**News You Can Use**
**15th May, 2019**

**Compiled By: ILSI-INDIA**

**Source**
Journals, Websites & Newspapers Articles

**Spotlight**
**ILSI-India Monograph on “Eating Right for a Healthy You”**

Visit ILSI-India Website To Download: [www.ilsi-india.org](http://www.ilsi-india.org)

**Presentations of ILSI-India Seminar on Value Addition To Agriculture Through Food Processing**
Uploaded On ILSI-India Website

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- Compendium of Conference on Role of Probiotics in Promoting Healthy Microbiome for Health and Immunity
- Compendium of Seminar on Food Additives: A Global Perspective on Safety Evaluation and Use
- Report of Seminar on Recent Developments in Food Science and Technology for Better Nutrition
- Report of Workshop on Alternatives to Animal Testing for Food Safety
Chicory Root Fiber May Maintain Microbiota Balance In Children Taking Antibiotics

A study suggests that daily consumption of chicory root fibre in children aged 3–6 can keep the level of bifidobacteria higher and more stable, even during antibiotic treatment.

Source: Beneficial Microbes

Walnuts May Help Lower Blood Pressure For Those At Risk Of Heart Disease

When combined with a diet low in saturated fats, eating walnuts may help lower blood pressure in people at risk for cardiovascular disease, according to a new study.

In a randomized, controlled trial, researchers examined the effects of replacing some of the saturated fats in participants’ diets with walnuts. They found that when participants ate whole walnuts daily in combination with lower overall amounts of saturated fat, they had lower central blood pressure.

Source: Penny Kris-Etherton, Distinguished Professor Of Nutrition, Penn State, Journal Of The American Heart Association

Right Combination Of Diet And Bacteria Limits Cancer Progression

A team of scientists has found that a combination of prebiotics, such as dietary fibre, and probiotics, i.e. specific beneficial bacteria, reduces the expression of pro-carcinogenic and drug resistance genes. The combination leads to metabolic changes that affect the growth of cancer cells and may help treat diseases such as colorectal cancer (CRC).

Source: Luxembourg Centre For Systems Biomedicine (LCSB) And The Life Sciences Research Unit (LSRU) At The University Of Luxembourg

Variety Of Protein Better For Health

New research suggests that while delivering muscle-building benefits, excessive consumption of branched-chain amino acids (BCAAs) may reduce lifespan, negatively impact mood and lead to weight gain. BCAAs great for adding muscle mass, but science says one could pay for it later.

What this new research has shown is that amino acid balance is important. It is best to vary sources of protein for best amino acid balance.

BCAAs are a group of three essential amino acids: leucine, isoleucine and valine. It is important to vary protein sources in order to get a variety of essential amino acids, through a healthy and balanced diet rich in fibre, vitamins and minerals. BCAAs are present in protein-containing foods, with red meat and dairy being the richest sources. Chicken, fish and eggs are also nutritious sources of BCAAs. Vegetarians can find BCAAs in beans, lentils, nuts and soy proteins.

Source: Professor Stephen Simpson And Dr Samantha Solon-Biet, University Of Sydney’s Charles Perkins Centre Nature Metabolism

Sniffing Chocolate Could Help You Quit Smoking

Now, a study suggests that smelling pleasant odours, including chocolate, peppermint and apple could help smokers to quit.

Source: University Of Pittsburgh

Comfort Food Leads To More Weight Gain During Stress

A team led by discovered in an animal model that a high-calorie diet when combined with stress resulted in more weight gain than the same diet caused in a stress-free environment. The researchers revealed a molecular pathway in the brain, controlled by insulin, which drives the additional weight gain.

Source: Professor Herbert Herzog, Head Of The Eating Disorders Laboratory At The Garvan Institute Of Medical Research, Cell Metabolism

It’s OK To Indulge Once In A While, Study Suggests: The Body Adapts To Occasional Short-Term Overeating

Researchers in Australia studied a small group of healthy, lean men with an average age of 22. Volunteers participated in a short-term trial consisting of five days "indicative of humans overeating during festivals and holidays" and a long-term model of chronic overeating lasting 28 days. The nutritional composition of the volunteers’ diet was representative of a typical Australian diet (55 percent carbohydrates, 35 percent fat and 15 percent protein). The "overfeeding" portion of the diet included high-calorie snacks such as chocolate, meal replacement drinks and potato chips to add approximately 1,000 more calories to the men’s normal food consumption each day. The research team measured the volunteers’ weight, fat mass, blood sugar and insulin levels before the trial began and again after five and 28 days.

