School of Medicine

Department of Health Sciences

Master's degree in Medical Biotechnology

Thesis Title: The Role of the Ketogenic Diet in Brain Cancer: Translating Research into Public Health Insights. "News of the week project."

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Academic Year: 2023/2024

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SUMMARY

Rationale of the Study

The alarming rate of non-communicable diseases, including brain cancer, stresses the need for an alternative approach in addition to standard treatments. The lifestyle one follows contributes to the health outcome; hence, exploring metabolic interventions such as a ketogenic diet, integrating it with lifestyle medicine, may provide insight into enhancing the treatment and survival of people with brain tumors. The "News of the Week" project aims to provide up-to-date information on the role of the Ketogenic diet (KD) in the management of brain cancer and translate the findings into a less complex form for public understanding.

Methodology

This project was designed to assess the effects of the KD on tumor growth, patient survival, safety, and feasibility, and overall well-being in individuals with brain cancer by using the following databases: PubMed and Scopus. The project used a clear search strategy and inclusion criteria to select relevant human studies published in 2023-2025. Studies that do not show an association between the ketogenic diet and brain cancer, and non-human studies were excluded.

Results

Adherence to KD intervention, Glucose ketone index (GKI), Isocitrate dehydrogenase gene (IDH) mutation status, age, and stage of the disease play a role in the outcome of patients. KD effects are through its ability to reduce glucose availability to tumor cells, induce a metabolic shift toward ketone utilization, and affect the mechanism of tumor progression. In this research the final result contains 7 studies that met the inclusion criteria associated with KD in the management of brain cancer.

Conclusion

Integrating the KD as an adjunct treatment in Brain cancer patients may help in slowing tumor growth, prolonging survival, and improving the well-being of some patients with brain tumors. "News of the Week" help in providing information on the influence of lifestyle and diet on disease progression in less complicated words for the public.

1. INTRODUCTION

1.1 Lifestyle Medicine

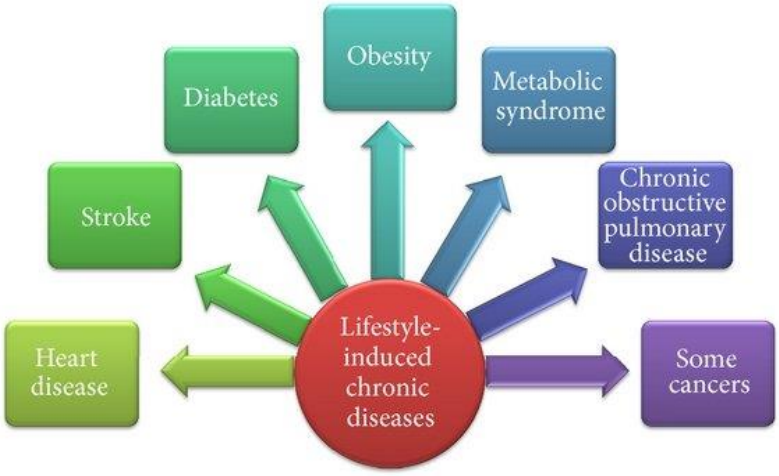
Ernst Wynder, in 1988, was the first to articulate lifestyle medicine, and since then, it has evolved into an integrated, evidence-based approach in the modern healthcare system as a preventive measure for non-communicable diseases (NCDs) by integrating diet, physical activity, stress management, and other lifestyle factors to achieve better health outcomes. Additionally, it addresses the root causes of chronic diseases through sustainable and evidence-based interventions, which can transform global health outcomes and reduce the burden of chronic diseases on individuals, communities, and healthcare systems. According to the American College of Lifestyle Medicine, it can also manage up to 80% of chronic diseases by helping reduce their rising prevalence and related costs. The modern model enhances patients' and healthcare providers' satisfaction while emphasizing better health outcomes, lower costs, and health equity. Moreover, this approach also supports planetary health, making it key to a more effective and equitable healthcare system (American College of Lifestyle Medicine).

1.2 Lifestyle Medicine and Chronic Disease

In 2021, 43 million deaths were estimated to be linked to chronic diseases, also known as non-communicable diseases (NCDs) (World Health Organization (WHO, 2024). NCDs are responsible for 75% of non-pandemic-related deaths globally, which makes them a global burden on health (WHO, 2024). Premature death happens among individuals under the age of 70, which accounts for nearly 18 million deaths, and around 82 % of these occur in low and middle-income countries (WHO, 2024).The reason behind 80% of premature deaths was NCDs of four major diseases, namely: Cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes. Cardiovascular diseases contributed to 19 million fatalities, being the top in the list, followed by cancer, resulting in 10 million deaths, chronic respiratory diseases being responsible for 4 million deaths, and finally diabetes and its complications over 2 million fatalities (WHO, 2024). Recently, the number of people living with diabetes has increased globally, affecting 1 in 10 people. It is projected to rise from 537 million cases today to 643 million by 2030(IDF Atlas, 10th Edition; International Diabetes Federation, 2024). Similarly, the obesity rate has been seen to increase in rates since 1990, both in adults and adolescents. WHO reported in 2022 that 1 in 8 people globally

had obesity. In 2019, an elevated BMI contributed to an estimated 5 million deaths from non-communicable diseases (NCDs) like cardiovascular diseases, diabetes, cancers, neurological disorders, chronic respiratory diseases, and digestive issues (GBD 2019 Risk Factor Collaborators, 2020). Above all, Key risk factors such as tobacco use, physical inactivity, harmful alcohol consumption, unhealthy diets, and air pollution significantly increase the likelihood of NCD-related mortality (WHO, 2024).

Figure 1: Illustrating the impact of lifestyle choices on chronic diseases.

