same manufacturer suggests that "feeding pigs with a well-balanced diet that is highly palatable is essential for optimal growth performance and production efficiency" and that "flavors are useful tools to improve palatability and feed intake" [40]. Another manufacturer states that "addition of flavors to ruminant diets is a useful tool to improve palatability, increase feed intake and performance parameters" [38].

Various studies have assessed the impact of added flavors on feed intake, as well as body weight, in animals and the main results are summarized below and in Additional file 2. Furthermore, the species used, period of life, duration of intervention period, and added flavor tested are presented for each study in Additional file 2. There is a large diversity in reports assessing the use of added flavors in animal nutrition. In general, three different study designs and endpoints can be distinguished:

1) The first kind of studies tested the preference of animals regarding flavored and non-flavored feed. The same animals were exposed at the same time period to one or more feeds with added flavors (intervention) and a non-flavored feed (control). Feed intake per time unit was the primary outcome in these experiments. It was significantly higher for at least one added flavor tested in the intervention as compared to the control in studies in goats [41] and ponies [42]. However, one preference study did not find differences between flavored and non-flavored feed in lactating cows [43] and another study even described a significantly lower intake of flavored feed in post-weaning piglets [44].
2) In a second type of studies using a within-subject design, the same animals were exposed consecutively to one or more feeds with added flavors (intervention) and non-flavored feed (control). Feed intake and body weight gain per time interval were the primary outcomes in these experiments. They were higher in the intervention as compared to the control for orange flavor in a study with calves but no difference was found in the feed intake of second-lactation cows [45]. In another study in baboons, there was a trend towards higher feed intake for one (chocolate, fruit punch, lemon, orange) but not another (apple, lemon, orange, sugar) set of added flavors [46]. In a second experiment, consecutive application of a punch and orange flavor increased the feed intake [46]. The authors concluded that the results "may be useful for producing a nonhuman primate model of obesity" [46]. However, the study had two major drawbacks which might bias the findings: First, the proportion of simple carbohydrates was different between flavored (25%) and unflavored (5%) chow. Second, the unflavored feed was also offered during the intervention period.
3) In a third kind of studies, applying a between-subject design, groups of different animals were exposed to either one or more feeds with added flavors (intervention) or non-flavored feed (control). Comparisons of feed intake, body weight gain, and final body weight between the intervention and control groups were the primary outcomes in these experiments. Feed intake was significantly higher in the intervention as compared to the control for at least one added flavor in various studies in pre-weaning piglets

[47–50], post-weaning piglets [47, 49, 51], lactating sows [52], and pre-weaning calves [53], and there was a trend towards higher feed intake in pre-weaning and post-weaning piglets [47], as well as post-weaning calves [54]. Body weight gain was significantly higher in the intervention as compared to the control for at least one added flavor in several reports in pre-weaning piglets [52], post-weaning piglets, and growing pigs [47–50, 55, 56], as well as in pre-weaning calves [53, 54] and in calves generally [57]. There was a trend towards higher body weight gain in post-weaning piglets [51] and post-weaning calves [54]. Furthermore, final body weight was significantly higher in the intervention as compared to the control group in pre-weaning piglets [47, 52], post-weaning piglets [47, 55], and pre-weaning and post-weaning calves [53]. In some reports, body weight tended to be higher in post-weaning piglets [50] and in calves [57]. However, several studies did not observe differences between the intervention and control groups in at least one period of life concerning feed intake [44, 48, 50, 51, 53–62], body weight gain [44, 47–49, 51–53, 58–61], and final body weight [44, 49, 50, 52, 56, 58–60]. One study shows convincingly that novel flavors unconditionally suppress weight gain but not feed intake in the absence of flavor-calorie associations in rats [62].

Combined, these studies indicate that added flavors can increase feed intake, body weight gain, and final body weight. However, none of these animal studies focused on the mechanisms for these effects. Therefore, additional studies should assess how promotion of hedonic eating, disruption of flavor-nutrient learning, and other potential mechanisms contribute to increased feed intake, body weight gain, and final body weight. Moreover, results were heterogeneous and changes in feed intake, body weight gain, and final body weight were not always in the same direction. A major drawback is that several between-subject design studies did not assess all three endpoints (Additional file 2). Furthermore, flavor preference cannot be elucidated in animals directly, e.g., with consumer sensory evaluation as in humans [63], but only indirectly by measuring differences in feed intake. It needs to be elucidated in future studies how these data in animals related to flavored versus non-flavored diets can be translated to human obesity.

Use of added flavors in human nutrition

Within the European Union, flavor substances must be approved before they can be added to food in human nutrition [2]. Their safety is evaluated by the European Food Safety Authority and approved flavor substances are listed in a positive list in Annex I of regulation 1334/2008 [2, 64]. In the US, the Food Additives Amendment from 1958 distinguishes between food additives which have to be approved by the Food and Drug Administration and substances graded as “generally recognized as safe” by qualified experts [65–67]. Nevertheless, approval of added flavors within the European Union and the US does not require testing concerning endpoints like body weight gain and no such studies in humans have been published to the best of our knowledge.

The use of added flavors in human nutrition reaches far back in the past with monks in the medieval age already using natural substances obtained by distillation from plant material to flavor food [68]. The industrial production of flavors started in the nineteenth century with the first flavor compounds being isolated from natural sources [69]. Soon, chemical synthesis of flavor substances started, e.g., the production of vanillin synthesized by Tiemann and Haarmann in 1874 [69, 70]. The production of flavors and fragrances has been closely linked within one industry, called the flavor and fragrance industry, with almost equal market shares of the flavor and fragrance parts [71]. In the twentieth century, some decisive changes advanced the flavor and fragrance industry. These include the discovery of spray-drying flavors in 1930 [72] and the invention of gas chromatography in the 1960s which led to further exploration and discovery of flavors [73, 74]. Around the same time, there was a trend towards a healthier lifestyle and consumers attached importance to the naturalness of their food [75, 76]. This led to a shift from synthetic to natural flavors and was a challenge for the flavor and fragrance industry which at that time was focused on the development of new synthetic flavors [75]. Due to this increasing consumer demand, natural flavors in flavored food novelties increased from about 35% in 1965 to 80% in 1995 with a concomitant decrease in prices for naturals [75].

In the second half of the twentieth century, the worldwide flavor and fragrance industry expanded tremendously. For the US flavor and fragrance industry, sales adjusted for 2020 US$ value increased from US$ 1.9 billion in 1963 to US$ 7.0 billion in 2013 (Additional file 3) [77–90]. In parallel to the growth of the flavor and fragrance industry, there was an increase in US obesity prevalence from 13.4% in 1961 to 38.2% in 2013/2014 (Additional file 3) [91]. The parallel increase in obesity rates and flavor and fragrance industry sales does not serve as a proof in itself for weight-inducing effects of added flavors since there is no evidence available that shows a correlation between the two factors. Furthermore, the flavor and fragrance industry is a broad category and does not necessarily reflect the increase in sales of added flavors.

Conclusions

The present opinion article analyzes the potential contribution of added flavors to excessive calorie intake and body weight gain in animals and humans. Added flavors are extensively tested concerning toxicity but no studies in humans exist examining the link between added flavors, food intake, and body weight gain. Therefore, only indirect evidence is available at present that added flavors might contribute to obesity in humans.

Based on the arguments presented in the current opinion article, the role of added flavors in human food intake regulation and body weight control needs to be assessed in future studies. More specifically, the following three knowledge gaps should be addressed within the next 10 years:

1. Differences in food intake between food items with added flavors and their non-flavored counterparts need to be assessed by consumer sensory evaluations and double-blind controlled trials in human volunteers.
2. The effectiveness of obesity interventions specifically targeting food items with added flavors should be elucidated within randomized controlled trials and compared to established treatments.
3. Independent associations between added flavor intake and relevant health outcomes including metabolic, as well as cardiovascular, morbidity, and mortality, should be defined in epidemiological cohorts.

Furthermore, it needs to be assessed how promotion of hedonic eating, disruption of flavor-nutrient learning, and other potential mechanisms might contribute to the overconsumption of flavored food and obesity risk in humans. In addition, policy strategies should be implemented which enable consumers to choose unflavored food items more easily. In most countries, added flavors are labeled on the ingredient list of packaged food [3, 92]. However, added flavors usually cannot be readily recognized in food prepared outside the home. Identification in this type of food is of importance since its consumption in the US has increased from 17% of average energy intake in 1977/1978 to 34% in 2011/2012 [93].

Addressing these gaps, outcomes, and policy strategies will better define the role of added flavors in human body weight control and potentially pave the way for novel, effective obesity treatment modalities which are urgently needed [94, 95].

Abbreviations

EAH: Eating in the absence of hunger; US: United States of America.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-022-02619-3.

Additional file 1. Literature search.

Additional file 2. Studies on feed with added flavors (intervention) as compared to unflavored feed (control) in animal experiments.

Additional file 3. Obesity prevalence in the US and inflation-adjusted US flavor and fragrance industry sales since 1960.

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Authors' contributions

NJN and MF conceived the research and wrote the article. The authors read and approved the final manuscript. MF is the guarantor of the manuscript and accepts full responsibility for the work, had access to the data, and controlled the decision to publish. He attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information file.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details
[1]Institute of Nutritional Science, Justus-Liebig-University of Giessen, 35390 Giessen, Germany. [2]Department of Internal Medicine (Endocrinology, Nephrology, and Rheumatology), University of Leipzig, Leipzig, Germany.

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Publisher's Note

Additional file 1. Literature search

The Opinion article is based on a literature search in PubMed, PMC, ScienceDirect, and Google Scholar up to September 1, 2021 with the following search terms or their combinations: “flavor”, “aroma”, “feed intake”, “hedonic eating”, “flavor-nutrient learning”, “body weight”, and “obesity”.

In addition to the keyword-based literature search, the following journals of the flavor and fragrance industry, as well as animal nutrition and livestock farming, were searched by hand (years in parentheses): Perfumery and Essential Oil Record (1951 to 1969), The Flavor Industry (1970 to 1974), International flavors and food additives: IFFA (1975 to 1979), Food: food ingredients & processing international (1980 to 1991), American Perfumer and Cosmetics (1959 to 1971), Perfumer and Flavorist international (1976 to 1980), Perfumer and Flavorist (1980 to 2017), FeedMagazine (2001 to 2020), Pig Progress (2016 to 2020), Dairy Global (2016 to 2020), All About Feed (2016 to 2020), World Poultry (2016 to 2020), Future Farming (2017 to 2020), including special editions. A further literature search was performed based on references cited in the articles found.

The literature was analyzed and structured by both authors. Inclusion criteria were as follows: Only studies with relevant obesity-associated endpoints including food/feed intake, body weight gain, and final body weight were included. In addition, the development of the flavor and fragrance industry including basic information about flavors, legal aspects, and sales, as well as time trends in obesity prevalence in humans and mechanistic studies concerning hedonic eating and flavor-nutrient learning were researched. Exclusion criteria were as follows: Research with a focus on phytogenic feed additives was excluded since they show various physiologic effects beyond flavoring of feed [8, 9]. Furthermore, studies on sweeteners were not included since their role in body weight control has been well summarized in recent reviews [10–13]. Animal studies elucidating the influence of flavors on feed intake and body weight were excluded if no adequate control group without flavor addition was present of if flavors were added combined with phytogenic feed additives and/or sweeteners.

Additional file 2. Studies on feed with added flavors (intervention) as compared to unflavored feed (control) in animal experiments[1]

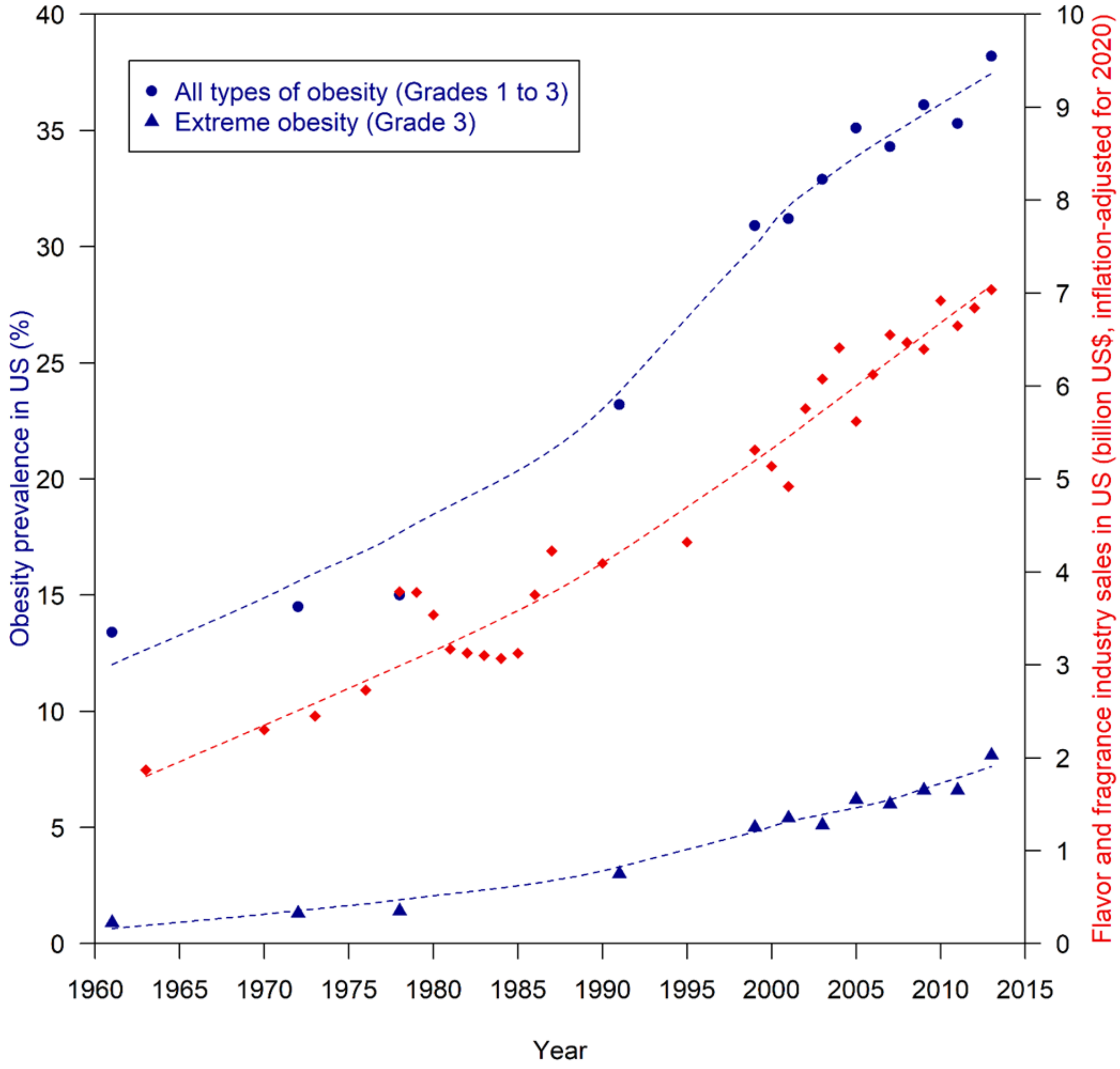
Study type	First author Year (Ref.)	Animals in I and C groups	Species	Period of life	Duration of I	Added flavor tested	Feed intake	Body weight gain	Final body weight	Further comments
1	De Rosa 2002 [41]	Same	Goat	2 to 3 y	6 d within 14 d	Clover, Ryegrass	↑[a]	n.p.	n.p.	[a]$p < 0.001$ for ryegrass in two of two sessions; $p < 0.05$ for clover in one of two sessions
	Khelil-Arfa 2021 [42]	Same[#]	Pony	4 to 13 y	5 d	Anis, Apple, Caramel, Raspberry	↑[a]	n.p.	n.p.	[a]$p < 0.05$ only for apple
	Harper 2016 [43]	Same[#]	Cattle	Lactation	6 d	Anise, Fenugreek, Honey, Molasses, Orange, Thyme, Vanilla	↔	n.p.	n.p.	Experiment not adequately controlled for strong effect of bin position and C feed not included on each day
	Seabolt 2010 [44]	Same	Pig	Post-weaning	2 d	Creamy and milky cheese profile with sweet and vanilla bottom notes (Luctarom®)	↓[a]	n.p.	n.p.	[a]$p < 0.01$
2	Thomas 2007 [45]	Same[†,#]	Cattle	Calves	21 d (3x7 d)	Orange, Vanilla added to water	↑[a]	↑[b]	n.p.	[a]$p < 0.05$; [b]$p < 0.05$ only for orange
		Same[†]		Second-lactation	28 d (4x7 d)	Orange added to water	↔	n.d.	n.p.	-
	Wene 1982 [46]	Same[†,#]	Baboon	7 to 15 y	48 d	Chocolate, Fruit punch, Lemon, Orange	(↑)[a]	n.d.	n.p.	[a]$p = 0.052$; The proportion of simple carbohydrates was different between flavored (25 %) and unflavored (5 %) chow which might bias the findings; Unflavored feed was also offered in I period
		Same[†,#]			48 d	Apple, Lemon, Orange, Sugar	↔	n.d.	n.p.	
		Same[†,#]			185 d	Orange, Punch	↑[a]	n.d.	n.p.	[a]$p = 0.034$
3	Danielsen 1991 [47]	Different	Pig	Pre-weaning	14 d	Cream, Strawberry	↑[a], (↑)[b]	↔	↑[c]	[a]$p < 0.05$ for cream; [b]$p \leq 0.1$ for strawberry; [c]p not given, 0.2 kg higher; [d]p not given,
				Post-weaning	21 d		↑[a], (↑)[b]	↑[a]	↑[d]	