Although the amount of visceral fat that surrounds internal organs increased substantially, short-term overeating did not have a significant effect on the men’s weight or fat mass. In addition, fasting levels of blood sugar and C-peptide -- an amino acid the body releases in response to increased production of insulin -- did not change. Chronic overeating increased the amount of total body fat and visceral fat as well as post-meal blood sugar and C-peptide levels. However, it did not alter fasting blood sugar levels, endogenous glucose production or the rate of glucose removal from the body (glucose disposal). This may be because the nutrient profile in the long-term trial was consistent with a typical diet and dietary fat percentages did not increase.

Long-term overindulgence in fatty foods, instead of more nutritionally balanced foods, may be an important factor that causes rapid changes in blood sugar control.

These findings "suggest that early adaptations in response to carbohydrate overfeeding are directed at increasing glucose disposal in order to maintain whole-body insulin sensitivity," the researchers wrote.

Source: Deskin University In Australia, American Journal Of Physiology-Endocrinology And Metabolism

Junk Food Linked To Stress During Exams

Eating poor quality diet, including less fruits and vegetables and more fast food, is associated with increased stress during university examinations, according to a new study.

Source: Nathalie Michels From Ghent University In Belgium.
Eating a bacon sandwich, beef or sausages on just four days a week significantly increases the risk of bowel cancer, despite being well within Government dietary guidelines, experts have warned. The equivalent of one bacon rasher or lamb chop a day on average, raises and individual’s risk of bowel cancer by around 20%.

Source: University of Oxford

U.S. children and teens who consumed low-calorie or zero-calorie sweetened beverages took in about 200 extra calories on a given day compared to those who drank water, and they took in about the same number of calories as youth who consumed sugary beverages, according to a new study. The study is based on dietary recalls collected from 7,026 children and teens enrolled in the National Health and Nutrition Examination Survey from 2011 until 2016.

Allison C. Sylvetsky, PhD, Assistant Professor of Exercise and Nutrition Sciences at the George Washington University Milken Institute School of Public Health, Pediatric Obesity

EFSA is seeking feedback from stakeholders and other interested parties on its scientific opinion on the appropriate age for introduction of complementary feeding of infants. The Panel on Nutrition, Novel Foods and Food Allergens (NDA) reviewed around 300 studies for the opinion. Its main conclusions are that:

- The appropriate age to introduce complementary foods depends on the infant’s characteristics and development, even more so in pre-term infants. In most infants, this age is between about 3-4 and 6 months.
- Most infants do not need complementary foods for nutritional reasons until around 6 months, except some exclusively breast-fed infants at risk of iron depletion.
- There is insufficient data to determine a precise age at which complementary foods should be introduced to all infants in Europe.
- There is no evidence that early introduction of potentially allergenic foods – such as egg, cereals, fish and peanuts – increases the risk of children developing allergies.
- There is no evidence for either beneficial or adverse effects of introducing foods containing gluten earlier than 6 months of age.

The opinion considers the introduction of complementary foods from a developmental, nutritional and health perspective. It is not an evaluation of the optimal duration of exclusive breast-feeding, as the assessment is applicable irrespective of whether infants are initially exclusively breast-fed or formula-fed.

The deadline for submitting comments is 29 May 2019.

Source: https://www.efsa.europa.eu

A new study suggests that meals that include fresh avocado as a substitute for refined carbohydrates can significantly suppress hunger and increase meal satisfaction in overweight and obese adults.

Source: Center for Nutrition Research at Illinois Institute of Technology, Nutrients

EFSA, the EU Member States and the European Commission are jointly launching a campaign called #EUandMyFood. The aim is to remind EU citizens of the benefits of the European food safety system that was created in 2002 under the General Food Law.

https://www.efsa.europa.eu

A 12-year long impasse started to gradually unravel during the 51st session of the Codex Committee on Food Additives (CCFA51) in March 2019, when Codex Members found a new compromise on how to mutually respect their regulatory differences while not preventing international harmonization.