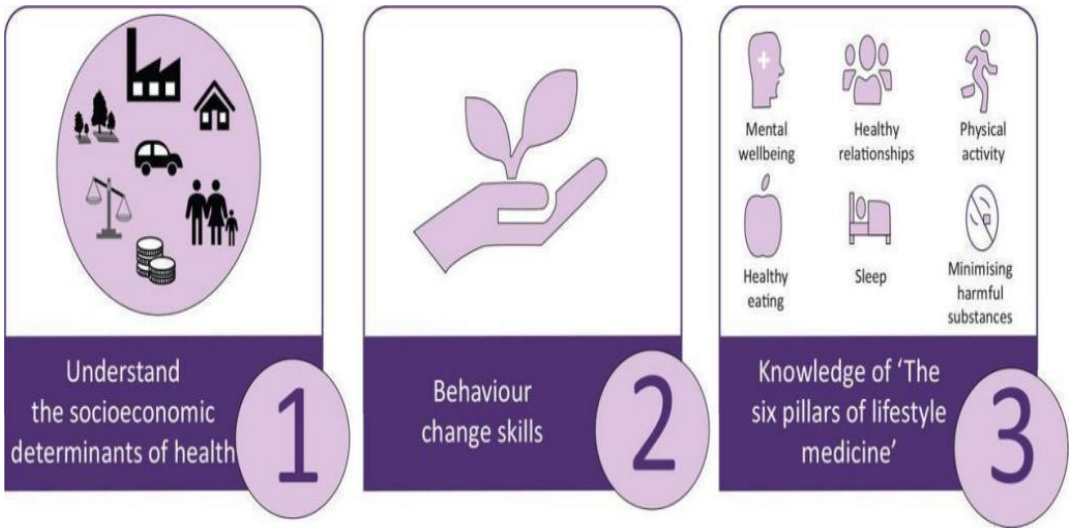


As shown in the diagram, lifestyle choices contribute to the development of various chronic conditions like diabetes, heart disease, obesity, metabolic syndrome, and certain cancers. Adopted from Minich and Bland (2013), The Scientific World Journal https://doi.org/10.1155/2013/129841.

Non-communicable diseases like diabetes, cardiovascular disease, certain cancers, obesity, and chronic respiratory diseases are caused by a combination of factors, including genetics, lifestyle behaviors, healthcare system limitations, community influences, and environmental determinants of health (Mirsky & Artz, 2023), and they are leading causes of morbidity and mortality, based on the statistics by the WHO (WHO,2024).These chronic diseases are impacted by the type of lifestyle an individual chooses to live, highlighting the fact that NCDs can be prevented through modification and following a better lifestyle: Diet, Physical activity, stress management, hygienic sleep, and avoidance of substance use like illicit drugs and other substances. These, with preventive health policies and strategies, will make a huge difference (WHO 2024). As stated by Mirsky and Artz, the challenge is not in the "what" (lifestyle medicine's importance) but in the "how" (effective implementation) (Mirsky & Artz,

2023). Given the increasing burden of chronic diseases, interventions targeting these modifiable risk factors are crucial, and lifestyle medicine offers an evidence-based approach, emphasizing the modification of behavioral risk factors such as diet, physical activity, stress management, and sleep hygiene to prevent and manage chronic illnesses, with the integration of lifestyle-based strategies into healthcare poised to enhance patient outcomes, reduce healthcare costs, and improve both patient and provider satisfaction (American College of Lifestyle Medicine).

Figure 2:-The three major foundations for the implementation of lifestyle medicine.



The British Society of Lifestyle Medicine (BSLM) explains 3 Major components in the practice of lifestyle Medicine: 1. understanding the socioeconomic determinants of health, 2.The use of behavior change techniques (tools and techniques that healthcare providers and individuals need to promote and sustain healthy lifestyle changes), and 3. Knowledge of the six pillars. Adopted from Fallows, E. S. (2023). Lifestyle medicine: A cultural shift in medicine that can drive integration of care. Future Healthcare Journal, 10(3), 226. https://doi.org/10.7861/fhj.2023-0094.

1.3 Pillars of Lifestyle Medicine

Lifestyle medicine comprises six pillars, such as nutrition, exercise, stress management, social support, sleep, and avoiding risky behaviors.

Figure 3: Pillars of Lifestyle Medicine

Lifestyle medicine has six pillars: nutrition, exercise, stress management, social support, sleep, and avoiding risky behaviors, such as smoking tobacco and using illicit drugs. Adherence to the six pillars helps to reduce the risk of chronic disease. Adapted from Arora, Sarah, et al. "Diet and Lifestyle Impact the Development and Progression of Alzheimer's Dementia." Frontiers in Nutrition, vol. 10, 2023, p. 1213223, https://doi.org/10.3389/fnut.2023.1213223.

1.3.1 Whole Food, Plant-based Nutrition

Looking out for what we eat has a great impact on health. Studies show that diets that are low in saturated fat, Trans fat, sodium, added sugars, and healthy dietary patterns reduce the risk of the major diet-related chronic diseases, such as diabetes, cardiovascular disease, and some cancers (Neuhouser, 2019). Various scientific evidence supports the use of a whole food, predominantly plant-based diet (Consuming a fiber-filled, nutrient-dense, antioxidant-rich eating pattern based predominantly on a variety of minimally processed vegetables, fruits, whole grains, legumes, nuts, and seeds), which can be a crucial step in preventing chronic

disease (American College of lifestyle medicine). Another study done by Ornish Lifestyle Medicine supports this idea by stating nutritional interventions as a key contributor to reversing the progression of chronic diseases such as severe coronary artery disease, type 2 diabetes, high cholesterol, and high blood pressure(Ornish Lifestyle Medicine).In addition, another study conducted shows that dietary factors also have effects on mood and are linked to mood disorders such as anxiety and depression (Melanson, 2007).

1.3.2 Physical Activity

As per the definition provided by WHO, physical activity refers to a bodily movement carried out by the skeletal muscles that require energy consumption (WHO, 2024). According to the Centers for Disease Control and Prevention (CDC), about 1 in 2 adults in the US live with a chronic disease, and only 1 out of 4 fully meet the guidelines of physical activity (CDC). Getting engaged with enough physical activity could prevent the following: 1 in 8 Breast cancer cases, 1 in 10 premature deaths, 1 in 12 diabetes cases, and 1 in 15 cases of heart disease (CDC). Regular exercise for a week has a substantial health benefit. Many studies show that an adult who is less sedentary and engages in more activity experiences health benefits. It improves cardiovascular fitness, strengthens the musculoskeletal system, and enhances metabolic function. Additionally, it has been shown to reduce symptoms of anxiety and depression, improve cognitive function, and lower the risk of cognitive decline and dementia (Fedorchenko et al., 2024).

1.3.3 Restorative Sleep

The Sleep Research Society suggests that for optimal health, one should sleep 7 or more hours per night. Healthy sleep is as beneficial as eating healthy and physical activity (Meltzer, Moreno, & Johnston, 2014). Sleep has a relationship with brain function, especially in regulating and expressing at the brain and behavioral level, which will also later affect societal structure (Goldstein & Walker, 2014). Lack of proper sleep, which includes long duration of sleep, is also related to various risks of developing chronic conditions such as obesity, diabetes (Type 2), by disrupting whole-body energy metabolism and increased adiposity due to disruptions in circadian rhythms and hormonal imbalances (Tan et al., 2018).