				Entire period	35 d		$\uparrow^{a}$, $(\uparrow)^{b}$	$\uparrow^{a,e}$	$\uparrow^{d}$	0.7 kg higher; $^{e}p < 0.05$ for strawberry
	Yan 2011 [48]	Different	Pig	Pre-weaning	17 d	Cheese, Vanilla	$\uparrow^{a}$	↔	n.d.	$^{a}p < 0.05$ only for cheese; $^{b}p < 0.05$
				Post-weaning	7 d		↔	$\uparrow^{b}$	n.d.	
	Wang 2014 [49]	Different	Pig	Pre-weaning	21 d	Fruit-milk, Fruit-milk-anis	$\uparrow^{a}$	↔	↔	$^{a}p < 0.05$ only for fruit-milk-anis; $^{b}p < 0.01$ only for fruit-milk-anis
				Post-weaning	8 d		$\uparrow^{b}$	$\uparrow^{b}$	↔	
	Adeleye 2014 [50]	Different$^{\#}$	Pig	Pre-weaning	19 d	Apple, Apricot, Butterscotch, Red fruit, Toffee	$\uparrow^{a}$	n.d.	↔	$^{a}p = 0.01$
				Post-weaning	14 d	-	↔	$\uparrow^{a}$	$(\uparrow)^{b}$	$^{a}p = 0.03$; $^{b}p = 0.07$
	King 1979 [51]	Different	Pig	Pre-weaning	27 d	Firanor	↔	↔	n.d.	$^{a}p < 0.05$ only for piglets receiving flavored starter weaned from sows receiving flavored feed; ^{b}Same comparison as above, no specific p given but trend described in text
				Post-weaning	31 d		$\uparrow^{a}$	$(\uparrow)^{b}$	n.d.	
	Silva 2018 [52]	Different	Pig	Lactation	24 d	Krave® AP in sow feed (2 concentrations)	$\uparrow^{a}$	↔	↔	$^{a}p < 0.001$
				Pre-weaning			n.d.	$\uparrow^{a}$	$\uparrow^{b}$	$^{a}p < 0.001$ only for higher concentration; $^{b}p < 0.001$
	Fathi 2009 [53]	Different	Cattle	Pre-weaning	~ 60 d	Vanilla	$\uparrow^{a}$	$\uparrow^{b}$	$\uparrow^{a}$	$^{a}p = 0.03$; $^{b}p = 0.01$; $^{c}p = 0.02$
				Post-weaning	~ 21 d		↔	↔	$\uparrow^{c}$	
				Entire period	81 d		$\uparrow^{c}$	↔	$\uparrow^{c}$	
	Thomsen 1980 [54]	Different	Cattle	Pre-weaning	30 d	Butter, Maple , Milk	↔	$\uparrow^{a}$	n.d.	$^{a}p < 0.05$ only for maple-flavored starter; $^{b}p < 0.1$ only for maple-flavored starter; $^{c}p < 0.1$ only for milk-flavored starter
				Post-weaning	21 d		$(\uparrow)^{b}$	$(\uparrow)^{b}$	n.d.	
				Entire period	51 d		$(\uparrow)^{b}$	$\uparrow^{a}$, $(\uparrow)^{c}$	n.d.	
	Torrallardona 2000 [55]	Different	Pig	Post-weaning	35 d	Luctarom® (4 profiles)	↔	$\uparrow^{a}$	$\uparrow^{a}$	$^{a}p = 0.01$ all profiles combined compared to C

3	Lv 2012 [56]	Different	Pig	95 d	14 d	Banana, Milk	↔	↑[a]	↔	[a]p < 0.05
	Dusel 2006 [57]	Different	Cattle	Calves	70 d	CuxArom Toffee Vanilla	↔[a]	↑[b]	(↑)[c]	[a]Intake of feed with added flavor only which was restricted from day 43 onwards; [b]p = 0.045; [c]p = 0.078
	Seabolt 2010 [44]	Different	Pig	Post-weaning	35 d	Creamy and milky cheese profile with sweet and vanilla bottom notes (Luctarom®)	↔	↔	↔	-
	McLaughlin 1983 [58]	Different	Pig	Post-weaning	35 d	Cheese, Sweet-molasses-caramel	↔	↔	n.d.	-
				Pre-weaning	8 d	Cheese, Commercial flavor, Sweet-molasses-caramel	n.d.	↔	↔	-
				Post-weaning	35 d		↔	↔	n.d.	
	Sulabo 2010 [59]	Different	Pig	Pre-weaning	4 d	Luctarom®	↔	↔	↔	-
				Post-weaning	28 d		↔	↔	↔	
	Danielsen 1981 [60]	Different	Pig	Pre-weaning	21 d	Suk-aroma	↔	n.d.	↔	-
				Post-weaning	35 d		↔	↔	↔	
	Naim 1985 [61]	Different[#]	Rat	n.d.	23 d	Bacon, Beef, Bread, Cheddar cheese, Cheese paste, Chicken, Chocolate, Liver, Nacho cheese, Peanut, Salami, Vanilla	↔	↔	n.d.	I group was exposed to both flavored and unflavored feed throughout the I period
	Seitz 2020 [62]	Different	Rat	n.d.	21 d	Peppermint	↔	↓[a]	n.d.	[a]p < 0.05 observed at three different flavor intensities

[1] Abbreviations used: C, Control; d, Days; I, Intervention; n.d., No data; n.p., Not possible due to study design; y, Years; ↑ indicates significant increase, ↓ significant decrease, ↔ no significant difference of intervention as compared to control, () trend, i.e., p < 0.10 and/or authors describe trend in text; [†]Intervention and control at different time points with same animals (i.e., within-subject design); [#]More than one added flavor was fed during one experimental setting to animals in the intervention group; Different animals refers to between-subject design; If a time range for the intervention was given, the shortest period was chosen as duration of intervention; Half days were rounded off; Start and end days of the intervention were counted as full days; Intervention groups with additional sweeteners or without added flavors were excluded from the table.

Additional file 3. Obesity prevalence in the US and inflation-adjusted US flavor and fragrance industry sales since 1960[1]



[1] Estimates for prevalence of obesity and extreme obesity are based on the National Health and Nutrition Examination Survey (NHANES) cohort, ages 20 to 74 years [91]. Years on the x-axis for NHANES data were assigned to the rounded off midpoint of the respective study period [91]. Estimates for sales of US flavor and fragrance industry are based on market figures [77–89]. In case of worldwide sales, US market share was calculated at 26.5 % using the average of three US market share data at different time points [80, 82, 83]. The sales in 1963 were calculated through the reported 6.6 % annual growth of the US flavor and fragrance industry from 1963 to 1973 based on sales in 1973 [77]. US flavor and fragrance industry sales are inflation-adjusted for 2020 US$ value [90]. Lines were fitted by locally estimated scatterplot smoothing.

2.2 Publication 2: Flavour, emulsifiers, and colour are the most frequent markers to detect food ultra-processing in a UK food market analysis.

Author information

Nathalie Judith Neumann[1,*], Gerrit Eichner[2] and Mathias Fasshauer[1,3]
[1]Institute of Nutritional Science, Justus Liebig University Giessen, 35390 Giessen, Germany
[2]Mathematical Institute, Justus Liebig University Giessen, 35392 Giessen, Germany
[3]Center for Sustainable Food Systems, Justus Liebig University Giessen, 35390 Giessen, Germany
*Correspondence: nathalie.neumann@ernaehrung.uni-giessen.de

Authors' contributions

NJN, GE and MF conceived the research and wrote the first draft. NJN researched commercial food items from the two market leaders of groceries in the UK. Statistical analyses were performed by all authors. All authors have read, redacted and approved the final manuscript. NJN is the guarantor of the manuscript and accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Summary

Research gap 2 was addressed in the publication “Flavour, emulsifiers, and colour are the most frequent markers to detect food ultra-processing in a UK food market analysis.”(88).

Within this publication, the NOVA classification was formalised by defining NOVA group 4 through all mentioned MUP(3,13) and their corresponding search terms. Moreover, it was analysed which MUP and which MUP combinations are the best to detect UPF in a British food market analysis.

The analysis was based on the Oxford WebQ, a web-based 24-hour dietary assessment tool of 206 food and 32 beverage items which include all major foods consumed in the UK(89,90). For each Oxford WebQ item, up to ten matching commercial products were researched online with data from the two UK grocery market leaders, i.e., Tesco and Sainsbury’s(91). In total, 2146 different products were researched. No ingredient lists could be found for 310 food items, e.g., meat, fish, fruit, vegetables, eggs, oils, nuts, and seeds, as well as water and alcoholic beverages such as wine and spirits. These products were excluded because European law does not require the listing of ingredients for this type of food(92). Therefore, the final analysis included ingredient lists of 1836 food items.

According to two publications by Monteiro et al.(3,13), sixty-five MUP and their corresponding search terms were classified in nine categories, i.e., flavours, flavour enhancers, colouring agents, sweeteners, processing aids, varieties of sugar, modified oils, protein sources, and fibres. The ingredient lists of the 1836 foods were searched for the sixty-five MUP. If at least one of the MUP was present in a product, this food items was classified as UPF.

In total, 990 of the 1836 food items (53.9 %) were positive for at least one of the MUP and, therefore, defined as UPF. The most prevalent MUP were flavour (578 products, 58.4 % of all UPF), emulsifier (353, 35.7 %), colour (262, 26.5 %), dextrose (163, 16.5 %), whey (145, 14.6 %), and gluten (100, 10.1 %). In addition, 24 MUP were found in 1 % to 10 % of all UPF and 13 MUP were present in less than 1 % of all UPF.

The best combination of two MUP for UPF detection was flavour and emulsifier with 720 detected UPF (72.7 %). With the most successful combination of three, i.e., flavour, emulsifier, and colour, 784 UPF were detected (79.2 %). The best combination of four was flavour, emulsifier, colour, and fibre detecting 820 UPF (82.8 %). Detection rate increased to 85.8 % of all UPF if ingredient lists were analysed concerning one additional of the MUP, i.e., dextrose.

Almost 90 % of all UPF could be detected by six MUP, i.e., flavour, emulsifier, colour, fibre, dextrose, and firming agent (88.4 %).

In conclusion, the study shows that the NOVA classification can be formalised with a MUP-based reproducible approach to detect UPF. This approach enables consumers to identify almost 80 % and 90 % of all UPF by searching the ingredient lists for three and six MUP, respectively.

The published manuscript is attached.

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Public Health Nutrition

Flavour, emulsifiers and colour are the most frequent markers to detect food ultra-processing in a UK food market analysis

Nathalie Judith Neumann[1,]*, Gerrit Eichner[2] and Mathias Fasshauer[1,3]
[1]Institute of Nutritional Science, Justus-Liebig University of Giessen, Goethestr. 55, Giessen, Hessen 35390, Germany: [2]Mathematical Institute, Justus-Liebig University of Giessen, Giessen, Germany: [3]Center for Sustainable Food Systems, Justus-Liebig University of Giessen, Giessen, Germany

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Abstract

Objective: To elucidate which markers of ultra-processing (MUP) and their combinations are best suited to detect ultra-processed food (UPF).
Design: The study was based on the 206 food and 32 beverage items of the Oxford WebQ which encompass all major foods consumed in the UK. For each Oxford WebQ question, ingredient lists of up to ten matching different commercial products (*n* 2146) were researched online using data from the two market leaders of groceries in the UK sorted by relevance (Tesco) and by top sellers (Sainsbury's), respectively. According to the NOVA classification, sixty-five MUP were defined, and if the ingredient list of a food product was positive for at least one MUP, it was regarded as UPF. The percentage of UPF items containing specific MUP was calculated. In addition, all combinations of two to six different MUP were assessed concerning the percentage of identified UPF items.
Setting: Cross-sectional analysis.
Participants: None.
Results: A total of 990 products contained at least one MUP and were, therefore, regarded as UPF. The most frequent MUP were flavour (578 items, 58·4 % of all UPF), emulsifiers (353 items, 35·7 % of all UPF) and colour (262 items, 26·5 % of all UPF). Combined, these three MUP detected 79·2 % of all UPF products. Detection rate increased to 88·4 % of all UPF if ingredient lists were analysed concerning three additional MUP, that is, fibre, dextrose and firming agent.
Conclusions: Almost 90 % of all UPF items can be detected by six MUP.

Keywords
Food additives
Markers of ultra-processing
NOVA classification
Ultra-processed food

Over the decades, the rising prevalence of obesity has become a major public health threat that is increasingly evident around the world(1). Obesity has a significant impact on the global incidence of CVD, type 2 diabetes mellitus, cancer, osteoarthritis, work disability and sleep apnoea(1).