Among the standards that CCFA51 will send for adoption to the Codex Alimentarius Commission in July 2019 are revised provisions for the General Standard for Food Additives (GSFA) that concern the use of sweeteners in some food categories. The provisions would recognize that in some countries sweeteners can only be used in foods with significant (caloric) energy reduction, foods with no added sugars or as a sweetener to improve flavor.

Source: http://www.fao.org
When Could Cell-Cultured Food Products Appear On The Codex Agenda?

In a search for alternative sources of meat and in response to concerns over meat consumption, animal welfare and greenhouse gas emissions, scientists have developed the ability to grow meat from animal cells in a laboratory. The process involves taking tissue from a live animal and extracting stem cells which are then grown into muscle fibers in a bioreactor.

Developing awareness of emerging issues such as this is a key component of strategic planning in Codex. “Every committee in Codex has a responsibility to look ahead and examine issues that may require internationally harmonized standards in the future”, said Tom Heilandt, Secretary of the Codex Alimentarius Commission. When new technologies become available consumers can often be skeptical and uncertain about the risks and benefits involved. “The standard-setting environment has a part to play regarding the quality and safety of new products and as lab-grown meat becomes more important, Codex will be a necessary part of that discussion. And beyond quality and safety, Codex labeling requirements will make sure that consumers have all the information they need”, he said.

Source: http://www.fao.org/

Fat Cell Discovery Could Help Combat Obesity-Related Health Issues

Researchers have discovered differences in fat cells that could potentially identify people predisposed to metabolic diseases such as diabetes and fatty liver disease. The world-first discovery also identified ‘fast burning’ fat cells that if unlocked might help people lose weight.

Source: Matthew Watt, Who Is Head Of Physiology, University Of Melbourne’s School Of Biomedical Sciences, Cell Reports

Obesity And Emotional Problems Appear To Develop Together From Age 7

The analysis of a large nationally representative sample of over 17,000 children in the UK finds that regardless of their socioeconomic status, girls and boys with obesity at age 7 were at greater risk of emotional problems at age 11, which in turn, predicted high body mass index (BMI) at 14 years of age.

While the study did not investigate the reasons why obesity and emotional problems develop together during childhood, the researchers say that a range of factors are likely to be involved. Children with higher BMI may experience weight-related discrimination and poor self-esteem, which could contribute to increased depressive symptoms over time (as has been shown in adults), while depression may lead to obesity through increased emotional eating of high-calorie comfort foods, poor sleep patterns, and lethargy.

Source: Dr Charlotte Hardman From The University Of Liverpool, UK

Pig ‘Ebola’ Virus Sends Shock Waves Through Global Food Chain

What started with a few dozen dead pigs in northeastern China is sending shock waves through the global food chain. Last August, a farm with fewer than 400 hogs on the outskirts of Shenyang was found to harbor African swine fever, the first ever occurrence of the contagious viral disease in the country with half the world’s pigs.

Forty-seven head had died, triggering emergency measures including mass culling and a blockade to stop the transportation of livestock. Within days, a government notice proclaimed the outbreak “effectively controlled.”

However, the disease had literally gone viral, dispersed across hundreds of miles in sickened animals, contaminated food, and in dirt and dust on truck tires and clothing. Nine months later, the contagion has spread nationwide, crossed borders to Mongolia, Vietnam and Cambodia, and bolstered meat markets globally.

While official estimates count 1 million culled hogs, slaughter data suggest 100 times more will be removed from China’s 440 million-strong swine herd in 2019, the Chinese zodiac’s “year of the pig.”

The contagion is also highlighting the urgent need for government investment in outbreak preparedness, This is an unprecedented situation and will impact food prices globally.

Source: https://www.bloomberg.com

Lifestyle Factors That Could Harden Arteries

A new study pinpoints lifestyle factors that could lead to hardened arteries. The study is one of the largest of its kind, performed an untargeted metabolomics profile of over 1,200 participants of the Bogalusa Heart Study to identify metabolites linked to the hardening of arteries.

The study found 27 new metabolites associated with arterial stiffness. The majority of these were associated with other known risk factors of arterial stiffness like high blood pressure, high cholesterol or diabetes.

But some of these metabolites are food additives and cooking ingredients found in many U.S. kitchens. For example, the team identified two peptides -- gamma-glutamylvaline and gamma-glutamylisoleucine -- that are commonly used to enhance the savory taste of chicken broth.