1.3.4 Stress Management

According to the American Journal of Lifestyle Medicine, more than 75% of doctor visits are related to stress (American College of Lifestyle Medicine). The American Psychological Association shows, chronic stress can have detrimental effects on the body, contributing to both physical and mental health issues. Prolonged stress increases the risk of conditions such as anxiety, depression, digestive disorders, headaches, muscle tension, reproductive health, cardiovascular diseases, including high blood pressure, heart disease, heart attacks, and strokes, as well as sleep disturbances, weight gain, and cognitive impairments affecting memory and concentration. Stress is an inevitable part of daily life, influencing individuals in both positive and negative ways. While certain levels of stress enhance motivation and performance, prolonged and excessive stress disrupts the equilibrium of the body by affecting proper sleep, physical activity, and eating habits (Harvard T.H. Chan School of Public Health, 2021).

1.3.5 Avoidance of Risky Substances

Research consistently shows that the use of tobacco, alcohol, and illicit drug substances is associated with a range of adverse health outcomes, including cardiovascular diseases, cancer, liver diseases, and mental health disorders (American Heart Association, 2020; World Health Organization, 2021).

1.3.6 Social Connection

Social connections play a crucial role in lifestyle medicine, significantly impacting both mental and physical health. Studies from the US Department of Health and Human Services (HHS) show that being isolated makes it harder to thrive, and people who experience social isolation face a 29% higher risk of early death (HHS). For older adults, feeling chronically lonely or socially isolated can nearly double the risk of developing dementia (HHS). Another study highlights the dual impact of social ties on aging health. Strong relationships enhance well-being and lower disease risks; persistent conflicts and loss of close ties can harm health. As global aging accelerates, understanding these effects is crucial (Rook & Charles, 2017).

2. BRAIN CANCER

2.1 Overview and Types of Brain Cancer

Brain cancer is the uncontrolled growth of cells within the brain or central nervous system (CNS). The brain is a highly complex organ, which makes it difficult when it comes to neurological damage, including brain cancer. Due to its aggressive nature and limited treatment options, brain cancer is considered to be the most challenging malignancy. It has a high mortality rate, with a median age of diagnosis of 61. The chances of surviving depend on the age of diagnosis and other factors like tumor type (National Brain Tumor Society). Around 72% of brain tumors are benign, and 28% are malignant. Brain cancer encompasses diverse tumor types that vary in origin, growth patterns, and clinical implications, as given by the National Brain Tumor Society. There are over 150 identified types of brain tumors, broadly categorized into malignant (cancerous) and benign (noncancerous) forms (National Brain Tumor Society).

Brain tumors are a heterogeneous group of neoplasms that vary widely in incidence, behavior, and patient demographics. While some tumor types, such as meningioma and pituitary adenomas, are generally benign, others, like glioblastomas and embryonal tumors, are highly aggressive and associated with poor prognosis. Tumor prevalence also varies by age and sex; for instance, glioblastoma occurs more frequently in older adults and males, whereas meningiomas are more common in females. A summary of common brain tumor types and their demographic distribution is presented in Table 1 (Ostrom et al., 2019).

Table 1. Classification of Common Brain Tumors by Frequency, Behavior, and WHO Grade.

Tumor Type	**Tumor Behavior**	**Common Age Group**	**Gender Predominance**	**WHO Grade (Typical)**[1]
Meningioma	Usually, benign	Adults	Female > Male	I (can be II or III)
Glioblastoma (GBM)	Highly malignant	Older adults	Male > Female	IV
Pituitary Tumors	Usually, benign	Adults	No strong bias	I (some can be II/III)
Nerve Sheath Tumors	Benign	Adults	Slightly Female > Male	I
Embryonal Tumors (e.g., Medulloblastoma)	Malignant	Children	Male > Female	IV
Ependymoma	Can be benign or malignant	Children and young adults	No strong bias	I–III (depends on subtype)
Oligodendroglioma	Malignant	Young to middle-aged adults	Male > Female	II–III
Other Gliomas	Mixed	Adults	Varies	II–IV

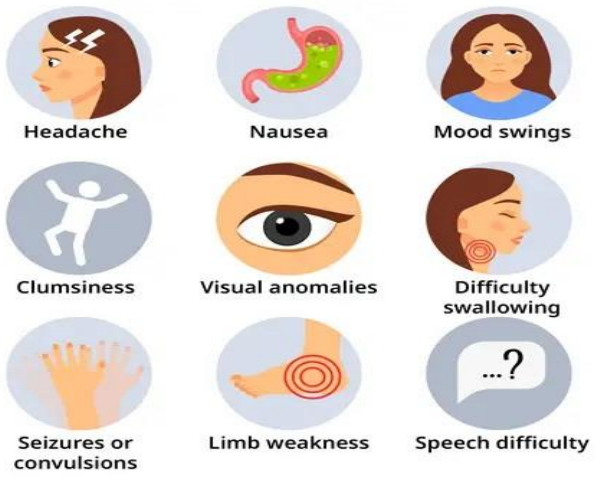
[1]WHO Grade from grade ^{I} to grade ^{IV} = World organization classification system indicating the tumor aggressiveness.

Brain tumors are mainly grouped as malignant or benign tumors, and can be graded from grade ^{I} to grade ^{IV} as specified by the WHO. The above table is based on Ostrom, Quinn T., et al." Risk Factors for Childhood and Adult Primary Brain Tumors." Neuro-Oncology, vol.21, no. 11, 2019, p.1357, https://doi.org/10.1093/neuonc/noz123.

2.2 Symptoms and Diagnosis

The symptoms of brain cancer differ depending on the kind of tumor it is, the location, and the size. The general symptoms include increased intracranial pressure, headaches, nausea, vomiting, and Visual disturbances, such as blurred vision, double vision (diplopia), or vision loss (Schaff, L. R., & Mellinghoff, I. K., 2023, Healthline, 2024, Cancer.Net). Additionally, cognitive impairments such as memory problems, confusion, and personality changes may arise due to tumor-induced pressure on adjacent brain structures (Mayo Clinic, 2024).

Figure 4: Major Symptoms of Brain Cancer



Adopted from Adobe stock. Vector medical poster brain cancer. Symptoms of the disease by Irina Strelnikova. Vettoriale stock di Vector medical poster brain cancer. Symptoms of the disease. | Adobe Stock.

For improved treatment results, an early and accurate diagnosis of a brain tumor is essential. Especially since brain cancer symptoms mimic other conditions' symptoms. The diagnostic process for brain cancer begins with a thorough assessment, including inquiries into the patient's symptoms, medical history, and family history. Various examinations are conducted to evaluate neurological function, vision, hearing, memory, sense of touch, and reflexes. If these examinations indicate potential issues, further investigations are conducted taking biopsy and using imaging technologies like: MRI

(Magnetic Resonance Imaging): Used to locate tumors, assess swelling, and identify areas affected by strokes, CT Scan (Computed Tomography): Helps detect fresh bleeding and changes in the skull or brain tissue, Magnetic Resonance Spectroscopy (MRS): Conducted alongside an MRI to analyze biochemical processes in the brain, further aiding in differentiating between cancerous and non-cancerous lesions(American Cancer Society,2023). There are emerging technologies for better diagnosis, including AI, Nanotechnologies, sono biopsy, and Biomarkers that can overcome challenges with the present imaging technologies and biopsy.