A strong positive link exists between the consumption of ultra-processed food (UPF) and the risk of overweight and obesity(2). UPF is defined as ready-to-consume or heat-up food items high in fat, salt and sugar, as well as low in dietary fibre, protein and micronutrients, usually packaged attractively and marketed intensively(3). Ultra-processing is used to create products that are convenient, hyper-palatable, and highly profitable and can replace other food groups(3). There is a substantial expansion in the types and quantities of UPF sold worldwide, representing a transition towards a more highly processed global diet(4). Limiting highly processed food or UPF has been recommended in several nutrition guidelines, including Brazil(5), Canada(6), Ecuador(7), France(8), Israel(9), Japan(10), New Zealand(11) and Peru(12).

Industrial food processing is assessed by the NOVA classification, a food-rating scheme based on the extent and purpose of processing and, thus, distance from nature, which classifies food and food products into four groups(3,13). Processing according to the NOVA classification includes physical, biological and chemical methods during the manufacturing process(3). Unprocessed and minimally processed food together form NOVA group 1(13). NOVA group 2 contains processed culinary ingredients like oil, sugar and salt which are obtained from group 1 or directly from nature(13). Processed industrial products made by adding those culinary ingredients belong to NOVA

GE and MF contributed equally to this work and are joint senior authors

**Corresponding author*: Email nathalie.neumann@ernaehrung.uni-giessen.de

group 3[13]. UPF is defined as NOVA group 4, and several cosmetic additives, as well as non-culinary ingredients, are exclusively found in this group[13]. Cosmetic additives, for example, flavours, colouring agents and sweeteners, make the final products more palatable or appealing[13]. Non-culinary ingredients are food substances never or rarely used in the kitchen, for example, varieties of sugars such as dextrose or fructose, modified oils and protein sources such as casein or soya protein isolates[13]. The use of these additives and ingredients can mask undesirable sensory characteristics and improve sensory properties[13]. A food product is defined as NOVA group 4 if its ingredient list contains at least one cosmetic additive or non-culinary ingredient[13]. Even in the absence of cosmetic additives or non-culinary ingredients, a food item is also regarded as UPF if some drastic processes are applied directly to the food, for example, extrusion, hydrogenation, hydrolysation, moulding, pre-frying or puffing[3,13,14].

Focusing on cosmetic additives and non-culinary ingredients has been suggested as one approach to simplify the assessment of UPF[13]. Davidou and co-workers were the first to define a specific and exhaustive list of markers of ultra-processing (MUP) for the NOVA-based Siga classification[14]. However, more than 100 different MUP have been described[3,13,14] which makes the detection of UPF difficult. Therefore, the present study elucidates which MUP and combinations of them are best suited to detect UPF in a UK food market analysis.

Methods

Search strategy to select food products

All assessments concerning MUP were based on the Oxford WebQ. The Oxford WebQ is an online dietary questionnaire assessing food and beverage intake from the previous day[15]. Similar to a 24-h dietary recall by an interviewer, the Oxford WebQ provides quantitative information on all foods and beverages consumed[15]. A total of 206 food and 32 beverage items are assessed in the Oxford WebQ[16]. These food and beverage items encompass all major foods consumed in the UK and, therefore, the Oxford WebQ is best suited to study UK populations[15]. Food items are evaluated independent from specific brands, for example, intake of 'chocolate biscuits (e.g. choc chip cookies, chocolate digestive biscuits)' is assessed but not consumption of specific chocolate biscuits brands.

For each Oxford WebQ question, ingredient lists of up to ten matching commercial products from the two market leaders of groceries in the UK, that is, Tesco and Sainsbury's[17], were analysed. Online research within the subcategories best matching the Oxford WebQ questions was primarily done at Tesco (https://www.tesco.com/groceries/en-GB) and in case of fewer than ten items found there also at Sainsbury's (https://www.sainsburys.co.uk/shop/gb/groceries). Food products within the chosen categories were sorted by relevance (Tesco) or by top sellers (Sainsbury's). The first ten products matching the Oxford WebQ questions were chosen. If different flavours of the same brand, for example, chocolate and strawberry ice cream of the same brand, were listed within these top ten, they were included in the analysis. In case of fewer than ten matching products found at Tesco and Sainsbury's combined, all available products were included in the analysis.

The Oxford WebQ has been developed and validated for adult participants only[18–20]. Accordingly, the Oxford WebQ has been exclusively used in large studies with adult participants[15]. Therefore, food specifically targeting children, for example, having the words 'kids' or 'children' on the packaging, was excluded from the present analysis.

Ingredient lists of food products

In total, 2146 different products were analysed in the present study concerning the 238 Oxford WebQ items. If no ingredient lists were given, a further internet search was performed on www.amazon.co.uk and other product information sites. For 310 food products, no ingredient lists could be found. These include unprocessed meat, fish, fruit, vegetables, eggs, oils, nuts, and seeds, as well as water and alcoholic beverages such as wine and spirits. European law does not require mandatory provision of ingredient lists for these types of food[21]. Items without ingredient lists were excluded from further analysis. The ingredient lists of the remaining 1836 food products were recorded.

MUPs

According to two recent publications by Monteiro and co-workers[3,13], sixty-five MUP were defined based on nine categories, that is, flavours, flavour enhancers, colouring agents, sweeteners, processing aids, varieties of sugar, modified oils, protein sources, and fibres, and their individual compounds (see online Supplemental Table 1). All MUP were optimised for maximal detection of individual compounds, for example, the MUP 'glutam*' identifies individual compounds such as glutamic acid, monosodium glutamate and magnesium diglutamate (see online Supplemental Table 1). Ingredient lists of the 1836 food products were analysed concerning the sixty-five MUP. If a food product was positive for at least one MUP, it was regarded as UPF. If an additive was not a MUP in all circumstances, for example, maltodextrin is a MUP if used as a bulking agent but not if used as a stabiliser (i.e. in this context a marker for NOVA group 3[3]), it was regarded as a MUP nevertheless. If a MUP could be classified into different functional classes, for example, maltodextrin in the categories processing aids and varieties of sugar, the decision about the most appropriate category was reached by the consensus of all authors.

Statistical analysis

All data analyses and graphical representations were performed using R version 4.0.5. The sixty-five MUP were extracted from the ingredient lists and sorted by frequency. The percentage of UPF items containing specific MUP was calculated. In addition, all combinations of two to six different MUP were assessed, and the percentage of UPF items identified by these combinations was calculated. The respective combinations with the highest UPF detection rate were graphically represented using Venn diagrams.

Results

Frequency of single MUP in UPF

Of the 1836 food products with ingredient lists, 990 (53·9 %) were positive for at least one MUP and, therefore, defined as UPF. Within these 990 UPF products, forty-three MUP were detected at least once, whereas twenty-two MUP were not found in the ingredient lists (Table 1). The most frequent MUP with a frequency >10 % of all UPF were flavour (578 products, 58·4 % of all UPF), emulsif* (353 products, 35·7 % of all UPF), colour (262 products, 26·5 % of all UPF), dextrose (163 products, 16·5 % of all UPF), whey (145 products, 14·6 % of all UPF) and gluten (100 products, 10·1 % of all UPF) (Table 1). From the MUP identified in at least one product, a total of twenty-four and thirteen MUP were present in 1 % to 10 % and in less than 1 % of UPF, respectively (Table 1).

Combinations of MUP

Flavour was the MUP detecting the highest proportion of UPF products (578 of 990; 58·4 %; Table 1 and Fig. 1(a)). Next, it was assessed how many UPF products can be detected maximally by two to six combinations of MUP. The most successful combination of two was flavour and emulsif*. Thus, flavour and emulsif* alone detected 367 and 142 UPF items, respectively, and the combination of both terms detected an additional 211 UPF items, resulting in a total of 720 out of 990 UPF products (72·7 %; Fig. 1(b)). The most successful combination of three was flavour, emulsif* and colour detecting 784 UPF items (i.e. 245 flavour alone, 134 emulsif* alone, 64 colour alone, 143 combination of flavour and emulsif*, 122 combination of flavour and colour, 8 combination of emulsif* and colour, 68 combination of flavour, emulsif*, and colour; 79·2 %; Fig. 1(c)). With the most successful combination of four, that is, flavour, emulsif*, colour and fibre, 820 UPF products were detected (82·8 %, Fig. 1(d)). The most successful combination of five consisting of flavour, emulsif*, colour, fibre and dextrose detected 849 UPF items (85·8 %, Fig. 1(e)). With a combination of six MUP, that is, flavour, emulsif*, colour, fibre, dextrose and firming, almost 90 % of the UPF products were identified (875 UPF products, 88·4 %, Fig. 1(f)).

Discussion

Principal findings

In the present study, MUP are assessed for the first time in a large sample of commercial products to elucidate the most successful combinations for UPF detection. The results enable consumers to strike the optimal individual balance between the number of MUP to remember on the one hand and the proportion of UPF items identified correctly on the other hand. Thus, already 58·4 % and 72·7 % of UPF can be detected with a single MUP, that is, flavour, and the MUP combination of flavour and emulsif*, respectively. Almost 90 % of UPF can be identified with the combination of six MUP, that is, flavour, emulsif*, colour, fibre, dextrose and firming. Future studies should assess whether consumers can successfully identify UPF in the supermarket by using this MUP-based approach. In particular, experiments should elucidate which number of MUP can be recalled and correctly applied to specific products.

Comparison with other studies

In the current study, 53·9 % of the 1836 food products with ingredient lists are positive for at least one MUP and, therefore, defined as UPF. Using a similar approach in a large-scale database of foods and beverages available on the French market, 53·8 % of products with an ingredient list, that is, 68 110 out of 126 556, contained at least one food additive(22). Interestingly, 17·8 % had one, 11·6 % two, 7·8 % three, 5·3 % four and 11·3 % five or more food additives(22). In a study from Australia, 4794 out of 7322 food items (65·5 %) are defined as UPF(23). Similarly, 67 % of 24 932 packaged food items from France are UPF(14). In a study by the same authors, the percentage of MUP dextrose is similar to the current findings, whereas other MUP including protein isolates are more frequently observed on the French market as compared to the present UK sample(24). In agreement with the current results, most MUP are present in less than 10 % of UPF items(24). However, to the best of our knowledge, the present study is the first to assess which MUP combinations detect the maximum number of UPF products.

Added flavours are by far the most prevalent MUP being detected in 58·4 % of UPF. In accordance with the present findings, extracts/natural flavours and synthetic flavours are present in 42·7 % and 26·5 % of UPF, respectively, in a representative and weighted food offer found in overall French supermarkets(24). Evidence has recently been presented that added flavours might induce overeating and body weight gain(25). Thus, added flavours override homoeostatic control of food intake by the promotion of hedonic eating(25). Furthermore, they impair the ability to predict nutrients in food items via disruption of flavour-nutrient learning(25). Taking these results and our current findings into consideration, added flavours might not only be the MUP detecting the maximum number of UPF, but

Table 1 MUP sorted by frequency†

Ranking	MUP	Frequency	% UPF‡
1	Flavour	578	58·4
2	Emulsif*	353	35·7
3	Colour	262	26·5
4	Dextrose	163	16·5
5	Whey	145	14·6
6	Gluten	100	10·1
7	Fibre	93	9·4
8	Barley malt extract	79	8·0
9	Sweetener	76	7·7
10	Maltodextrin	74	7·5
11	Fructose	72	7·3
12	Gelling	65	6·6
13	Thickener	64	6·5
14	Humectant	63	6·4
15	Invert*	62	6·3
16	Lactose	56	5·7
17	Firming	44	4·4
18	Caking	28	2·8
19	Sucralose	28	2·8
20	Acesulfame	27	2·7
21	Glazing	26	2·6
22	Flavour enhancer	25	2·5
23	Glutam*	20	2·0
24	Steviol	20	2·0
25	Aspartame	17	1·7
26	Ribonucleotide*	17	1·7
27	Isomalt	16	1·6
28	Sorbitol	14	1·4
29	Bulking	10	1·0
30	Hydrolysed	10	1·0
31	Maltitol	8	0·8
32	Saccharin	8	0·8
33	Erythritol	7	0·7
34	Hydrogenated	7	0·7
35	Isolate*	5	0·5
36	Inosin*	4	0·4
37	Guanyl*	3	0·3
38	E95*	2	0·2
39	Sequestrant	2	0·2
40	E62*	1	0·1
41	E63*	1	0·1
42	Foaming	1	0·1
43	Xylitol	1	0·1

All variations after the word are possible (e.g. glutamic and glutamate are possible for glutam).

†The following twenty-two MUP were not found in any of the ingredient lists: advantame, carbonating, casein, cyclam*, dye, E420, E421, E640, E650, E96*, glycine, interesterified, lactitol, maltol, mannitol, mechanically separated meat, msg, neohesperidine, neotame, polyglycitol, thaumatin and zinc acetate.

‡% UPF indicates which percentage of UPF items (*n* 975) were positive for the respective MUP.

they might also be ingredients actively promoting obesity and its consequences.

Besides added flavours, emulsifiers, colouring agents, dextrose, whey and gluten are found in more than 10 % of all UPF. It has been suggested that some common food emulsifiers induce metabolic and chronic inflammatory disease by altering the gut microbiome and intestinal barrier(26). Dextrose is a monosaccharide which is regarded as a free sugar when added to food items by the manufacturer(27). Free sugars have been convincingly linked to body weight gain and, therefore, the WHO suggests to limit free sugar consumption to less than 10 % of total energy intake per day(27). Moreover, the addition of gluten to a normal chow and a high-fat diet increases body weight and fat deposits without changing food intake in mice(28). Whereas colour variety can enhance selection, no increase on continuous food intake has been demonstrated(29). Furthermore, whey protein supplementation might improve body weight and total fat mass in overweight and obese subjects(30). Together these data suggest that emulsifiers, dextrose and gluten are not only relevant as MUP, but they might also directly contribute to conditions favouring metabolic disease, that is, low-grade inflammation (emulsifiers), increased food intake (dextrose) and body weight gain (dextrose and gluten). Further studies need to elucidate their role, as well as the role of other MUP, in the development of metabolic disease in more detail.

Health and policy implications

Besides overweight and obesity(2), increased UPF consumption has been convincingly linked with other adverse outcomes. Thus, a significant 1·6-fold increase in all-cause mortality is detected in a Spanish prospective cohort study (*n* 19 899) if subjects with the highest UPF consumption are compared to the lowest UPF intake(31). In agreement with these findings, all-cause and CVD mortality are increased 1·4-fold and 1·7-fold, respectively, in subjects from Italy presenting with a history of CVD (*n* 1171) when comparing the highest with the lowest quartile of UPF intake(32). Risk for CVD is also significantly increased 1·2-fold in a large prospective cohort study from France (*n* 105 159) in the highest as compared to the lowest consumption category for UPF(33). Dementia risk is increased 1·3-fold if the proportion of UPF in the diet increases by 10 % in subjects from the UK (*n* 72 083)(34). Incident depression risk is increased 1·2-fold for a 10 % increase in UPF consumption in a study from France (*n* 26 730)(35). Furthermore, the risk of inflammatory bowel disease increases 1·8-fold in a prospective cohort study in twenty-one low-, middle- and high-income countries (*n* 116 087) in the highest as compared to the lowest UPF consumption group(36). Moreover, UPF consumption in the highest as compared to the lowest quartile is associated with a 1·2-fold and 1·1-fold increase in overall cancer mortality and morbidity, respectively, in a prospective UK study (*n* 197 426)(37).