The relationship between some of the metabolites and arterial stiffness over time is unclear, and researchers plan to run this study again using longitudinal data.

Source: Changwei Li., assistant professor of epidemiology and biostatistics at UGA’s College of Public Health, American Journal of Hypertension

Non Communicable Diseases

Circadian Rhythm Plays A Part In Weight Loss

Weight watchers worldwide need to not only be careful about what to eat but also about the timing of the food intake finds a new study. The research finds that late night meals may desynchronize the body clock. The effects can be seen on the digestion, sugar levels, skin, stress levels etc.

Source: Dr David Bechtold, University Of Manchester, Journal Cell

Bad News: Astronauts’ Brains Are Filling With Liquid

Fluids float upward into astronauts’ brains during long spaceflights, causing their brains to expand. A study by Russian scientists on 11 astronauts shows that even months after their return to Earth, the astronauts’ ventricles — the sacs in the...
Training For First-Time Marathon ‘Reverses Aging Of Blood Vessels’

Training for and completing a first-time marathon reverses aging of major blood vessels, according to new research. The study found that older and slower runners benefit the most. The study included 139 healthy first-time marathon runners aged 21-69 years.

Novice runners who trained for six months and complete their first marathon had a four-year reduction in arterial age and a 4 mmHg drop in systolic blood pressure. This compares to the effect of medication, and if maintained translates to approximately 10% lower risk of stroke over lifetime.

Source: Dr Anish Bhuva, a British Heart Foundation Fellow at University College London, UK, European Society of Cardiology

Is Dancing The Kale Of Exercise?

Research shows that dance offers a wealth of anti-aging benefits. It’s also fun. According to a study of 11 totally different bodily actions social dance is the only one related to much less dementia danger. Researchers speculate that dance functions like an involved intellectual activity because it’s complex.

Unlike walking on a treadmill, dance calls for sustained psychological effort to grasp new steps and requires cooperation with an associate and the music. This observational study showed that dance is associated with reduced risk of developing dementia.

Source: Dr. Joe Verghese, Chief of Geriatrics at Albert Einstein College of Medicine

Surveys

Social Media Influencers Give Bad Diet And Fitness Advice Eight Times Out Of Nine, Research Reveals

People who wish to lose weight have been warned to stay away from social media influencers who claim to have the latest diet fix, researchers say.

A study by a team at University of Glasgow found that just one out of nine leading UK bloggers making weight management claims actually provided accurate and trustworthy information.

The health researchers studied the country’s most popular influencers, based on those who had more than 80,000 followers on at least one social media site, verification from at least two sites such as Twitter, and who had an active weight management blog.

Source: Christina Sabbagh, University Of Glasgow, https://www.independent.co.uk/

The Obesity Crisis Is Growing Faster In Rural Areas Than In Major Cities

A new global study led by Imperial College London crunched a huge amount of data to help paint a picture of where increasingly overweight people tend to reside, and the conclusions are actually incredibly interesting. Obesity is increasing more rapidly in the world’s rural areas than in...
cities, according to a study of global trends in body-mass index (BMI).

The study, published analyzed the height and weight data of over 112 million adults across urban and rural areas of 200 countries and territories between 1985 and 2017. The study found that from 1985 to 2017:

- **BMI rose by an average of two kilograms per square meter (kg/m²) in women and 2.2 kg/m² in men globally, equivalent to each person becoming five to six kg heavier.**
- **Over half of the global rise over these 33 years was due to increases in BMI in rural areas.**
- **In some low- and middle-income countries, rural areas were responsible for over 80 per cent of the increase.**
- **Since 1985, average BMI in rural areas has increased by 2.1 kg/m² in both women and men.**
- **In cities, the increase was 1.3 kg/m² and 1.6 kg/m² in women and men respectively.**

The study reveal important differences between high-, middle-, and low-income countries. In **high-income countries**, the study showed that BMI has been generally higher in rural areas since 1985, especially for women. Rural areas in **low- and middle-income countries** have seen shifts towards higher incomes, better infrastructure, more mechanized agriculture and increased car use. These factors not only bring numerous health benefits, but also lead to lower energy expenditure and to more spending on food, which can be processed and low-quality when sufficient regulations are not in place.

The main exception to the global trend was sub-Saharan Africa where women gained weight more rapidly in cities.