2.3 Risk Factors

Although the exact causes of brain tumors remain unclear, for convenience, we can classify them as non-modifiable risk factors and lifestyle and environmental risk factors (Vienne-Jumeau, Tafani, & Ricard, 2019).

2.3.1 Non-modifiable risk factors

Age, sex (some types of brain cancer are common in men than women), family history (hereditary syndromes like Li-Fraumeni), and some immune system disorders are categorized under the non-modifiable risk factors and potential risks (Cancer Research UK 2023, Ostrom et al., 2019).

2.3.2 Environmental and lifestyle factors

Certain environmental exposures and some occupations are strongly related to brain cancer. Ionizing radiation is the most clearly established risk factor, and has been consistently associated with an increased risk of CNS tumors in both children and adults (Ostrom et al., 2019; Vienne-Jumeau, Tafani, & Ricard, 2019). A study conducted in Canada showed that there is an increased risk of brain cancer associated with some occupations that involve exposure to asbestos, benzene, mineral oil, or lubrication oil, and isopropyl alcohol. (Pan, Ugnat, &Mao, 2005).

Additionally, a comprehensive meta-analysis by Onyije et al. (2024) found that maternal and paternal exposure to insecticides or herbicides and benzene exposure are associated with an increased risk of childhood brain tumors before conception and during pregnancy (Onyije et al. 2024).

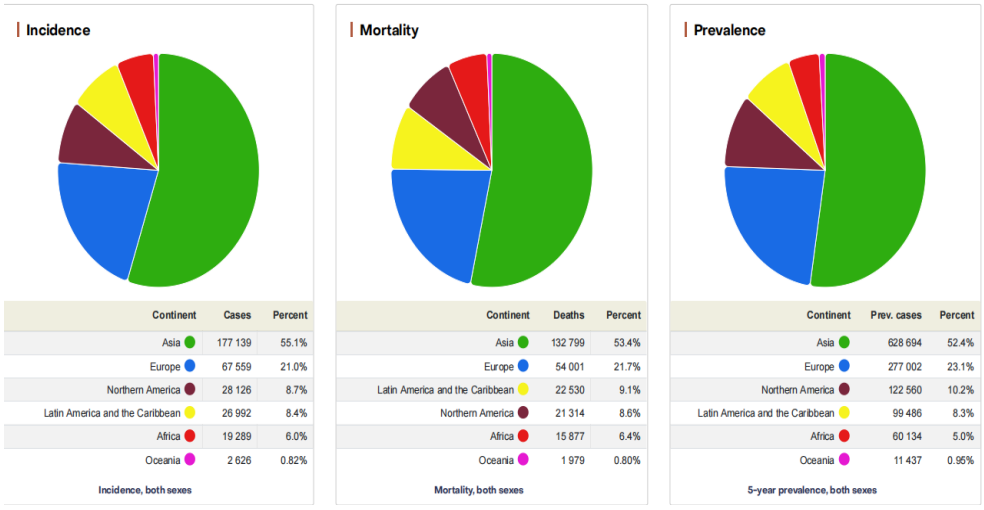
Prenatal and maternal lifestyle can be associated with increased childhood brain tumors (CBT) as per onyije et al. (2024) consuming cured meat which contains nitrites or nitrates during pregnancy was linked to 51% increased of risk of cured meats (containing nitrites) but also drinking ≥ 2cups/day, smoking 10 cigarettes/day are moderately associated to CBT, additional birth weight >4000g is associated to high risk of CBT (onyije et al., 2024).

Various studies have been done regarding brain cancer and its association with diet, but the results were less definitive. Instead, consumption of fruits and vegetables may have protective effects due to antioxidant properties. In general, having a healthy nutritional diet can be a preventive lifestyle (Ostrom et al., 2019).

2.4 Global Trends and Future Projections of Brain Cancer

According to the report of GLOBOCAN 2022, estimated by the International Agency for Research on Cancer (IARC), there were around 322,731 new cases and 248,500 deaths globally related to Brain cancer and CNS. It ranked 19th in incidence and 12th in cancer-associated mortality worldwide (IARC, 2022).

Figure 5: Incidence and prevalence of Brain and CNS cancers.