Therefore, consumers should recognise and consciously avoid UPF. The present study enables consumers to identify almost 80 % and 90 % of all UPF items by searching the ingredient lists for three and six MUP, respectively. This MUP-based approach considerably simplifies UPF detection. However, consumers still need to study ingredient lists to identify UPF and ingredient lists are not always available, for example, in food prepared outside the home. Therefore, public policy strategies should be implemented which enable consumers to avoid UPF items more easily without the need for studying ingredient lists. The WHO

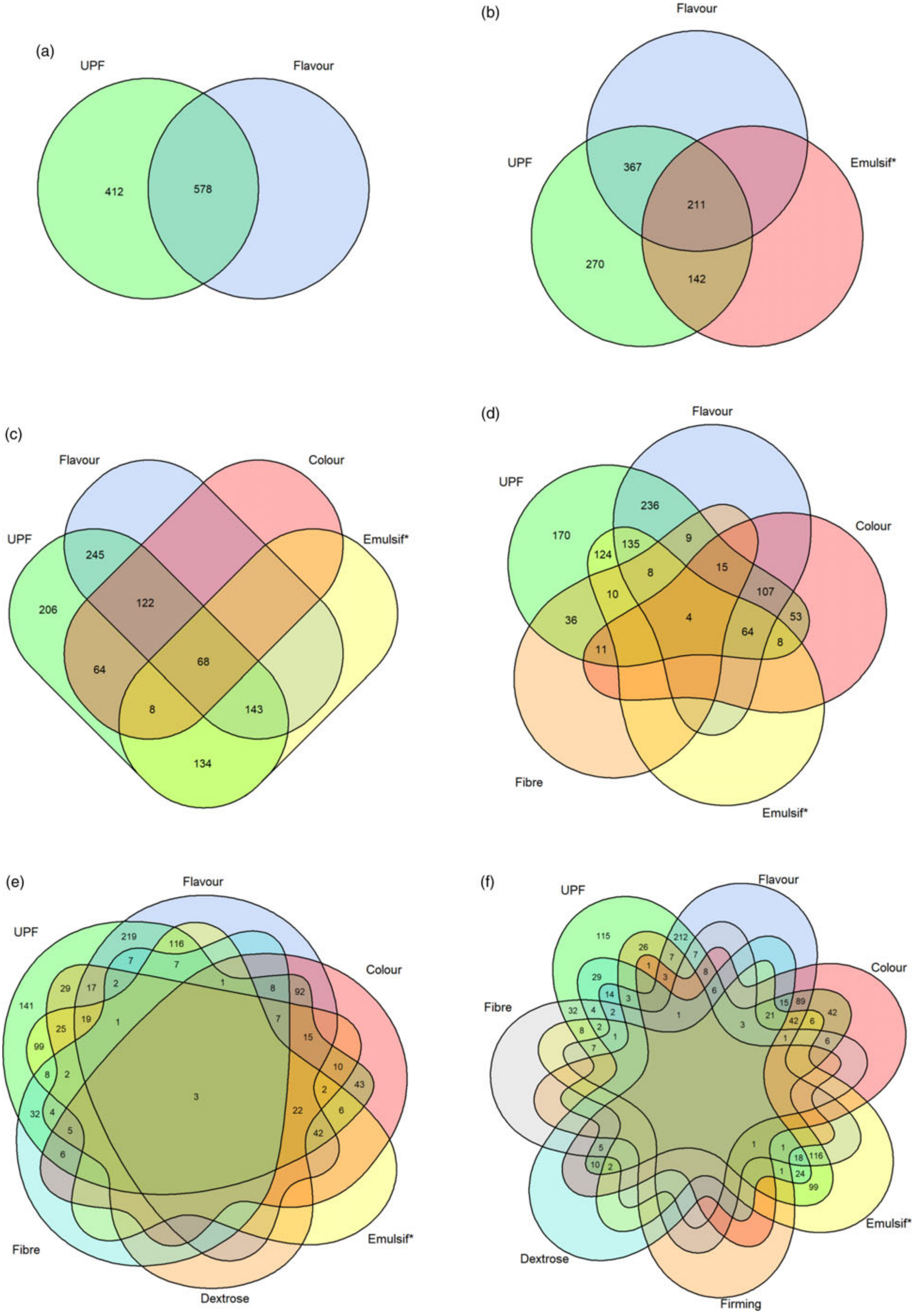

Fig. 1 Venn diagrams depicting combinations of (a) one, (b) two, (c) three, (d) four, (e) five and (f) six MUP which detected the maximum number of UPF products (total *n* 990)

recommends the use of front-of-package labelling (FOPL) and reformulation of food products to create healthy food and drink environments(38). FOPL like the Nutri-Score improves the ability of participants to rank products according to healthiness correctly and offers the potential to increase sales of healthy food items(39,40). Furthermore, FOPL provides incentives for manufacturers to decrease the level of processing by changing product compositions(41,42). The NOVA group of food items can be depicted by a FOPL(43). Furthermore, a novel nutrition classification scheme combining level of processing and nutrient thresholds for Na and free sugars has recently been proposed(23). Similarly, the Pan American Health Organization Nutrient Profile Model not only defines UPF but also sets thresholds for critical nutrients, including free sugars, Na, total fat, saturated fat, trans fat and sweeteners(44). Identification of UPF items enables policymakers to reduce UPF consumption on a population level, for example, by taxation(45,46). Real-world evaluation studies suggest that taxation of sugar-sweetened beverages reduces purchases and consumption of this important UPF category(47). Further, public health policies to limit UPF intake besides FOPL and taxation include restrictions on the marketing of unhealthy food targeting children, regulation of school food environments and reexamination of agricultural subsidies(44).

Strengths and limitations of this study

Strengths of the current study include a large sample size of commercial food items, structured detection of UPF with defined MUP and analyses not only of single MUP but also of their combinations.

A limitation is that only the UK market was analysed and the distribution of MUP in UPF might be different in other countries. Furthermore, food items without an ingredient list had to be excluded from the analysis. In most cases, it can be assumed that these products are not UPF, for example, fruits, vegetables, and eggs, and, thus, their exclusion has no impact on the results of the current study. However, other food items without ingredients lists might be in part UPF, especially some types of alcoholic beverages.

It has been convincingly shown recently that detection of UPF items differs depending on the approach used and the selection of individual MUP(48). Furthermore, food can also be UPF in the absence of MUP if processes like extrusion, hydrolysation and, pre-frying are applied(3,13,14). Therefore, the MUP-based approach used in the current study might underestimate the proportion of UPF items. However, information on processes like extrusion, hydrolysation and pre-frying cannot be easily obtained by individual consumers in contrast to information about MUP which can be extracted from ingredient lists. Moreover, the possibility of hidden additives in food products, for example, compound ingredients not thoroughly described in the ingredient list, cannot be excluded and might underestimate the proportion of UPF items. On the other hand, some additives defined as MUP in the current study are not MUP in all circumstances, for example, maltodextrin if used as a stabiliser, which might incorrectly identify some food items as UPF. Moreover, the proportion of UPF detected by MUP and the number of MUP per product might depend on the type of food or food category. However, food groups are not studied separately in the present analysis, since its aim is to elucidate which MUP and their combinations are best suited to detect UPF over the whole range of food.

In the present study, food specifically targeting children has been excluded from the analysis, since the Oxford WebQ has only been developed for and used in adult participants. It is important to note in this context that in a recent study from France, 88 % of food specifically targeting children over the age of 3 years is UPF(49). Furthermore, in a report from Portugal, 56 % of food products for children aged 0 to 3 years are UPF(50).

Conclusions

Based on research of commercial food items from the two market leaders of groceries in the UK, the present study enables consumers to identify almost 80 % and 90 % of all UPF items by searching the ingredient lists for three and six MUP, respectively. These findings might help consumers to make healthier choices when shopping for groceries by avoiding UPF which has been consistently linked with a broad range of adverse outcomes. In addition, they can also help researchers in food classification in dietary surveys.

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Conflicts of interest

There are no conflicts of interest.

Authorship

N.J.N., G.E. and M.F. conceived the research and wrote the first draft. N.J.N. researched commercial food items from the two market leaders of groceries in the UK. Statistical analyses were performed by all authors. All authors have read, redacted and approved the final manuscript. N.J.N. is the guarantor of the manuscript and accepts full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethics of human subject participation

Not applicable.

Supplementary material

For supplementary material accompanying this paper visit https://doi.org/10.1017/S1368980023002185

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Supplementary Table 1

MUPs and their individual compounds within the nine categories[1]

Category	**MUPs**	**Individual compound**
Cosmetic additives		
1. Flavours	1. Flavour	Flavor Flavour
2. Flavour enhancers	2. E62*	E620 – E629
	3. E63*	E630 – E637
	4. E640	E640
	5. E650	E650
	6. Flavour enhancer	Flavour enhancer
	7. Glutam*	Calcium diglutamate Glutamic acid Magnesium diglutamate Monoammonium glutamate Monopotassium glutamate Monosodium glutamate
	8. Glycine	Glycine Glycine and its sodium salt
	9. Guanyl*	Calcium guanylate Dipotassium guanylate Disodium guanylate Guanylic acid Sodium guanylate
	10. Inosin*	Calcium inosinate Dipotassium inosinate Disodium inosinate Inosinic acid
	11. Maltol	Ethyl maltol Maltol
	12. MSG	MSG
	13. Ribonucleotide*	Calcium 5'-ribonucleotides Disodium 5'-ribonucleotides
	14. Zinc acetate	Zinc acetate
3. Colouring agents	15. Colour	Colour Colour stabiliser
	16. Dye	Dye
4. Sweeteners	17. Acesulfame	Acesulfame K Salt of aspartame-acesulfame
	18. Advantame	Advantame
	19. Aspartame	Aspartame Salt of aspartame-acesulfame
	20. Cyclam*	Cyclamate Cyclamic acid
	21. E420	E420
	22. E421	E421
	23. E95*	E950 – E959
	24. E96*	E960 – E969
	25. Erythritol	Erythritol

	26. Isomalt	Isomalt
	27. Lactitol	Lactitol
	28. Maltitol	Maltitol Maltitol syrup
	29. Mannitol	Mannitol
	30. Neohesperidine	Neohesperidine DC
	31. Neotame	Neotame
	32. Polyglycitol	Polyglycitol
	33. Saccharin	Saccharin
	34. Sorbitol	Sorbitol Sorbitol syrup
	35. Steviol	Steviol glycoside
	36. Sucralose	Sucralose
	37. Sweetener	Sweetener
	38. Thaumatin	Thaumatin
	39. Xylitol	Xylitol
5. Processing aids	40. Bulking	Anti-bulking Bulking agent
	41. Caking	Anti-caking agent Anticaking agent
	42. Carbonating	Carbonating agent
	43. Emulsif*	Emulsifier Emulsifying salts
	44. Firming	Firming agent
	45. Foaming	Anti-foaming agent De-foaming agent Foaming agent
	46. Gelling	Gelling agent
	47. Glazing	Glazing agent
	48. Humectant	Humectant
	49. Sequestrant	Sequestrant
	50. Thickener	Thickener
Non-culinary ingredients		
6. Varieties of sugar	51. Barley malt extract	Barley malt extract#
	52. Dextrose	Dextrose Polydextrose#
	53. Fructose	Fructose Fructose-glucose syrup# Glucose-fructose syrup# High-fructose corn syrup
	54. Invert*	Inverted refiners syrup# Inverted sugar syrup# Invert sugar
	55. Lactose	Lactose
	56. Maltodextrin	Maltodextrin
7. Modified oils	57. Hydrogenated	Hydrogenated oil
	58. Interesterified	Interesterified oil
8. Protein sources	59. Casein	Casein
	60. Gluten	Gluten

	61. Hydrolysed	Hydrolysed protein
	62. Isolate*	Isolated soy protein Protein isolate# Soy protein isolate
	63. Mechanically separated meat	Mechanically separated meat
	64. Whey	Dried whey# Whey# Whey derivatives# Whey permeate# Whey powder# Whey protein Whey solids#
9. Fibres	65. Fibre	Fibre Fibre isolate# Insoluble fibre Soluble fibre

[1] Individual compounds are based on NOVA group 4(3,13). *Indicates that all variations of the word are possible (e.g., glutamic and glutamate are possible for glutam*). #Indicates individual compounds which are not literally mentioned in the two publications(3,13) but which are related to the ultra-processing compounds mentioned.

2.3 Publication 3: Ultra-processing markers are more prevalent in plant-based meat products as compared to their meat-based counterparts in a German food market analysis.

Author information

Kemja-Maria Metz[1], Nathalie Judith Neumann[1,*] and Mathias Fasshauer[1,2]

[1]Institute of Nutritional Science, Justus Liebig University Giessen, 35390 Giessen, Germany

[2]Center for Sustainable Food Systems, Justus Liebig University Giessen, 35390 Giessen, Germany

*Correspondence: nathalie.neumann@ernaehrung.uni-giessen.de

KMM and NJN contributed equally to this work and are joint first authors.

Authors' contributions

KMM, NJN and MF conceived the research and wrote the first draft. The product selection was done by two authors (KMM and MF) and ingredient lists, as well as nutritional information, were extracted from the chosen PBMP and MBP by one author (KMM). Statistical analyses were performed by all authors. All authors have read, redacted and approved the final manuscript. KMM and NJN are the guarantors of the manuscript and accept full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Summary

Research gap 3 was addressed in the publication "Ultra-processing markers are more prevalent in plant-based meat products as compared to their meat-based counterparts in a German food market analysis."(93).

Within this publication, MUP (called ultra-processing markers in the manuscript) and nutrient composition in PBMP were compared with equivalent meat-based products (MBP) on the German food market.

For the analysis, a total of 282 PBMP were assessed, first in local stores of the top four German food store chains, i.e., Edeka, Rewe, Lidl, and Aldi, and second through an online search of all companies selling PBMP at these chains. Based on principles of the German Food Book for meat and meat products(94), as well as for fish, crustaceans, and molluscs(95), PBMP were grouped in 18 product categories. For each product category, comparable MBP were researched via the Rewe (www.rewe.de) and Bofrost (www.bofrost.de) online stores, as well as through local Aldi and Lidl stores. A total of 149 MBP were included in the final analysis. For all PBMP and MBP, ingredient lists and nutrient compositions were extracted. Based on the NOVA classification(3,13), MUP were identified in English and their German equivalents were researched and adapted resulting in 33 German search terms. These MUP were classified in six ultra-processing bullet categories, i.e., flavour, flavour enhancer, sweetener, colour, other cosmetic additives, and non-culinary ingredients. All ingredient lists of the PBMP and MBP were analysed concerning these 33 MUP and six ultra-processing bullet categories. A product was regarded as UPF if it was positive for at least one of the MUP. Nutrient composition and proportion of MUP in PBMP and MBP were compared using chi-square test for categorical variables and Mann-Whitney U test for continuous parameters with $p < 0.05$ considered as statistically significant.

PBMP had a significantly higher proportion (88 % of all products) of UPF compared to MBP (52 %). Sweeteners were not found in any product. The proportion of the five remaining ultra-processing bullet categories was significantly higher in PBMP as compared to MBP. Of the 33 MUP, 23 were detected in at least one PBMP or MBP. Of these 23 MUP, 18 were more frequent in PBMP as compared to MBP. Flavour (70 %) and dextrose (41 %) were the most frequent MUP in PBMP and MBP, respectively. Concerning nutrient composition, median energy, total fat, saturated fat, and protein content of the PBMP were significantly lower compared to MBP. In contrast, the amounts of carbohydrate, sugar, fibre, and salt were significantly higher in PBMP.