**Source:** Professor Majid Ezzati, Imperial College London, Nature

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**Japan's Child Population At Record Low After Falling For 38th Consecutive Year**

Japan's child population has declined for the 38th year in a row and is now at a record low, the government said. The number of children younger than 15 stood at 15.22 million on April 1, down 180,000, or 1.2 per cent, from last year, the Statistics Bureau said.

It is the lowest number since comparable data became available in 1950. With children making up just 12.1 per cent of its population, Japan ranks with a population exceeding 40 million, followed by South Korea at 12.9 per cent and Italy and Germany at 13.4 per cent, according to the Statistics Bureau figures.

Japan’s total population fell by 448,000 people, a record decline, to 126 million.

**Source:** www.independent.co.uk

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**Indian Scientists Develop Colored Wheat Crops That Pack Nutrition**

Indian scientists develop colored wheat crops that pack nutrition. Agricultural biotechnologists have not on developed these colored wheat varieties, but also transferred the technology to various companies.

Common wheat varieties grown all over the world are white (or amber) in color. The unconventional ones get their color from natural antioxidants abundantly present in fruits such as blueberries, blackberries and jamun. While a very small quantity of anthocyanins is present in regular wheat varieties, the colored ones are rich in them. For instance, black wheat packs 28 times more anthocyanins than its conventional cousin.

The colored varieties offer a lot of health benefits, said Gar Black wheat, for instance, may help prevent fat deposition, control glucose levels, improve insulin tolerance and lower blood cholesterol, as indicated by mouse studies. Besides anthocyanins, the varieties have relatively higher levels of proteins and essential micronutrients such as zinc. These antioxidants present may also help ward off ageing, obesity and diabetes. The varieties have been developed using classical biotechnology tools that are commonly used by plant breeders.

**Source:** Monika Garg, National Agri-Food Biotechnology Institute (NABI), n Mohali, https://www.thehindubusinessline.com

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**EPA Reaffirms That Glyphosate Poses No Risk To Public Health**

After reviewing glyphosate, the U.S. Environmental Protection Agency (EPA) reaffirms its finding that “there are no risks to public health when glyphosate is used in accordance with its current label and that glyphosate is not a carcinogen.” The agency’s scientific findings on human health risk are consistent with the conclusions of science reviews by many other countries and other federal agencies.

Glyphosate is the most widely used herbicide in U.S. agriculture and has been studied for decades. Glyphosate is used on more than 100 food crops, including glyphosate-resistant corn, soybean, cotton, canola, and sugar beet.

**Source:** https://www.epa.gov

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**Australia Amends Genetic Editing Regs; Permits GM Wheat Field Trial**

After a thorough review of its gene technology regulations, the Australian government has decided it will not regulate the use of gene-editing techniques in plants, animals, and human cell lines that do not introduce new genetic material.

Previously, the use of such technologies, including CRISPR-Cas9, for research was restricted in practice because the techniques were governed by the same rules as conventional genetic modifications, which require approval from a biosafety committee accredited by the Office of the Gene Technology Regulator (OGTR).
The amended rules remove that requirement for the use of tools in which proteins cut DNA at a specific target site—as long as the tools allow the host cell to repair the break naturally, rather than using a template containing genetic material to direct the repair process.

The Australian changes will take effect October 8.

Source: http://www.ifst.org/

**Maharashtra Math**

1 Kg Sugar = 2,515 Liters Water

It takes 2,515 liters of water to produce a kilogram of sugar in Maharashtra, according to the Commission for Agricultural Costs and Prices (CACP). To put that in context, in rural areas of the State’s Aurangabad district, people pay around ₹1,000 to get 2,500 liters of tanker water for household use — as much as is needed to produce 1 kg of sugar.

In all, 195 sugar mills in Maharashtra have crushed 951.79 lakh tonnes of sugarcane to produce 1,071.94 lakh quintals of sugar this year, using 26.96 trillion litres of water. Twenty-six of the State’s 36 districts are reeling under water scarcity, but this has not affected cane cultivation and crushing as the State has surpassed last year’s (2017-18) sugar production of 1,067.81 lakh quintals.

The CACP, in its earlier reports, has observed that in Maharashtra, sugarcane cultivation, which takes place on less than 4 per cent of the total cropped area in the State, takes away almost 70 per cent of the State’s irrigation water, leading to massive inequity in its use.