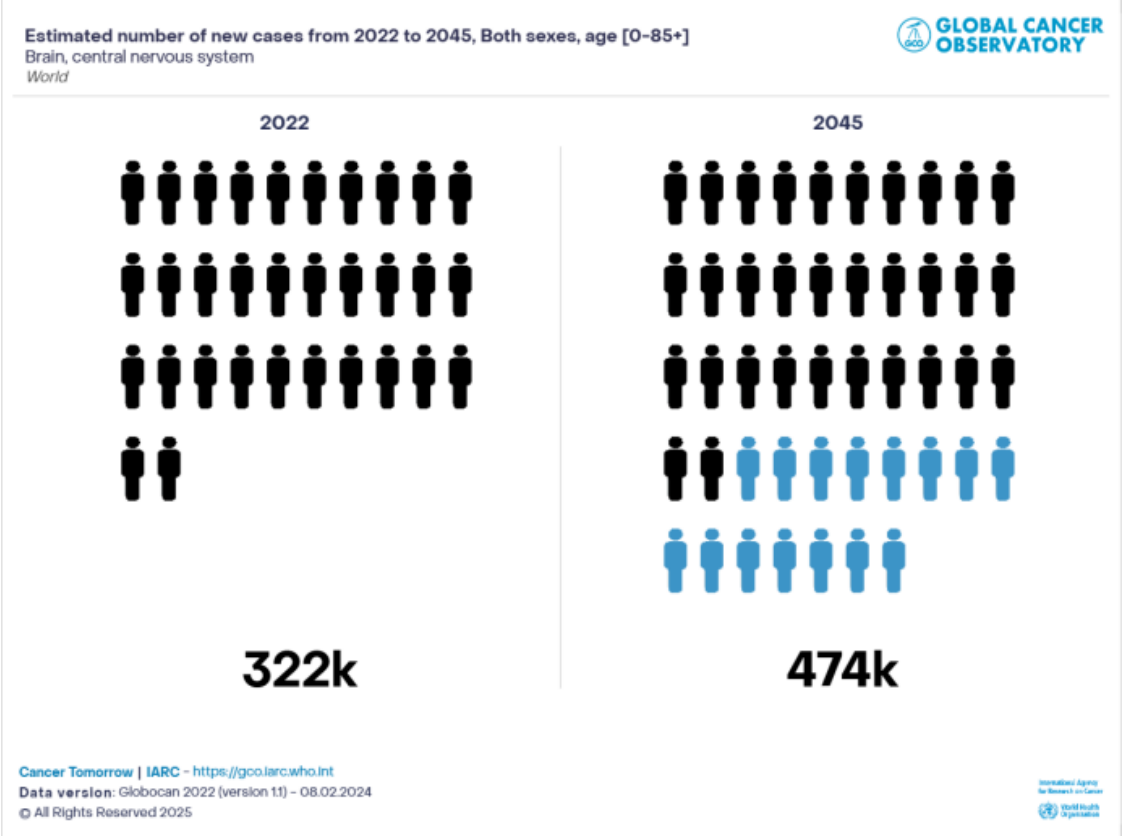


The figure illustrates that Asia comprises over 55% of cases and 53% of fatalities, followed by Europe, and then North America. Adopted from the International Agency for Research on Cancer. (2022). Global Cancer Observatory (GLOBOCAN 2022): Brain and CNS cancers. World Health Organization. https://gco.iarc.fr/

2.5 Current Standard Treatments and Challenges

Treatment of brain cancer is influenced by factors such as tumor size, location, histological grade, and the patient's overall health status. Standard care typically involves a combination of surgery, radiation therapy, and chemotherapy, though each approach faces notable limitations. Corticosteroids are routinely administered preoperatively to control cerebral edema and reduce seizure risk, but long-term use contributes to immunosuppression and metabolic complications (Harvard Health, 2024). Chemotherapy agents like temozolomide (TMZ) and bevacizumab offer modest survival benefits in glioblastoma multiforme (GBM); however, they come with systemic toxicity and hematologic side effects such as neutropenia often require dose adjustments or treatment delays (Schaff & Mellinghoff, 2023). Meanwhile, emerging options, including immune checkpoint inhibitors and molecularly targeted agents, remain investigational with mixed results and limited accessibility. Given the challenges of incomplete resection, treatment resistance, neurotoxicity, recurrence, and poor quality of life, attention is shifting to adjunctive approaches like metabolic therapy, the KD. Understanding its role within the broader framework of lifestyle medicine provides a foundation for exploring its therapeutic implications in brain cancer.

Figure 6:-Projected trend in the new cases of brain and central nervous system cancers to 2045.



In the future, there is a high probability of new and significantly high brain and central nervous system cancer cases expected (IARC, 2022). If the incidence rate continues at the same rate, cases will increase from 322,000 in 2022 to 474,000 in 2045(IARC, 2022).

3. KETOGENIC DIET AND BRAIN CANCER

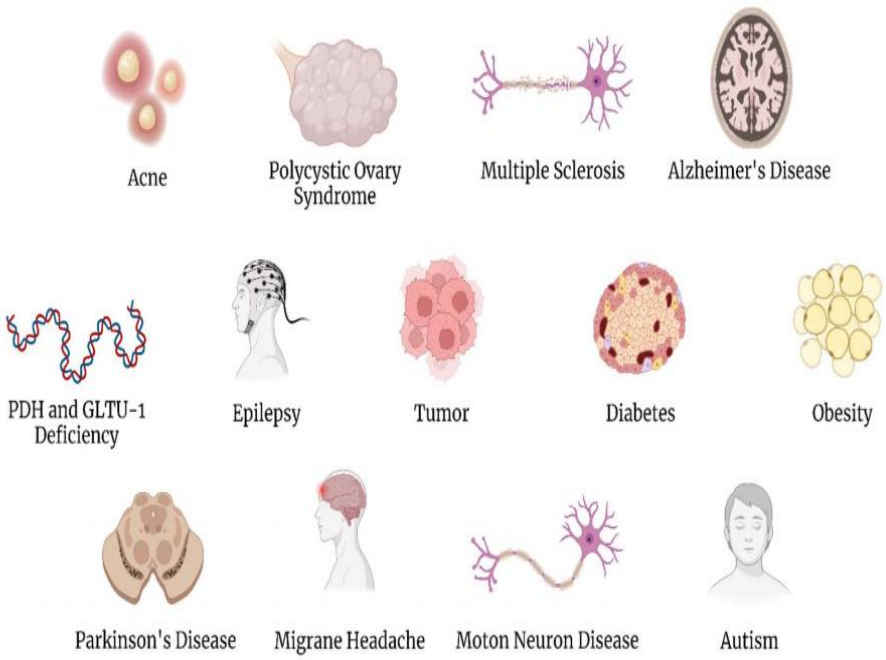
3.1 Understanding the Ketogenic Diet

The history of the KD takes us back to 1911, when it was used as a treatment for epilepsy by decreasing the severity of seizures in periods of starvation (Wheless, 2008). The term was developed by Dr. Russell Wilder and Dr.Rollin Turner at the Mayo Clinic. Then, in 1970, Dr. Robert Atkins introduced nutritional ketosis for weight loss in his published book. He described how a diet with low carbohydrates creates a different, in fact, unique metabolic alteration in the body (Atkins, R. C. (1972). Dr. Atkins' diet revolution.).The KD is a nutritional approach that majorly involves low carbohydrate intake, high fat consumption, and moderate or standard protein levels. Intake of this diet diverts the use of glucose as a main energy source into an alternative for ketones like Beta-hydroxybutyrate, acetoacetate, and acetone, resulting in decreased glucose availability (Santangelo et al., 2023; Liu et al., 2024). Lately, this diet is getting much attention from various researchers as a therapeutic mechanism for multiple issues, including obesity, acne, type 2 diabetes mellitus, cancer, and Alzheimer's disease (Westman et al., 2018; Weber et al., 2018; Rusek et al., 2019).

Figure 7: The Ketogenic Diet.

Adopted from https://nutritionstudies.org/ and Ketogenic diet Vector Images | Depositphotos. A ketogenic diet consists of low-carb (5-10%), protein (20%), and (70-80%) fat.