In conclusion, this publication shows that the MUP concept to assess UPF can be transferred to the German food market by translating the English MUP into adequate German search terms. Moreover, the data indicate that MUP are significantly more prevalent in PBMP compared to MBP whereas some aspects of the nutrient composition of PBMP appear favourable.

The published manuscript is attached.

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Ultra-processing markers are more prevalent in plant-based meat products as compared to their meat-based counterparts in a German food market analysis

Kemja-Maria Metz[1], Nathalie Judith Neumann[1,]* and Mathias Fasshauer[1,2]
[1]Institute of Nutritional Science, Justus-Liebig University of Giessen, Goethestr. 55, Giessen, Hessen 35390, Germany:
[2]Center for Sustainable Food Systems, Justus-Liebig University of Giessen, Giessen, Hessen, Germany

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Abstract

Objective: To compare ultra-processing markers and nutrient composition in plant-based meat products (PBMP) with equivalent meat-based products (MBP).
Design: A total of 282 PBMP and 149 MBP within 18 product categories were assessed. Based on the NOVA classification, 33 ultra-processing markers were identified and six ultra-processing bullet categories were defined, that is flavour, flavour enhancer, sweetener, colour, other cosmetic additives and non-culinary ingredients. The ingredient lists were analysed concerning these ultra-processing markers and ultra-processing bullet categories, as well as nutrient composition, for all PBMP and MBP. Differences between PBMP and MBP were assessed using chi-square and Mann-Whitney U tests, respectively.
Setting: Cross-sectional analysis.
Participants: 282 PBMP and 149 MBP.
Results: The percentage of ultra-processed food (UPF) items was significantly higher in PBMP (88 %) as compared to MBP (52 %) ($P < 0{\cdot}0001$). The proportion of UPF items was numerically higher in 15 out of 18 product categories with differences in six categories reaching statistical significance ($P < 0{\cdot}05$). Flavour, flavour enhancer, colour, other cosmetic additives and non-culinary ingredients were significantly more prevalent in PBMP as compared to MBP ($P < 0{\cdot}0001$). Concerning nutrient composition, median energy, total fat, saturated fat and protein content were significantly lower, whereas the amounts of carbohydrate, sugar, fibre and salt were significantly higher in PBMP ($P < 0{\cdot}05$).
Conclusions: Ultra-processing markers are significantly more prevalent in PBMP as compared to MBP. Since UPF intake has been convincingly linked to metabolic and CVD, substituting MBP with PBMP might have negative net health effects.

Keywords
Metabolic syndrome
NOVA classification
Nutrient composition
Plant-based meat products
Ultra-processed food

During recent decades, there has been a considerable shift towards more plant-based dietary patterns[1]. Thus, the proportion of 12- to 17-year-old adolescents in Germany following a vegetarian diet more than tripled within 10 years, that is it increased from 1·6 % in 2006 to 5·0 % in 2015 to 2017[2]. A plant-based diet not only has the potential to improve human health but also to reduce the impact on the environment as compared to animal-based food products[3]. Furthermore, ethical considerations play a major role when choosing a plant-based diet[1,2].

The growing interest in vegetarian diets is leading to an increasing demand for plant-based meat products (PBMP)[4]. PBMP replace meat in the human diet and are intended to mimic the texture, taste and appearance of meat[5,6]. About two-thirds of the US American population have eaten PBMP in the past year at least once according to a recent survey[7]. Interestingly, 22 % and 20 % consumed PBMP daily and at least weekly, respectively[7]. The market for PBMP has been growing rapidly worldwide and extends beyond the vegetarian market to include meat-loving consumers who want to reduce their meat consumption for health, environmental and ethical reasons[8]. Thus, in the USA the market value of plant-based food products grew from 680 767 to 939 459 $ between 2017 and 2019 corresponding to an 38 % increase in sales over 2 years[9]. Future sales of plant-based alternatives are expected to

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KMM and NJN contributed equally to this work and are joint first authors.

*Corresponding author: Email nathalie.neumann@ernaehrung.uni-giessen.de

increase globally from $29·4 billion in 2020 to $162 billion by 2030(10).

Previous studies on PBMP focused on potential health benefits by assessing nutrient composition as compared to meat-based products (MBP). Most studies show convincingly that PBMP have a lower energy density(4,11,12), as well as contain less total fat and SFA(11–15) as compared to MBP. In contrast, carbohydrates(4,12,14–16) and dietary fibre(4,11,12,14–16) are higher in PBMP than in MBP. The salt content of PBMP is higher compared to MBP in some(11,13) but not all(14) studies. The amount of protein is the same(15,16) or lower(11,12,14) but protein quality also needs to be considered.

Besides nutrient composition, the extent of processing is an important parameter to evaluate the quality of food items(17). The NOVA classification assesses the extent and purpose of food processing and classifies food products into four groups according to their distance from nature(17,18). Processing according to the NOVA classification includes physical, biological and chemical methods during the manufacturing process, as well as the use of additives(17,18). Cosmetic additives, including flavours, colouring agents and sweeteners, make food products more palatable or appealing(18). Non-culinary ingredients such as fructose, modified oils and protein sources are food substances never or rarely used in the kitchen(18). If an ingredient list contains at least one cosmetic additive or non-culinary ingredient, the product is defined as NOVA group 4, that is ultra-processed food (UPF)(18). Besides the NOVA classification, other systems based on food processing have also been proposed, for example systems suggested by the International Food Information Council Foundation, the International Agency for Research on Cancer, and the National Institute of Public Health in Mexico(19). Compared to these systems, the NOVA classification rates highest in terms of quality since it is most specific, coherent, clear, comprehensive and workable(19).

UPF is ready-to-consume or heat up, and it is usually packaged attractively and marketed intensively(17). It is high in fat, salt and sugar, as well as low in dietary fibre, protein and micronutrients(17). By ultra-processing, products are created that are convenient, hyper-palatable, highly profitable and can replace other food groups(17). Increased consumption of UPF items has been convincingly linked with increased all-cause mortality(20,21), cardiovascular mortality(21), cardiovascular morbidity(22), dementia(23), inflammatory bowel disease(24) and obesity(25). Based on this convincing evidence, avoiding highly processed or UPF has been recommended in several nutrition guidelines including Brazil(26), Canada(27), Chile(28), Japan(29), New Zealand(30), Peru(31) and Uruguay(32).

In the present study, the proportion of ultra-processing is compared between PBMP and MBP overall, as well as in 18 product categories. Furthermore, six ultra-processing bullet categories, that is flavour, flavour enhancer, sweetener, colour, other cosmetic additives and non-culinary ingredients, as well as 33 ultra-processing markers, are assessed in PBMP and MBP using an ingredient list-based approach.

Methods

All research of PBMP and MBP was performed in the period from March 3, 2022 to May 3, 2022. The study was not registered, and the a priori protocol was not published before conducting the study.

Plant-based meat product survey and categorisation

A first screen of PBMP was performed onsite in local stores of the top four German food store chains, that is Edeka, Rewe, Lidl and Aldi. Ingredient lists and nutrient composition of these PBMP were extracted. In a second step, the websites of all companies selling PBMP at Edeka, Rewe, Lidl and Aldi were researched online to identify further PBMP not sold in these local food store chains. Ingredient lists and nutrient composition were also extracted from these additional PBMP. PBMP were defined as products actively marketed as MBP replacements, for example vegan/vegetarian minced meat, steak or sausage. Products traditionally used in vegetarian diets and not sold as MBP replacements such as tofu, tempeh and legumes were excluded from the search. However, if these traditional products were part of an actively marketed MBP replacement, for example tofu meat cut or tofu minced meat, they were included in the analysis. A total of 282 PBMP were included.

PBMP were grouped according to their product description, for example meatball, burger or steak. The guiding principles of the German Food Book for meat and meat products(33), as well as for fish, crustaceans and molluscs(34), were used to further specify the categorisation and to group similar meat alternatives into a single category. PBMP that were not listed in the guidelines(33,34), such as the south-eastern European specialty cevapcici, were assigned their own category due to their traditional recipe. If a minimum number of five PBMP were not reached within a category, they were assigned to the product categories ‘Others fish-based’ and ‘Others meat-based’. Using this approach, 18 separate product categories were obtained as shown in Table 1.

Meat-based product survey and categorisation

For all 18 PBMP categories, comparable MBP were researched using the Rewe online store (www.rewe.de) and sorted by popularity. The names of the product categories served as search terms. The number of comparison MBP was based on the number of PBMP as follows: If PBMP within a category were ≥ 10, ten

Table 1 Percentage of ultra-processing and six ultra-processing bullet categories in the total sample, as well as in the 18 product categories, of PBMP and MBP*

					Ultra-processing bullet categories									
			Ultra-processing		Flavour		Flavour enhancer		Colour		Other cosmetic additives		Non-culinary ingredients	
Product category	Group	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*
Total	MBP	149	52	77	8	12	5	8	1	1	7	11	48	71
	PBMP	282	**88**	**248§**	**70**	**198§**	**21**	**58§**	**17**	**48§**	**63**	**179§**	**77**	**216§**
Minced meat	MBP	10	0	0	0	0	0	0	0	0	0	0	0	0
	PBMP	26	**77**	**20‡**	**50**	**13†**	19	5	4	1	38	10	**62**	**16†**
Meatball	MBP	10	90	9	20	2	30	3	0	0	40	4	80	8
	PBMP	21	90	19	**81**	**17†**	29	6	5	1	62	13	90	19
Burger	MBP	10	10	1	10	1	10	1	0	0	10	1	10	1
	PBMP	33	**82**	**27‡**	**61**	**20†**	24	8	3	1	**64**	**21†**	**76**	**25‡**
Steak	MBP	5	0	0	0	0	0	0	0	0	0	0	0	0
	PBMP	6	67	4	67	4	0	0	17	1	67	4	50	3
Fillet strips	MBP	10	40	4	0	0	0	0	0	0	0	0	40	4
	PBMP	13	**100**	**13†**	**77**	**10†**	38	5	8	1	15	2	85	11
Sausage	MBP	10	70	7	10	1	0	0	0	0	0	0	70	7
	PBMP	26	96	25	**77**	**20†**	12	3	12	3	**69**	**18‡**	85	22
Kebab	MBP	5	100	5	20	1	20	1	0	0	20	1	100	5
	PBMP	7	86	6	57	4	14	1	0	0	14	1	71	5
Cevapcici	MBP	5	80	4	20	1	0	0	0	0	0	0	80	4
	PBMP	7	86	6	71	5	0	0	0	0	57	4	86	6
Schnitzel	MBP	10	80	8	0	0	0	0	0	0	0	0	80	8
	PBMP	31	97	30	**77**	**24§**	23	7	10	3	**84**	**26§**	90	28
Meat cut	MBP	10	30	3	20	2	20	2	10	1	0	0	10	1
	PBMP	14	64	9	36	5	0	0	0	0	29	4	64	9
Nuggets	MBP	10	70	7	20	2	0	0	0	0	0	0	70	7
	PBMP	25	**100**	**25†**	**80**	**20†**	32	8	8	2	**88**	**22§**	88	22
Salami	MBP	5	40	2	0	0	0	0	0	0	0	0	40	2
	PBMP	9	89	8	**78**	**7†**	44	4	**89**	**8†**	**89**	**8†**	89	8
Lunchmeat	MBP	10	70	7	10	1	10	1	0	0	0	0	70	7
	PBMP	22	73	16	**59**	**13†**	5	1	**41**	**9†**	**68**	**15†**	59	13
Meat paste	MBP	10	70	7	0	0	0	0	0	0	50	5	40	4
	PBMP	10	100	10	**100**	**10§**	40	4	**70**	**7†**	70	7	70	7
Pork sausage	MBP	10	90	9	10	1	0	0	0	0	0	0	90	9
	PBMP	12	83	10	**75**	**9†**	17	2	**50**	**6†**	**75**	**9†**	50	6
Fish fingers	MBP	10	20	2	0	0	0	0	0	0	0	0	20	2
	PBMP	11	**100**	**11‡**	**91**	**10‡**	18	2	18	2	**82**	**9‡**	**73**	**8†**
Others fish-based	MBP	5	0	0	0	0	0	0	0	0	0	0	0	0
	PBMP	5	**100**	**5†**	**100**	**5†**	20	1	40	2	80	4	**100**	**5†**
Others meat-based	MBP	4	50	2	0	0	0	0	0	0	0	0	50	2
	PBMP	4	100	4	50	2	25	1	25	1	50	2	75	3

*Ultra-processing and six ultra-processing bullet categories are presented as percentage and number.

†$P < 0{\cdot}05$.

‡$P < 0{\cdot}001$, and §$P < 0{\cdot}0001$ as assessed by chi-square test.

Values with statistically significant differences as compared to MBP are further indicated in bold.

PBMP, plant-based meat products; MBP, meat-based products.

comparison MBP were used; if PBMP within a category were < 10, five comparison MBP were chosen. If the required number of MBP was not reached by search in the Rewe online store, additional sources, that is local Aldi and Lidl stores, as well as the online Bofrost store (www.bofrost.de), were used. Based on this approach, 149 comparison MBP were included.

Assessment of ultra-processing and nutrient composition

According to Monteiro and co-workers(17,18), 33 ultra-processing markers were identified in English and their German equivalents were researched and adapted as summarised in Supplemental Table 1. Based on these ultra-processing markers, the following six ultra-processing bullet categories were defined: Flavour, flavour enhancer, sweetener, colour, other cosmetic additives and non-culinary ingredients (see online Supplemental Table 1). The ingredient lists for all PBMP and MBP were extracted and analysed concerning ultra-processing markers and bullet categories. If PBMP and MBP were positive for at least one ultra-processing marker, they were regarded as ultra-processed.

All nutritional information to be listed according to the European Union Food Information Regulation

No. 1169/2011[35], that is energy in kJ/100 g, as well as fat, saturated fat, carb, sugar, protein and salt in g/100 g, were recorded for all PBMP and MBP. Furthermore, dietary fibre in g/100 g was also captured.

Additional robustness analyses

Since raw meat product categories are typically non-ultra-processed, they were removed in one set of robustness analyses. More specifically, PBMP and MBP were compared after excluding the product categories of minced meat, burger, steak, fillet strips and meat cut.

An additional onsite robustness analysis was performed at two of the studied food retailers, that is at Rewe (4 Fernie Street, 35 394 Giessen, Germany; *n* PBMP = 87, *n* MBP = 243) and at Lidl (1–3 Georg Elser Street, 35 394 Giessen, Germany; *n* PBMP = 20, *n* MBP = 36). Here, information on all PBMP and all matching MBP was collected, that is the number of matching MBP was not restricted.

Statistical evaluation

Data were imported, processed, analysed and graphically displayed with R version 4.0.5[36]. PBMP and MBP overall and within product categories were compared using chi-square test for categorical variables and Mann-Whitney *U* test for continuous parameters. A *P*-value of < 0·05 was considered as statistically significant in all analyses.