Source: https://www.thehindubusinessline.com

**Miscellaneous**

Superbugs Could Kill 10 Million By 2050, Warns A UN-Backed Panel

Superbugs can take a whopping 10 million lives a year globally by 2050 if there was no sustained effort to contain antimicrobial resistance, an expert committee set up by the United Nations (UN) warned.

Globally, 7,00,000 people die because of drug-resistant diseases a year, including 2,30,000 deaths from multi-drug-resistant tuberculosis, it said.

In high-income countries alone, 2.4 million people could die between 2015 and 2050 due to antimicrobial drug resistance, which is being exacerbated by the abuse and overuse of antimicrobials agents such as antibiotic, antiviral, antifungal as well as antiprotozoal drugs.

Source: Inter-Agency Coordination Group (IACG)

Free Radicals May Not Be All Bad, Say Scientists

Free radicals are hyper reactive molecules that are implicated in a range of diseases ranging from cancers to neurodegenerative disorders to cardiovascular complications. But, these biological molecules, which are perceived to be villains and are destroyed using antioxidants, may have a positive role to play too, according to a team of Indian scientists.

In a finding that may alter our fundamental understanding about free radicals, or reactive oxygen species (ROS) as they are called in scientific parlance, a team of Indian researchers has found that these unstable and highly reactive molecules may be vital in regulating growth and the size of organisms. To unearth the spectacular role of free radicals, the scientists used fruit flies as model organism.

Source: Sudip Mandal, Associate Professor off biological sciences, Indian Institute of Science Education and Research (IISER), Mohali, Journal Developmental Cell

**Activities Update**

**ILSI-India**

**Activities Completed**

ILSI-India Annual Meeting – 26 April, 2019, New Delhi
Seminar on Value Addition to Agriculture through Food Processing – 26 April, 2019, New Delhi

**More Activities (Conferences, Seminars, Workshops) For 2019 Under Discussion**

Research Projects / Monographs
Monograph Of Role Of Probiotics In Promoting Healthy Microbiome For Health And Immunity - Ongoing
Assessment Of Sugar Consumption Levels Among Rural And Urban Population In India- Ongoing
Assessment Of Fat / Saturated Fat Consumption Levels Among Rural And Urban Population In India- Ongoing
Monograph On Risk Assessment - Ongoing
Study On Healthy Foods and Healthy Diets- Ongoing
Standardization Of Methodologies for Research on Microbiome –Under Discussion

Contact: ILSI-India for further Information
Email: info@ilsi-india.org

**Other ILSI Entities**

ILSI Europe
Workshop on Application of Threshold of Toxicological Concern (TTC) in Risk Assessment
2019-05-22 – 2019-05-23, Beijing, China

ILSI Brasil
Atualização Sobre Suplementos Alimentares e Probióticos
2019-05-16, São Paulo, Brasil

II Hot Topics em Pediatria
2019-05-18, São Paulo, Brasil

XI Atualidades em Food Safety
2019-05-21, São Paulo, Brasil

Participação Pint of Science Brasil

Simpósio Alimentos Fortificados e Suplementos
2019-06-04, São Paulo, Brasil

Café Da Manhã Com Palestra: Métodos Alternativos
2019-06-25, São Paulo, Brasil

ILSI China
Workshop on Application of Threshold of Toxicological Concern (TTC) in Risk Assessment
2019-05-22 – 2019-05-23, Beijing, China
Lead Article
Randomized Controlled Trials Investigating The Relationship Between Dietary Pattern and High-Sensitivity C-Reactive Protein: A Systematic Review

Association Between Consumption of Fruit or Processed Fruit and Chronic Diseases and Their Risk Factors: A Systematic Review of Meta-Analyses

Special Articles
International Approaches to Developing Healthy Eating Patterns for National Dietary Guidelines

A Proposed Nutrient Density Score that Includes Food Groups and Nutrients to Better Align with Dietary Guidance

Association Between Dairy Intake and the Risk of Contracting Type 2 Diabetes and Cardiovascular Diseases: A Systematic Review and Meta-Analysis with Subgroup Analysis of Men Versus Women

Nutrition In Clinical Care
Effects of Oral Supplementation with Probiotics or Symbiotic in Overweight and Obese Adults: A Systematic Review and Meta-Analyses of Randomized Trials