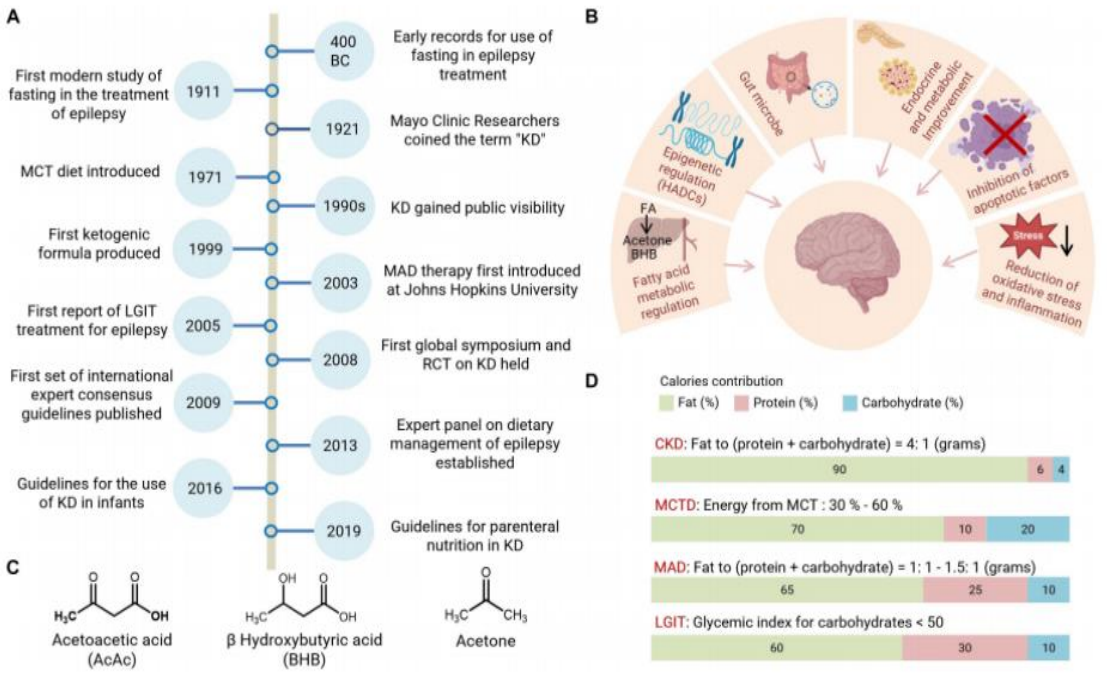
Figure 8: Importance of the Ketogenic Diet in various diseases.



The above visual diagram shows various conditions like acne, tumors, epilepsy, obesity, and some neurological diseases. In which adherence to the ketogenic diet has positive effects. Adopted from (Dal Bello, S., Valdemarin, F., Martinuzzi, D., Filippi, F., Gigli, G. L., & Valente, M. (2022)). Ketogenic Diet in the Treatment of Gliomas and Glioblastomas. Nutrients, 14(18), 3851. https://doi.org/10.3390/nu14183851).

There are various KDs, such as the classic KD, medium-chain triglyceride (MCT) diet, very low-calorie KD (VLCKD), modified Atkins diet, and low glycemic index treatment. Low glycemic index treatment is easier to follow for adults because it doesn't require strict restriction of carbohydrates (Sant'Angelo et al., 2023). KD has various side effects like hypoglycemia, dyslipidemia, gastrointestinal symptoms, and symptoms that are temporarily seen initially when starting the diet, nausea, vomiting, and headache, commonly referred to as "Keto flu," that can be easily managed. As observed by Kiryttopoulos et al., there is a weight loss initially, but then it gets stabilized (Kiryttopoulos et al., 2025; Sant'Angelo et al., 2023), and at the same time, potential complications like pancreatitis, cardiac abnormalities, and vascular changes can happen (Sant'Angelo et al., 2023). Therefore, understanding the role of KD in brain cancer requires extensive research on the pros and cons and an understanding of the physiological basis of the KD.

Figure 9:- History and classification of KD Therapy.



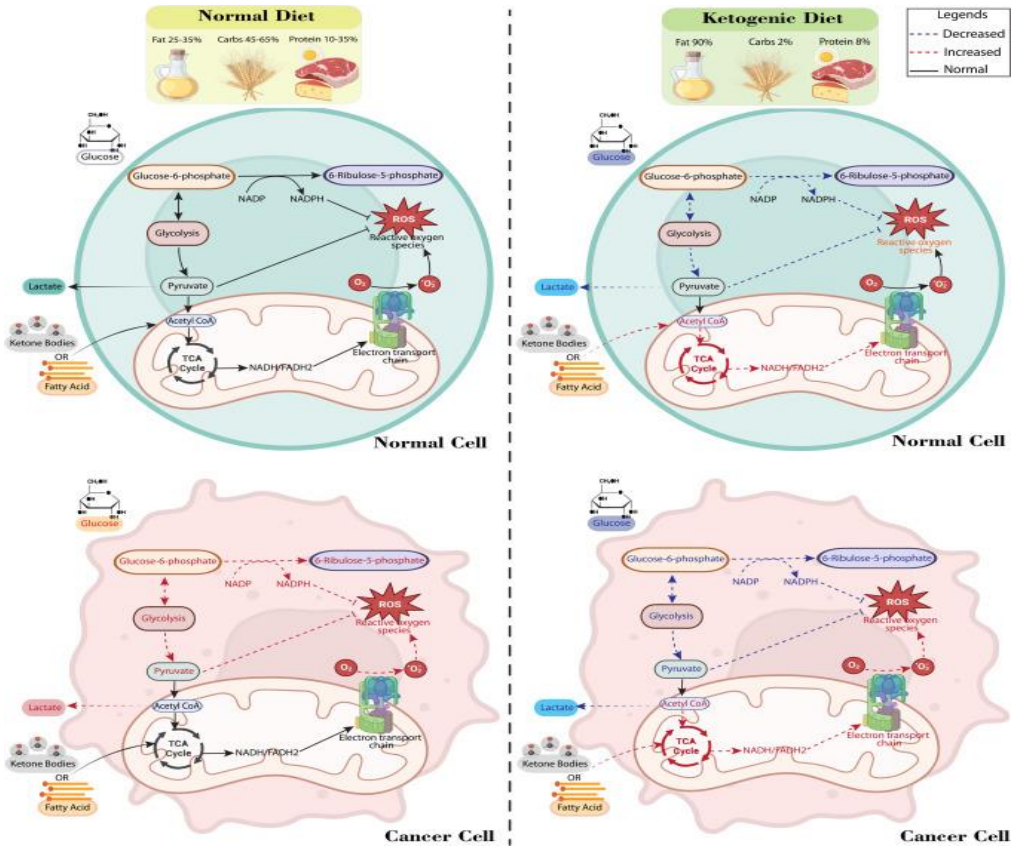
History and classification of KD therapy. (A) Highlighted events in the development of ketogenic diet therapy. (B) Mechanistic hypothesis for KD treatments. (C) Structure of ketones, Acetoacetate (AcAc), β-hydroxybutyrate (BHB), and acetone. (D) Nutrient composition for the main KD variants. RCT, randomized clinical trial; CKD, classic ketogenic diet; MCTD, medium-chain triglyceride diet; HDACs, histone deacetylases. Adopted from (Liu, Y., Fan, L., Yang, H., Wang, D., Liu, R., Shan, T., & Xia, X. (2024). Ketogenic therapy towards precision medicine for brain diseases. Frontiers in Nutrition, 11, 1266690. https://doi.org/10.3389/fnut.2024.1266690).