Results

Proportion of ultra-processed food items in plant-based meat products and meat-based products

Overall, 282 PBMP were compared to 149 MBP and the main results are summarised in Table 1. The proportion of UPF items was significantly higher in PBMP (88 %) as compared to MBP (52 %) ($P < 0{\cdot}0001$; Table 1). Within the product categories, the proportion of UPF items was also significantly higher in PBMP *v.* MBP for minced meat (77 % *v.* 0 %), burger (82 % *v.* 10 %), fillet strips (100 % *v.* 40 %), nuggets (100 % *v.* 70 %), fish fingers (100 % *v.* 20 %) and others fish-based (100 % *v.* 0 %) (all $P < 0{\cdot}05$; Table 1). The proportion of UPF items was numerically but not significantly higher in PBMP *v.* MBP for steak (67 % *v.* 0 %), sausage (96 % *v.* 70 %), cevapcici (86 % *v.* 80 %), schnitzel (97 % *v.* 80 %), meat cut (64 % *v.* 30 %), salami (89 % *v.* 40 %), lunchmeat (73 % *v.* 70 %), meat paste (100 % *v.* 70 %) and others meat-based (100 % *v.* 50 %) (all $P > 0{\cdot}05$; Table 1). The proportion of UPF items was the same or numerically lower in PBMP *v.* MBP for meatball (90 % *v.* 90 %), kebab (86 % *v.* 100 %) and pork sausages (83 % *v.* 90 %) (all $P > 0{\cdot}05$; Table 1).

Ultra-processing bullet categories and markers in plant-based meat products and meat-based products

Sweeteners were not found in any PBMP and MBP. Of the remaining five ultra-processing bullet categories, non-culinary ingredients (77 %), flavour (70 %) and other cosmetic additives (63 %) were more frequently detected in PBMP as compared to flavour enhancer (21 %) and colour (17 %) (Table 1). In MBP, non-culinary ingredients was by far the most common ultra-processing bullet category (48 %) followed by flavour (8 %), other cosmetic additives (7 %), flavour enhancer (5 %) and colour (1 %) (Table 1). The proportion of all five ultra-processing bullet categories was significantly higher in PBMP as compared to MBP ($P < 0{\cdot}0001$, Table 1). In total, 23 out of the 33 ultra-processing markers summarised in Supplemental Table 1 were detected in at least one PBMP or MBP (Fig. 1). Of those, flavour (70 %) and dextrose (41 %) were the most frequently found in PBMP and MBP, respectively (Fig. 1). Of the 23 ultra-processing markers, 18 were more frequently found in PBMP as compared to MBP (Fig. 1).

The proportion of food items with flavour was also significantly higher in PBMP *v.* MBP in 13 out of the 18 product categories, that is minced meat, meatball, burger, fillet strips, sausage, schnitzel, nuggets, salami, lunchmeat, meat paste, pork sausage, fish fingers and others fish-based (all $P < 0{\cdot}05$; Table 1). PBMP did not show a significantly higher percentage of flavour enhancer compared to MBP in any of the 18 product categories. The share of colour in PBMP *v.* MBP was significantly higher in salami, lunchmeat, meat paste, and pork sausage (all $P < 0{\cdot}05$; Table 1). For other cosmetic additives, eight product categories showed a significantly higher proportion in PBMP as compared to MBP, that is burger, sausage, schnitzel, nuggets, salami, lunchmeat, pork sausage and fish fingers (all $P < 0{\cdot}05$; Table 1). The proportion of items with non-culinary ingredients was significantly higher in PBMP *v.* MBP in four product categories, that is minced meat, burger, fish fingers and others fish-based (all $P < 0{\cdot}05$; Table 1).

Nutrient composition of plant-based meat products and meat-based products

Median (range) values for the nutrient composition of PBMP and MBP are summarised in Table 2. Median energy (880·5 *v.* 972·0 kJ/100 g), total fat (11·0 *v.* 15·8 g/100 g), saturated fat (1·2 *v.* 4·0 g/100 g) and protein (14·1 *v.* 17·0 g/100 g) contents of the PBMP were significantly lower than the values of the MBP (all $P < 0{\cdot}05$; Table 2). In contrast, the amounts of carbohydrate (7·1 *v.* 1·0 g/100 g), sugar (1·5 *v.* 0·5 g/100 g), fibre (4·5 *v.* 0·3 g/100 g) and salt (1·6 *v.* 1·3 g/100 g) were significantly higher in PBMP as compared to MBP (all $P < 0{\cdot}05$; Table 2). There was significant heterogeneity in nutrient composition between PBMP and MBP within the 18 different product categories (Table 2).

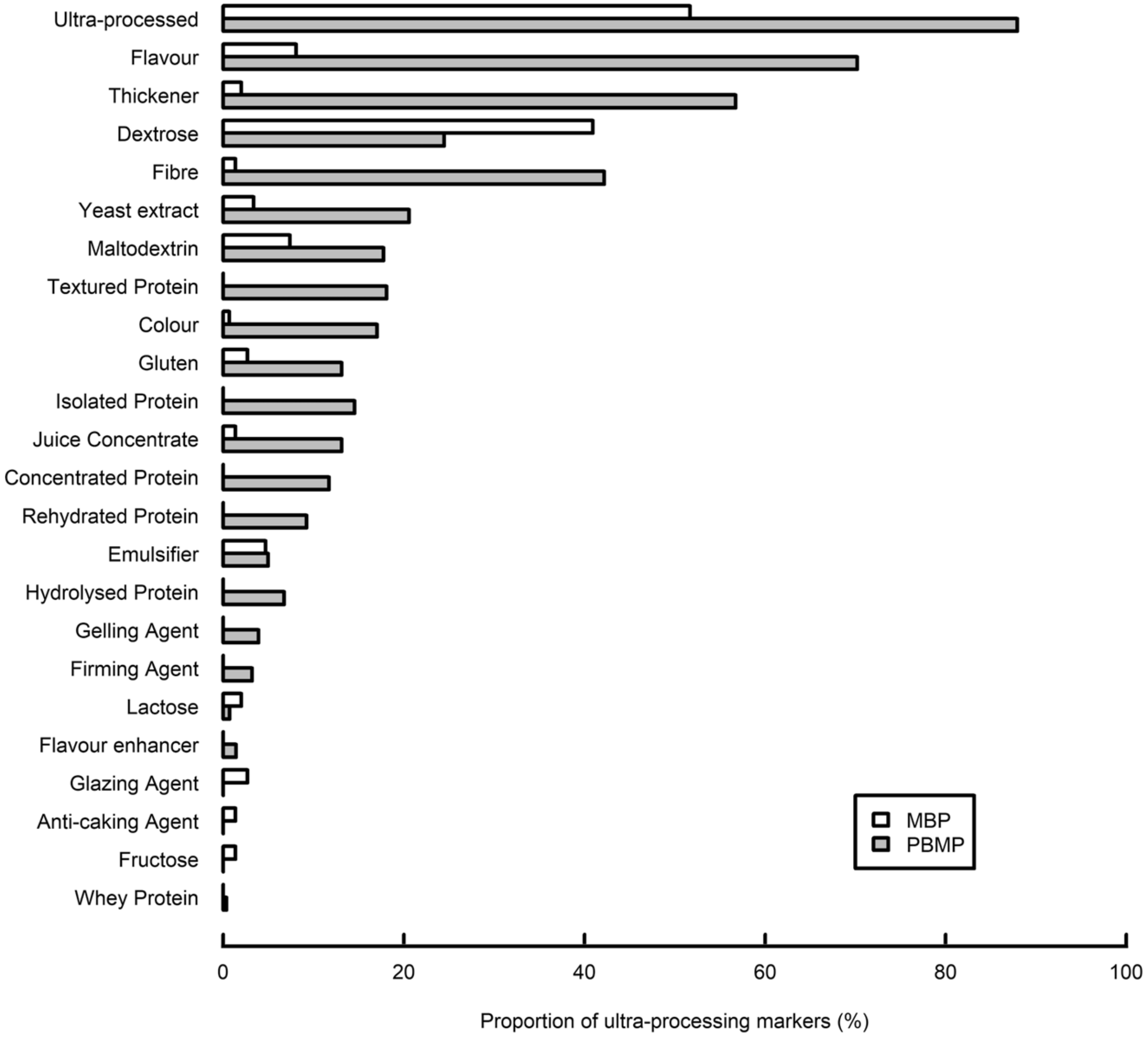

Fig. 1 Proportion of ultra-processing markers in MBP (*n* 149) and PBMP (*n* 282). All ultra-processing markers defined in Supplemental Table 1 which were used at least once are depicted

Additional robustness analyses

If raw meat product categories were removed from the analysis, the proportions of UPF items, flavour, flavour enhancer, colour, other cosmetic additives and non-culinary ingredients remained all significantly higher in PBMP as compared to MBP (all $P < 0{\cdot}05$; see online Supplemental Table 2).

In the onsite robustness analyses, the proportions of UPF items, flavour and other cosmetic additives were significantly higher in PBMP as compared to MBP at both Rewe and Lidl (all $P < 0{\cdot}05$; see online Supplemental Table 3). Flavour enhancer, colour and non-culinary ingredients were all more prevalent in PBMP as compared to MBP with differences reaching statistical significance at Rewe (all $P < 0{\cdot}0001$) but not at Lidl ($P > 0{\cdot}05$) (see online Supplemental Table 3). Energy, total fat, saturated fat and protein contents were significantly lower, and carbohydrate and fibre amounts were significantly higher in PBMP as compared to MBP at both supermarkets onsite (all $P < 0{\cdot}05$; see online Supplemental Table 4).

Discussion

Principal findings

The present study systematically assesses the extent of ultra-processing, as well as ultra-processing bullet categories and ultra-processing markers, in PBMP and their meat-based counterparts. We demonstrate that about nine out of ten PBMP fulfil ultra-processing criteria according to the NOVA classification in contrast to about half of the MBP. Of the 18 product categories examined, 15 show

Table 2 Nutrient composition in the total sample and in the 18 product categories, of PBMP and MBP*