3.2 Brain Cancer Metabolism and the Warburg Effect

Healthy brain cells differ from cancer cells mainly because healthy cells use glycolysis under anaerobic conditions, where there is no oxygen; on the other hand, cancer cells, including brain cancer cells, consistently depend on glycolysis even in the presence of oxygen. These phenomena were described by Dr. Warburg in 1955, and the phenomena were named after his name as the Warburg effect. Aerobic glycolysis enhances cancer cells' uncontrolled growth and division, which enables cancer cells to use this process for efficient energy production for survival (Makuku et al., 2023). The mechanism followed by KD is targeting the Warburg effect (cancer cells' reliance on glycolysis), reducing the glucose availability, and then increasing ketone bodies, in which healthy neurons can use it but glioma cells often cannot. As described by Ceccchi et al 2023,and

Valerio et al 2024 KD modulates insulin signaling (Akt/mTOR pathways), epigenetics (microRNA expression, DNA methylation), and oxidative stress, potentially enhancing conventional therapies (Valerio et al., 2024; Cecchi et al., 2023).

Figure 10: Schematic of Metabolic Differences in Normal vs. Cancer Cells on a KD vs. Normal Diet.

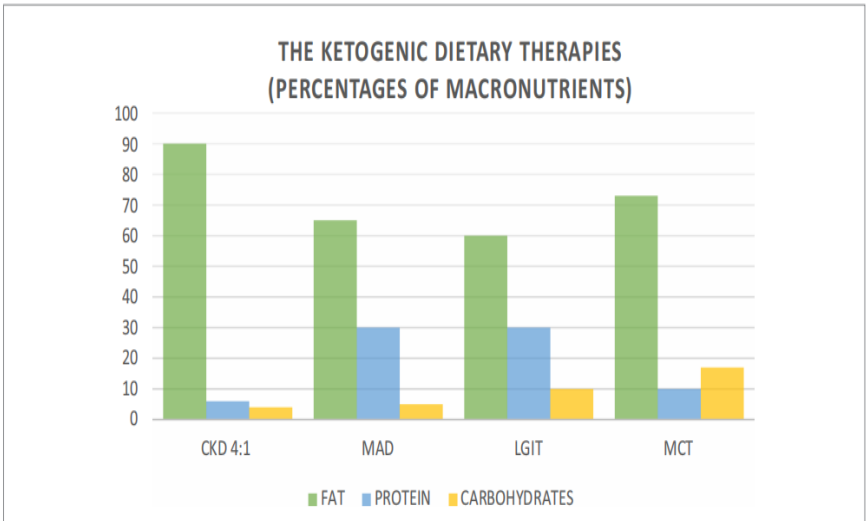


ROS generation is elevated in cancer cells due to a higher number of mitochondrial DNA mutations and changed mitochondrial protein expression. They mostly rely on glucose metabolism to combat oxidative stress, generating pyruvate and NADPH through the pentose phosphate pathway and glycolysis. Hydro peroxides are reduced by NADPH, while NADPH synthesis is supported by pyruvate. Ketogenic diets limit the availability of glucose, which in turn limits the activity of the pentose phosphate and G-6-P pathways. Because of this decreased NADPH regeneration, cancer cells experience higher levels of oxidative stress than healthy cells.

Adopted from (Chaudhary, R. (2024). Ketogenic diet as a treatment and prevention strategy for cancer: A therapeutic alternative. Nutrition, 124, 112427. https://doi.org/10.1016/j.nut.2024.112427.

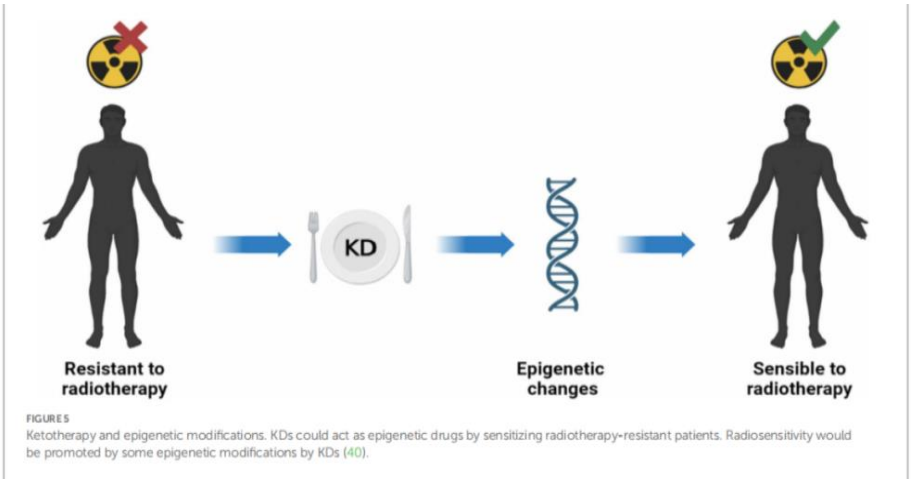
The other major difference between Normal brain cells and cancer cells is in their ability to utilize ketone bodies as an energy source or fuel. Under normal circumstances, normal brain cells can get energy from both ketones and glucose, but not cancer cells, which heavily depend on glycolysis, as several studies show it's mainly because they have reduced expression of ketolytic enzymes to utilize ketones. Severe restriction of carbohydrate intake and increasing a ketogenic-based diet causes the state of nutritional ketosis, which lowers the availability of glucose while increasing ketone body production, and the state of ketosis protects healthy cells from reactive oxygen species and enhances antioxidants, while it increases oxidative stress in the tumor cells (Cecchi et al., 2023). Additionally, the use of KD early and immediately after surgery to decrease the glucose inflow and prevent the Warburg effect, hence understanding the relationship between cell metabolism and proliferation control, may lead to an improvement in cancer treatment (Cecchi et al.,2023).

Figure 11: Nutritional Characteristics of Ketogenic Diet Therapies.