			Energy		Fat		Saturated fat		Carb		Sugar		Fibre		Protein		Salt	
Product category	Group	*n*	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range
Total	MBP	149	972·0	410·0–2107·0	15·8	1·0–45·0	4·0	0·0–19·0	1·0	0·0–28·4	0·5	0·0–8·9	0·3	0·0–5·6	17·0	6·9–25·0	1·3	0·0–4·2
	PBMP	282	**880·5**	**132·0–1592·0†**	**11·0**	**0·5–33·0§**	**1·2**	**0·1–17·7§**	**7·1**	**0·8–27·6§**	**1·5**	**0·0–10·0§**	**4·5**	**0·7–20·1§**	**14·1**	**1·3–62·0§**	**1·6**	**0·0–6·2†**
Minced meat	MBP	10	972·0	734·0–1018·0	18·0	11·0–19·0	7·0	0·0–8·1	0·0	0·0–0·5	0·0	0·0–0·3	0·0	0·0–0·5	18·0	18·0–20·0	0·0	0·0–0·2
	PBMP	26	840·5	441·0–1407·0	**8·5**	**0·5–20·6‡**	**1·1**	**0·1–16·0†**	**5·8**	**0·9–27·0§**	**1·6**	**0·0–8·7§**	**5·3**	**1·3–20·1§**	18·2	6·4–53·8	**1·4**	**0·0–6·2§**
Meatball	MBP	10	1085·0	410·0–1226·0	20·5	7·1–22·0	8·0	3·1–9·8	7·3	0·7–10·0	0·9	0·3–2·1	2·1	2·1–2·1	14·5	6·9–17·0	1·8	1·2–2·3
	PBMP	21	881·0	132·0–1300·0	**11·9**	**1·7–18·0†**	**1·5**	**0·2–7·4§**	8·3	1·0–21·4	**2·0**	**0·1–6·4†**	4·0	1·0–8·2	16·0	2·6–22·0	**1·4**	**0·3–2·0†**
Burger	MBP	10	1042·0	582·0–1246·0	20·0	1·7–21·9	8·2	0·2–9·5	0·1	0·0–28·4	0·0	0·0–2·9	0·0	0·0–0·0	17·1	9·7–18·0	1·1	0·9–1·7
	PBMP	33	**826·0**	**511·0–1134·0†**	**10·0**	**2·6–19·0‡**	**1·3**	**0·3–11·0†**	**6·5**	**1·8–22·0†**	**1·3**	**0·0–6·7†**	**4·6**	**1·3–9·7†**	14·0	5·9–29·0	**1·5**	**0·8–2·1†**
Steak	MBP	5	505·0	440·0–559·0	4·0	2·0–5·0	1·8	0·8–2·1	0·0	0·0–0·0	0·0	0·0–0·0	0·0	0·0–0·0	21·5	21·0–22·0	0·0	0·0–0·2
	PBMP	6	**917·5**	**528·0–1056·0†**	8·2	1·2–11·0	1·4	0·2–4·8	**7·6**	**6·5–27·0†**	**2·4**	**1·2–8·6†**	**4·8**	**4·5–5·4†**	17·7	13·0–49·0	**1·3**	**0·0–1·6†**
Fillet strips	MBP	10	477·0	443·0–607·0	2·0	1·0–4·0	0·6	0·0–2·0	0·1	0·0–5·0	0·1	0·0–2·0	0·0	0·0–0·1	23·0	22·0–23·9	0·2	0·0–3·0
	PBMP	13	**714·0**	**477·0–1497·0†**	**5·3**	**1·2–17·0†**	0·5	0·3–1·9	**3·3**	**1·1–19·0†**	0·5	0·0–4·4	**6·8**	**2·5–9·8‡**	**18·0**	**9·7–62·0†**	**1·3**	**0·6–2·5†**
Sausage	MBP	10	1152·0	941·0–1443·0	24·0	18·0–32·0	9·0	6·0–13·4	1·0	0·0–1·0	0·7	0·0–1·0	0·1	0·0–1·0	14·1	13·0–18·0	2·0	1·7–2·3
	PBMP	26	**831·0**	**481·0–1356·0†**	**13·1**	**6·6–24·4§**	**2·9**	**0·8–17·7‡**	**4·8**	**2·3–12·0§**	0·8	0·0–3·0	**4·8**	**0·7–7·2‡**	14·3	2·0–27·2	**1·7**	**1·0–5·3†**
Kebab	MBP	5	828·0	615·0–1345·0	11·4	7·8–24·0	3·2	1·0–5·6	3·4	1·4–5·7	1·0	0·7–2·4	0·4	0·4–0·4	18·5	14·0–25·0	1·7	1·3–2·7
	PBMP	7	799·0	544·0–1065·0	**6·9**	**3·9–14·0†**	**0·8**	**0·5–1·3†**	3·9	0·8–9·0	0·7	0·0–4·6	4·7	0·8–6·2	27·0	15·0–27·8	1·9	1·2–2·5
Cevapcici	MBP	5	1036·0	938·0–1078·0	19·5	14·0–20·0	9·3	3·3–10·6	1·0	1·0–5·6	0·5	0·5–1·1	0·9	0·9–0·9	16·0	14·5–23·0	1·5	1·3–2·5
	PBMP	7	972·0	654·0–1277·0	**16·0**	**9·0–18·0†**	5·0	1·8–8·6	**6·5**	**2·5–15·0†**	1·4	0·1–4·4	5·7	4·3–6·0	14·0	1·5–29·0	2·0	1·6–2·3
Schnitzel	MBP	10	933·5	691·0–979·0	10·4	3·6–12·0	2·2	0·9–3·9	16·2	11·0–19·5	1·2	0·5–6·7	0·6	0·4–0·9	16·7	12·9–17·2	1·3	0·9–1·4
	PBMP	31	938·0	353·0–1272·0	11·0	1·6–19·1	**1·2**	**0·4–3·8†**	17·0	1·9–26·1	1·3	0·0–5·1	**4·1**	**2·0–8·3†**	**13·1**	**5·3–20·0†**	**1·4**	**0·8–2·0†**
Meat cut	MBP	10	578·9	470·0–650·0	4·5	1·4–9·3	1·7	0·0–3·7	0·6	0·0–9·0	0·1	0·0–8·9	0·0	0·0–0·4	21·4	16·5–24·4	0·8	0·0–1·1
	PBMP	14	**832·5**	**417·0–1407·0†**	6·5	1·2–19·0	1·0	0·3–3·3	**3·3**	**1·2–27·0‡**	**1·1**	**0·0–8·6†**	**4·5**	**1·0–7·1‡**	26·0	9·7–49·0	**1·6**	**0·0–3·4‡**
Nuggets	MBP	10	1031·0	867·0–1239·0	13·5	11·0–20·0	3·0	1·5–7·9	18·4	2·7–22·0	0·7	0·4–2·1	0·8	0·0–1·1	15·0	9·7–22·0	1·0	0·8–2·1
	PBMP	25	**918·0**	**487·0–1144·0†**	**9·9**	**3·1–16·0†**	**0·9**	**0·3–2·3§**	16·1	4·4–27·6	1·6	0·0–10·0	**4·0**	**2·8–12·0†**	13·0	1·3–23·0	**1·5**	**1·0–2·2†**
Salami	MBP	5	1461·0	1269·0–1552·0	28·0	24·0–30·0	11·0	8·6–12·0	1·0	1·0–1·0	1·0	1·0–1·0	0·5	0·0–1·0	24·0	19·0–24·5	4·0	3·5–4·1
	PBMP	9	**759·0**	**559·0–1075·0†**	**11·0**	**9·1–19·0†**	**0·8**	**0·7–5·2†**	**6·0**	**4·8–8·5†**	1·5	0·8–4·8	3·2	2·8–3·2	11·5	4·0–29·0	**2·6**	**1·2–2·9†**
Lunchmeat	MBP	10	704·0	416·0–1162·0	10·8	1·2–26·0	3·2	0·4–17·0	1·0	0·5–1·2	0·8	0·3–1·2	0·5	0·3–0·5	16·7	11·0–21·0	2·1	2·0–2·8
	PBMP	22	739·5	525·0–1078·0	11·9	5·2–16·0	0·9	0·6–4·8	**4·9**	**3·0–9·3§**	**3·1**	**1·4–3·9§**	**2·5**	**0·8–7·7‡**	8·4	2·2–29·6	2·0	1·0–3·0
Meat paste	MBP	10	1396·5	1084·0–1771·0	31·0	21·0–42·0	12·7	6·3–16·0	0·7	0·5–3·5	0·6	0·3–1·4	0·5	0·3–5·6	14·0	11·0–15·5	2·0	1·4–2·8
	PBMP	10	**998·0**	**728·0–1094·0‡**	**22·4**	**12·0–25·5‡**	**1·6**	**1·3–3·6‡**	**5·2**	**2·9–15·0‡**	0·9	0·3–3·7	3·7	1·9–6·0	**2·7**	**2·5–6·2‡**	1·9	1·5–2·5
Pork sausage	MBP	10	1183·5	957·0–2107·0	26·0	20·0–45·0	10·5	6·0–19·0	1·0	0·5–1·1	0·7	0·5–1·1	0·5	0·0–0·5	12·0	11·0–25·0	2·1	1·8–4·2
	PBMP	12	**844·5**	**525·0–1592·0†**	**14·9**	**5·2–33·0†**	**1·1**	**0·6–2·6§**	**5·7**	**1·1–8·0§**	**2·8**	**1·0–3·9‡**	**2·4**	**1·0–5·5†**	8·4	4·0–29·6	2·3	1·4–3·5
Fish fingers	MBP	10	824·0	759·0–1034·0	8·2	7·7–14·0	1·0	0·6–1·2	17·8	13·4–20·5	0·9	0·5–2·0	0·9	0·8–1·1	13·0	11·0–13·5	0·9	0·7–1·2
	PBMP	11	**1029·0**	**822·0–1289·0†**	**11·9**	**7·3–20·0†**	**1·1**	**0·9–2·6†**	21·0	2·6–26	1·0	0·4–3·1	**3·2**	**2·0–8·4†**	11·0	2·9–15·7	**1·3**	**0·7–1·7†**
Others fish-based	MBP	5	815·0	439·0–924·0	11·0	1·3–15·7	2·0	0·2–3·3	0·0	0·0–0·3	0·0	0·0–0·3	0·0	0·0–0·0	21·0	20·0–24·0	0·5	0·1–3·1
	PBMP	5	864·0	543·0–1160·0	13·0	7·1–19·9	1·7	0·9–2·8	**6·8**	**1·7–8·6†**	**0·5**	**0·1–1·3†**	2·9	1·1–4·6	11·0	2·7–22·6	1·1	0·9–1·8
Others meat-based	MBP	4	989·0	448·0–1304·0	17·8	2·0–25·8	6·4	1·0–8·2	0·8	0·0–1·0	0·5	0·0–0·9	0·3	0·0–0·5	19·8	17·0–22·0	0·5	0·0–4·0
	PBMP	4	980·0	324·0–1282·0	15·0	0·5–20·0	2·6	0·1–9·0	**8·5**	**1·3–9·6†**	2·5	0·5–6·8	3·6	3·2–4·0	17·0	12·0–22·0	1·9	1·3–2·9

*Variables for the nutrient composition are presented as median and range. Fibre content was not given for all food items, and it was indicated for only one item within Meatball-, Kebab- and Cevapcici-MBP.

†$P < 0·05$.

‡$P < 0·001$ and §$P < 0·0001$ as assessed by Mann-Whitney *U* test.

Values with statistically significant differences as compared to MBP are further indicated in bold.

PBMP, plant-based meat products; MBP, meat-based products.

numerically higher proportions of ultra-processing for PBMP as compared to MBP. All ultra-processing bullet categories which are present in the studied products, that is flavour, flavour enhancer, colour, other cosmetic additives and non-culinary ingredients, are more frequently observed in PBMP than in MBP. Of 23 ultra-processing markers present in the products, 18 are detected in higher proportions in PBMP as compared to MBP. Concerning nutrient composition, median energy, total fat, saturated fat and protein content are significantly lower, whereas the amounts of carbohydrate, sugar, fibre and salt are significantly higher in PBMP as compared to MBP. Combined these findings suggest that a much higher proportion of PBMP fulfil ultra-processing criteria as compared to their meat-based counterparts whereas some aspects of the nutrient composition of PBMP appear favourable including higher fibre amounts, as well as lower energy, fat and SFA content.

Comparison with other studies

In an analysis comprising 148 PBMP sold by seven of the most common supermarket chains in Spain, the proportion of PBMP in NOVA group 4 is 94 %(37) which is similar to the 88 % found in the current analysis. In another study from Spain combining 198 PBMP and 33 plant-based dairy products within one analysis and using data from Open Food Facts, a lower proportion, that is 59 % of the plant-based foods with a NOVA classification label, is NOVA group 4(38). However, for 63 % of the plant-based foods in this study, no information concerning NOVA classification is available(38).

Various reports have elucidated the intake of UPF in vegetarians and vegans as compared to meat eaters. In a study conducted on 21 212 participants from the prospective observational NutriNet-Santé cohort in France between 2014 and 2018, higher avoidance of animal-based foods is associated with a higher consumption of UPF(39). Thus, the proportions of energy intake from UPF in relation to total energy intakes are 33·0 %, 32·5 %, 37·0 % and 39·5 % for meat eaters, pesco-vegetarians, vegetarians and vegans, respectively(39). However, standard deviations are rather large and no post hoc tests are presented besides the ANOVA result ($P < 0{\cdot}0001$) to elucidate which group means differ from one another significantly(39). In agreement with these findings, both healthy and unhealthy eating patterns exist in a convenience sample of 129 vegans(40). Two clusters, that is 'convenience' and 'traditional' are identified that consist of an array of ultra-processed vegan food items and represent almost half of the participants(40). In a German sample of 814 participants, PBMP consumption is predominant within a vegetarian diet while other ultra-processed product groups such as convenience, fast foods, snacks and ultra-processed beverages are mainly consumed by meat eaters(41). Of note, consumption of all types of UPF is lowest in flexitarians(41). Taking these published and the current data into consideration, different dietary patterns exist in vegetarians and vegans. A recent systematic review demonstrates convincingly that vegetarian and vegan diets have a higher overall diet quality(42). However, there are some dietary patterns in vegetarians and vegans that show higher UPF consumption than omnivores, and PBMP might contribute to this increased UPF intake.

A higher UPF intake has been convincingly linked to adverse outcomes(20–25). Moreover, flavours as the most prevalent ultra-processing marker in PBMP might induce overeating and body weight gain, thereby, contributing to the obesity epidemic(43). Taking these studies into consideration, it is well possible that PBMP consumption might have adverse effects on metabolic and cardiovascular endpoints due to a higher proportion of ultra-processing. However, some aspects of PBMP nutrient composition appear favourable in the current analysis including higher fibre amounts and lower energy content as compared to MBP which is in accordance with the majority of published evidence(44,45). Salt content is increased in the current analysis of PBMP which has also been described in various reports(44). It needs to be elucidated in future analyses how increased ultra-processing and altered nutrient composition affect the nutritional quality of PBMP as compared to MBP. The current study supports recent evidence that plant-based diets are not necessarily healthy(39–41,46). Besides ultra-processing and nutrient composition, further aspects of PBMP need to be assessed in future studies which include improving current production techniques, climate change and changing demographics(47,48).

Strength and limitations of this study

The present study systematically assesses ultra-processing bullet categories and ultra-processing markers in a broad range and variety of PBMP and MBP. Further strengths include that all PBMP are compared to their respective meat-based counterparts from the same local stores and that a search term-based approach according to the NOVA classification is used.

However, the study has some limitations. Thus, all assessments are performed exclusively for the German market and the composition of PBMP and MBP might differ in other regions. Furthermore, some product categories are rather small which affects the statistical power. Moreover, dietary fibre data in PBMP and MBP are incomplete since labelling is optional according to the German food law(35).

Various factors might introduce bias in favour of the MBP: Although PBMP sampling includes two discounters (Lidl and Aldi), MBP are sampled mostly from one relatively upmarket online supermarket (Rewe) which may offer a healthier product range than the cheaper discounters. Furthermore, the popularity ranking in the Rewe online store depends on the location from which the website is accessed and healthy foods might rank higher in affluent areas with many young, health-conscious consumers. Moreover, the range of foods offered in the online store might systematically be different from the brick-and-mortar ones. In addition, limiting the number of MBP as comparators to PBMP might introduce selection bias. However, independent robustness analyses examining all available PBMP and all matching MBP onsite under identical conditions at Rewe and Lidl show results comparable to the current findings. Furthermore, results remain similar if PBMP are compared to MBP excluding raw meat. Products traditionally used in vegetarian diets such as tofu, tempeh and legumes are frequently used as PBMP but are excluded from the current analysis as long as they are not marketed as MBP replacements which introduces further bias in favour of MBP.

The approach used in the current manuscript to identify UPF most closely resembles the ingredient marker method described by Ricardo and co-workers(49). However, it has been convincingly demonstrated that the detection of UPF items differs depending on the approach used and the selection of individual ultra-processing markers(49).

Conclusions

The current study indicates that the proportion of UPF items is higher in PBMP as compared to MBP overall, as well as in various product categories. In contrast, some aspects of the macronutrient composition of PBMP appear favourable including higher fibre amounts, as well as lower energy, fat and SFA content. Since UPF intake has been convincingly linked to metabolic and CVD, substituting MBP with PBMP might have negative net health effects.

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Conflicts of interest

There are no conflicts of interest.

Authorship

K.M.M., N.J.N. and M.F. conceived the research and wrote the first draft. The product selection was done by two authors (K.M.M. and M.F.) and ingredient lists, as well as nutritional information, were extracted from the chosen P.B.M.P. and M.B.P. by one author (K.M.M.). Statistical analyses were performed by all authors. All authors have read, redacted and approved the final manuscript. K.M.M. and N.J.N. are the guarantors of the manuscript and accept full responsibility for the work and/or the conduct of the study, had access to the data and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethics of human subject participation

Not applicable.

Supplementary material

For supplementary material accompanying this paper visit https://doi.org/10.1017/S1368980023002458

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Supplementary Table 1

Search terms for the six ultra-processing bullet categories and 33 ultra-processing markers[1]

Ultra-processing bullet categories	Ultra-processing markers in English		Ultra-processing markers in German
Flavour	1	Flavour	(A|a)rom(a|en)
Flavour enhancer	2	Flavour enhancer	Geschmacksverstärker
	3	Yeast (extract|flake)[#]	Hefe(extrakt|flocken)
Sweetener	4	Sweetener	Sü(ß|ss)ungsmittel
Colour	5	Colour	Farbstoff
Other cosmetic additives	6	Carbonating agent	Kohlendioxid
	7	Firming agent	Festigungsmittel
	8	Bulking agent	Füllstoff
	9	Defoaming agent	Schaummittel
	10	Anti-caking agent	Trennmittel
	11	Glazing agent	Überzugsmittel
	12	Emulsifier	Emulgator
	13	Sequestrant	Komplexbildner
	14	Humectant	Feuchthaltemittel
	15	Thickener	Verdickungsmittel
	16	Gelling agent	Geliermittel
Non-culinary ingredients	17	Fructose	Fru(c|k)tose, Fruchtzucker
	18	Fruit juice concentrate	(S|s)aftkonzentrat
	19	Invert sugar	Invertzucker
	20	Maltodextrin	Maltodextrin
	21	Dextrose	Dextrose
	22	Lactose	La(c|k)tose, Milchzucker
	23	Fibre	(F|f)aser
	24	Hydrogenated oil	Gehärtete Fette
	25	Hydrolysed protein	Hydrol(i|y)siert
	26	Rehydrated protein[#]	Rehydriert
	27	Textured protein[#]	(T|t)extur(at|iert)

	28	Protein isolate#	((E|e)iweiß|(P|p)rotein)isolat
	29	Protein concentrate#	((E|e)iweiß|(P|p)rotein)konzentrat
	30	Gluten	(G|g)luten,Weizenkleber
	31	Casein	(C|K)asein
	32	Whey protein	Molkenprotein
	33	Mechanically separated meat	Separatorenfleisch

[1] English search terms are based on NOVA group 4(17,18) and the indicated corresponding German search terms were used for the analysis. For various English search terms, more than one German equivalent exists and these equivalents are listed with the logical operator | indicating OR, i.e., the search term (A|a)rom(a|en) identifies words including “Aroma”, “Aromen”, “aroma” (like in “Raucharoma”), and “aromen” (like in “Raucharomen”). #Indicates search terms which are not literally mentioned in the publications by Monteiro and co-workers(17,18) but which are related to the ultra-processing markers mentioned.

Supplementary Table 2

Percentage of ultra-processing and six ultra-processing bullet categories in the total sample of PBMP and MBP excluding raw meat, i.e., excluding the product categories minced meat, burger, steak, fillet strips, and meat cut.[1]

Product category	**Group** (n)	**Ultra-processing** % (n)	**Ultra-processing bullet categories**				
			Flavour % (n)	**Flavour enhancer** % (n)	**Colour** % (n)	**Other cosmetic additives** % (n)	**Non-culinary ingredients** % (n)
Total	MBP (104)	66 (69)	9 (9)	5 (5)	0 (0)	10 (10)	63 (65)
	PBMP (190)	**92** **(175)**†	**77** **(146)**†	**21** **(40)**§	**23** **(44)**†	**73** **(138)**†	**80** **(152)**$^{\#}$

[1] Ultra-processing and six ultra-processing bullet categories are presented as percentage (number). $^{\#}p < 0.05$, $^{\S}p < 0.001$, and $^{\dagger}p < 0.0001$ as assessed by chi-square test. Values with statistically significant differences as compared to MBP are further indicated in bold.

Supplementary Table 3

Percentage of ultra-processing and six ultra-processing bullet categories of PBMP and MBP at Rewe and Lidl onsite markets[1]

Product category	Group	Ultra-processing	Ultra-processing bullet categories				
			Flavour	Flavour enhancer	Colour	Other cosmetic additives	Non-culinary ingredients
	(n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
Rewe	MBP (243)	62 (150)	7 (17)	3 (7)	3 (8)	13 (31)	58 (141)
	PBMP (87)	**100** **(87)**†	**95** **(83)**†	**20** **(17)**†	**26** **(23)**†	**68** **(59)**†	**86** **(75)**†
Lidl	MBP (36)	67 (24)	3 (1)	0 (0)	6 (2)	14 (5)	67 (24)
	PBMP (20)	**100** **(20)**$^{\#}$	**90** **(18)**†	5 (1)	15 (3)	**90** **(18)**†	90 (18)

[1] Ultra-processing and six ultra-processing bullet categories are presented as percentage (number). $^{\#}p < 0.05$, $^{\S}p < 0.001$, and $^{\dagger}p < 0.0001$ as assessed by chi-square test. Values with statistically significant differences as compared to MBP are further indicated in bold.

Supplementary Table 4

Nutrient composition of PBMP and MBP at Rewe and Lidl onsite markets[1]

Product category	**Group** (n)	**Energy** median (range)	**Fat** median (range)	**Saturated fat** median (range)	**Carb** median (range)	**Sugar** median (range)	**Fibre** median (range)	**Protein** median (range)	**Salt** median (range)
Rewe	MBP (243)	987.0 (215 to 2167.0)	19.0 (0.6 to 47.0)	6.0 (0.0 to 19.0)	1.0 (0.0 to 24.0)	0.5 (0.0 to 8.3)	0.3 (0.0 to 5.6)	18.0 (4.1 to 34.0)	2.1 (0.0 to 4.6)
	PBMP (87)	**840.0 (265.0 to 1306.0)**†	**11.0 (0.5 to 30.0)**†	**1.1 (0.1 to 8.7)**†	**6.0 (0.0 to 27.0)**†	**1.2 (0.0 to 4.5)**†	**5.7 (1.3 to 9.6)**†	**12.0 (0.6 to 32.0)**†	**1.6 (0.8 to 3.5)**$^{\#}$
Lidl	MBP (36)	993.0 (99.0 to 1463.0)	19.0 (3.3 to 34.5)	7.2 (0.5 to 12.2)	1.2 (0.0 to 19.0)	1.0 (0.0 to 5.6)	0.8 (0.0 to 0.9)	15.0 (4.9 to 22.9)	1.6 (0.1 to 2.3)
	PBMP (20)	**816.0 (314.0 to 1235.0)**$^{\#}$	**10.5 (1.5 to 26.1)**§	**1.1 (0.1 to 4.0)**†	**7.1 (0.0 to 30.6)**$^{\#}$	1.4 (0.0 to 6.5)	**4.7 (2.9 to 7.9)**$^{\#}$	**8.6 (1.6 to 19.0)**§	**1.8 (0.9 to 2.6)**$^{\#}$

[1] Variables for nutrient composition are presented as median (range). Fibre content was not given for all food items. $^{\#}p < 0.05$, $^{\S}p < 0.001$, and $^{\dagger}p < 0.0001$ as assessed by Mann-Whitney U test. Values with statistically significant differences as compared to MBP are further indicated in bold.

3. Discussion

Within the doctoral thesis, the three research gaps mentioned in subchapter 1.4 have been addressed through the publications summarised in chapter 2.

3.1 Major conclusions

The following major conclusions can be drawn based on the findings of the present doctoral thesis:

(1) Added flavours might induce overeating and obesity by promoting hedonic eating and disrupting flavour-nutrient-learning (publication 1).
(2) Added flavours increase feed intake and body weight as compared to non-flavoured control diets in a broad range of animal studies (publication 1).
(3) UPF can be detected objectively via a MUP- and ingredient list-based approach (publication 2).
(4) Among all MUP, flavour is the most frequent marker for UPF detection (publication 2).
(5) With a combination of three and six MUP, almost 80 % and 90 % of UPF are detected, respectively (publication 2).
(6) The MUP- and ingredient list-based approach can be transferred to the German food market (publication 3).
(7) The proportion of UPF in PBMP is higher than in MBP (publication 3).
(8) Flavour and dextrose are the most frequent MUP in PBMP and MBP, respectively (publication 3).

3.2 Comparison with other studies and future research

Taking into consideration the limitations of the NOVA classification, the results of this doctoral thesis give a clear outlook which further research has to be done (Figure 1). The overall aim should be to increase simplicity and objectivity of the NOVA classification.

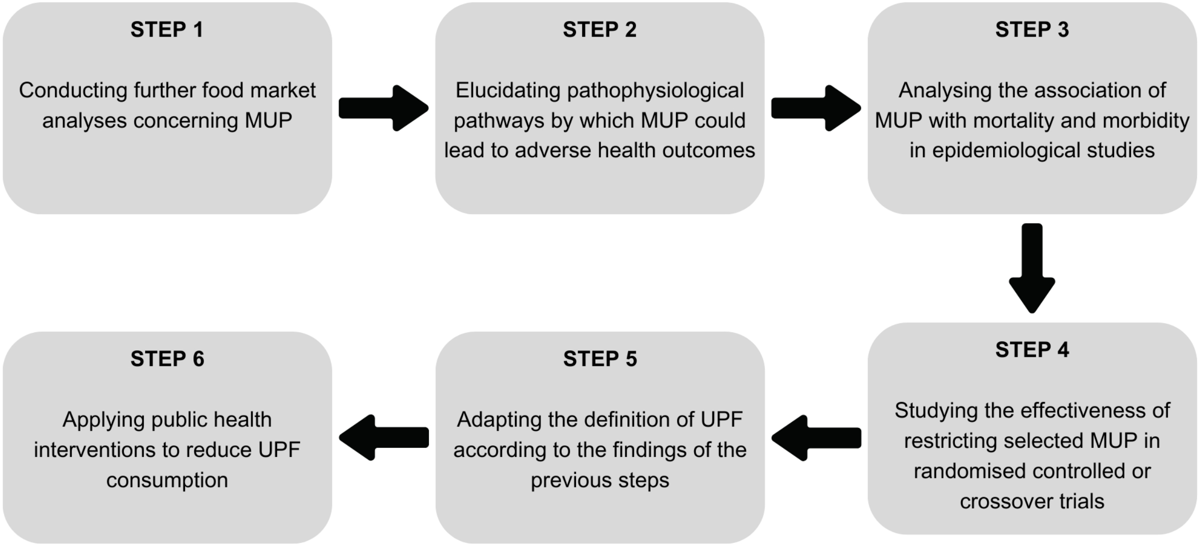

Figure 1: *Steps for further research*

In a **first step**, it is necessary to further analyse the worldwide food market concerning MUP in UPF. For this goal, the MUP concept described in the current thesis (publications 2 and 3) can be applied and transferred to further food markets, as well as languages, to guarantee reproducible and comparable results. It is important to note in this context that the proportion of UPF differs depending on the selection of individual MUP and the approach used(96). Therefore, clear definitions and consensus guidelines are necessary to ensure the comparability between different studies concerning UPF availability and intake levels(7,8). Until clear definitions become available, researchers should use coding procedures and best-practice examples for applying the NOVA system(7,97–99).

In a **second step,** pathophysiological pathways should be elucidated by which the large number of other MUP apart from added flavours could lead to adverse health outcomes. In the current thesis, flavour is the most frequent marker among all MUP in UPF on the British food market (publication 2) and in PBMP on the German food market (publication 3). Similar to the current results, extracts/natural flavours and synthetic flavours are found in 42.7 % and 26.5 % of UPF, respectively, in a French market analysis(43). In addition, added flavours are implicated in the pathophysiology of overeating and obesity (publication 1) and could, therefore, explain at least in part the associations of UPF with adverse health outcomes in several publications(18–26). However, similar data are sparse for other MUP. Current evidence suggests that emulsifiers might induce metabolic and chronic inflammatory disease due to changes in the gut microbiome and intestinal barrier(100). Moreover, all MUP consisting of mono- and disaccharides are free sugars which are linked to body weight gain(101). Sweeteners can cause overeating and impair glucose control by disrupting the association between sweet taste and energy, as well as altering the gut microbiome(102–104). Gluten increases body weight and fat deposits in mice(105). In contrast, no increase in food intake or body weight has been reported for colour and whey(106,107). Combined, these data suggest that various MUP might contribute to metabolic dysregulation. However, future analyses should address the role of MUP in metabolic control in a more systematic fashion, as well as cover the whole range of MUP.

In a **third step,** the association of MUP with mortality and morbidity should be analysed in epidemiological studies. Thus, the association of single MUP with diverse health outcomes could be studied in the UK Biobank cohort using a similar methodological approach as in recent studies on sugar subtypes(108–111). To perform these analyses, the probability for all MUP needs to be defined for each of the 206 food and 32 beverage items of the Oxford WebQ based on an existing UK food market analysis (publication 2). It is important to note in this context that associations between UPF and mortality(37,112), CVD(37,113), cancer(114), dementia(115), T2DM(116), adverse liver outcomes(24), chronic obstructive pulmonary disease(117), venous thromboembolism(118), new-onset chronic kidney diseases(119), Crohn's disease(36), irritable bowel syndrome(120), and gout(34) have already been shown in the UK Biobank cohort. However, it is necessary to extent these studies by elucidating the associations between single MUP and these endpoints.

In a **fourth step** the effectiveness of restricting selected MUP should be elucidated in randomised controlled or crossover trials, e.g., obesity interventions specifically targeting food items with added flavours should be compared to conventional treatments. Similar trials could also be performed restricting other MUP including sweeteners, as well as added mono- and disaccharides, alone or in combinations. It has been shown that energy intake and body weight increase were higher in an ad-libitum ultra-processed versus unprocessed diet in a randomised controlled trial(26). This relation should also be analysed for selected MUP.

In a **fifth step,** the UPF definition should be adapted according to the findings of the previous steps: It should focus on MUP, which are frequent (first step), lead to adverse health outcomes via defined pathophysiological pathways (second step), and are associated with mortality and morbidity in epidemiological studies (third step). Furthermore, restriction of these MUP should improve metabolic health (fourth step).

In a **sixth step**, consumers should be trained to detect and avoid UPF, e.g., by using MUP combinations (publication 2). However, they still need to study ingredient lists to identify UPF and ingredient lists are not always available, e.g., for many alcoholic beverages and in food prepared outside the home, as well as for products from the fresh food counters. Therefore, public health interventions should enable consumers to avoid UPF without the need for ingredient lists. Front-of-package labelling (FOPL) is one established way to improve the ability of participants to rank products according to healthiness correctly(121,122). A FOPL depicting the different NOVA groups has already been proposed(123). This FOPL should be improved using the refined UPF definition summarised in the fifth step. In addition, policymakers should aim to reduce UPF intake on a population level, e.g., by taxation(124,125). It has been convincingly shown that the taxation of one of the most important UPF categories, i.e., sugar-sweetened beverages, reduces their purchases and consumption(126). Furthermore, marketing of UPF to children and UPF in school food environments should be restricted by law(127). Moreover, agricultural subsidies supporting UPF production need to be re-examined(127). In addition, there is a need for the food market to change towards more non-UPF. Reasons for consumers choosing UPF include easy preparation and a long shelf-life(128). Therefore, it is desirable to offer non-UPF alternatives with similar characteristics making it easier for consumers to avoid UPF due to adequate alternatives.

In conclusion, the findings of the present doctoral thesis complemented by the steps mentioned above could enable a better understanding and a more objective application of the concept of ultra-processing, as well as decrease UPF consumption on a population level.

4. Summary

Consumption of ultra-processed foods (UPF) is associated with a broad range of adverse health outcomes in epidemiological studies. A large number of these publications use the NOVA classification to define UPF. There are two kinds of ingredients that are exclusively found in UPF, i.e., non-culinary ingredients and cosmetic additives, which combined are referred to as markers of ultra-processing (MUP). Critics point out that the NOVA classification is too inconsistent and is based on broad and ambiguous definitions that are not supported by scientific evidence.

Taking these studies into consideration, there are **three main research gaps** in the field of UPF that were analysed in the present work: (1) Which underlying mechanisms can explain the effects of UPF on overeating and body weight gain; (2) How can UPF be detected more objectively; (3) Can the MUP concept be adapted to the German food market? These research gaps have been addressed within three publications.

In the **first publication**, added flavours were suggested to induce overeating and obesity by promoting hedonic eating and disrupting flavour-nutrient-learning. They increased feed intake and body weight as compared to non-flavoured control diets in a broad range of animal studies.
In the **second publication**, UPF were detected objectively via a MUP- and ingredient list-based approach. Among all MUP, flavour was the most frequent marker for UPF detection. With a combination of three and six MUP, almost 80 % and 90 % of UPF were detected, respectively.
In the **third publication**, the MUP- and ingredient list-based approach was transferred to the German food market. The proportion of UPF in plant-based meat products (PBMP) was higher than in meat-based products (MBP). Flavour and dextrose were the most frequent MUP in PBMP and MBP, respectively.

Further research should focus on the following six steps: (1) Conducting further analyses of the worldwide food market concerning MUP; (2) Elucidating pathophysiological pathways by which the large number of other MUP apart from added flavours could lead to adverse health outcomes; (3) Analysing the association of the whole range of MUP with mortality and morbidity in epidemiological studies; (4) Studying the effectiveness of restricting selected MUP in randomised controlled or crossover trials; (5) Adapting the definition of UPF according to the findings of the previous steps; (6) Applying public health interventions to reduce UPF consumption and to change the food market towards more non-UPF.

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6. Declaration

Declaration in accordance with the Doctoral Regulations of the Faculty 09 in the version of 29.05.2019 § 17 (2)

“I declare that the doctoral thesis here submitted is entirely my own work, written without any unauthorised help by a third party and solely with the assistance referred to in the thesis. I have indicated in the text those texts that have been quoted from already published sources, either verbatim or by analogy and all statements based on verbally conveyed information. During the research carried out by me and referred to in the doctoral thesis, I have at all times followed the principles of good scholarly practice as defined in the Statute of Justus Liebig University Giessen for Ensuring of Good Academic Practice."

Giessen, 17.07.2024

Nathalie Judith Neumann

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