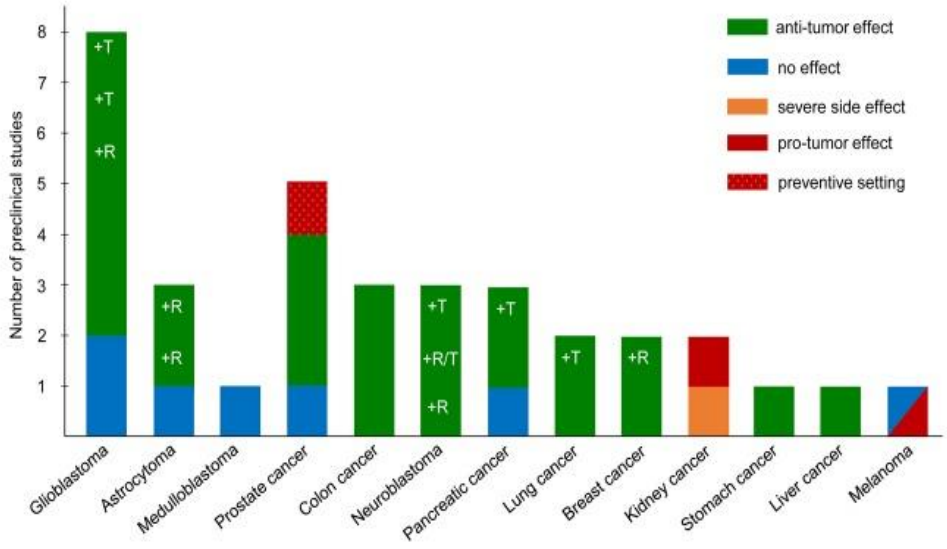
The bar graph shows that the ketogenic dietary therapies (KDTs) are the Classic Ketogenic Diet (CKD), the Ketogenic Diet with Medium Chain Triglycerides (MCT), the Modified Atkins Diet (MAD), and the Low Glycemic Index Treatment (LGIT). The common ratio is 4 g of fat for every 1 g of combined protein and carbohydrate, where 90% of the total energy comes from fat intake and 10% from the combined protein and carbohydrate intake. Adopted from Cecchi et al., 2023.Front. Nutr. 10:1222908.doi: 10.3389/fnut.2023.1222908.

Figure 12: The Ketogenic Diet acts as an epigenetic modification feature.



The image illustrates how tumor patients often exhibit radiation resistance as a result of modifications to the tumor tissue's epigenetic properties. To get around this, it has been demonstrated that several epigenetic inhibitors, including DNMT1 and KD, work similarly to these sensitizing medications.
Adopted from Cecchi et al., 2023.Front. Nutr. 10:1222908.doi: 10.3389/fnut.2023.1222908.

Figure 13: Showing the effect of Ketogenic Diet on tumor growth and progression.



The bar chart shows various pre-clinical studies of the KD effect on different types of cancer. R shows studies with a calorie-restricted KD, and T indicates using KD as adjuvant therapy to classic therapy. Adopted from Weber, D. D., Aminazdeh-Gohari, S., & Kotler, B. (2018). Ketogenic diet in cancer therapy. Aging, 10(2), 164–165. https://doi.org/10.18632/aging.101382.The preclinical studies show promising results.

4. AIM AND OBJECTIVE OF THE PRESENT WORK

This project aims to develop "News of the Week" content to identify the role of KD in the management of Brain Cancer, through the synthesis of recent human studies (2023–2025).

4.1 News of the week project

The increasing prevalence of lifestyle induced disease, such as some cancers affect the health outcome of individuals and this project focuses on presenting research insights in a comprehensible format to help and influence dietary and lifestyle choices, resulting in improved health outcomes. The "News of the Week" project aims to identify and summarize recent, human-based scientific articles, mainly focusing on lifestyle medicine, and translate findings in layman's terms to bridge the gap between academic research and public health by translating complex scientific findings into accessible, actionable knowledge for the broader community and presenting it on a platform in English and Italian. The News of the Week project explores KD and its impact on brain cancer. It is presented in the following structure: 1. Background of the study, 2. Identifying main findings of the study, 3. their practical implications for patients, 4. News of the week, presented engagingly for public understanding.

5. MATERIALS AND METHODS

5.1 Search strategy

In this review and News of the Week Project, a systematic search for the correlation of KD and brain cancer outcome on general population. It was conducted using PubMed and Scopus databases, encompassing studies available from 2023 up to 2025, this narrow timeframe was chosen to ensure that only the most recent human clinical evidence.

Search query used for "NEWS of The Week" project and review

- **PubMed** :-("Ketogenic diet "OR "Ketone diet") AND ("Brain cancer" OR" Brain tumor" OR "Brain neoplasm" OR "Glioma "OR"GBM").

- **Scopus** :-TITLE-ABS-KEY (("Ketogenic diet" OR "Ketone diet") AND ("Brain cancer" OR" Brain tumor" OR "Brain neoplasm" OR "Glioma " OR "GBM")) AND PUBYEAR > 2022 AND PUBYEAR < 2026 AND PUBYEAR > 2022 AND PUBYEAR < 2026 AND PUBYEAR > 2022 AND PUBYEAR < 2026.

Inclusion Criteria

1. Studies conducted on human beings, including all ages, races, or genders.
2. Studies that include the use of a KD in patients with brain cancer.
3. Types of studies: - clinical trials, observational studies, case reports, reviews, and systematic Reviews.
4. Published in 2023 - 2025.
5. Full text available.
6. Written in English.

Exclusion Criteria

1. Animal studies: Studies with mouse models or non-human studies.
2. Studies unrelated to KD and brain cancer.
3. Studies without full text available.
4. Non-English publication.

5.2 Data Extraction

Data were extracted from Microsoft Excel to ensure consistency across all included studies. The extracted variables include the following information: study characteristics (Author, year, country, study design, aim of the study, main findings), participants' demographics (sample size, sex, age, gender, cancer subtype), details about KD intervention as an adjunct therapy were recorded, including the type of KD protocol used and adherence to KD intervention. Clinical outcomes were also extracted, including (Tumor response, quality of life, survival outcomes, and metabolic markers like GKI and ketone levels). Moreover, additional information regarding adverse effects and limitations of the study was also documented.

6. RESULTS

6.1 Identification of Included Studies

The study selection process followed the PRISMA 2020 guidelines and was conducted in the timeframe of 2023 - 2025. The process began with the identification of 67 records from two databases: 20 from PubMed and 47 from Scopus. After removing 16 duplicate records, 51 articles remained and were screened by title and abstract. During this initial screening phase, 44 records were excluded for not meeting the inclusion criteria. The remaining 24 articles were then assessed in full text for eligibility. Of these, 17 were excluded for the following reasons: 7 were animal or non-human studies, 9 did not provide information about the effect of the KD on brain cancer, and 1 was of an ineligible publication type. Ultimately, 7 studies met the eligibility criteria and were included in the final review. The study selection process is presented in the PRISMA diagram in Figure 14.

Figure 14: flow diagram of study selection.

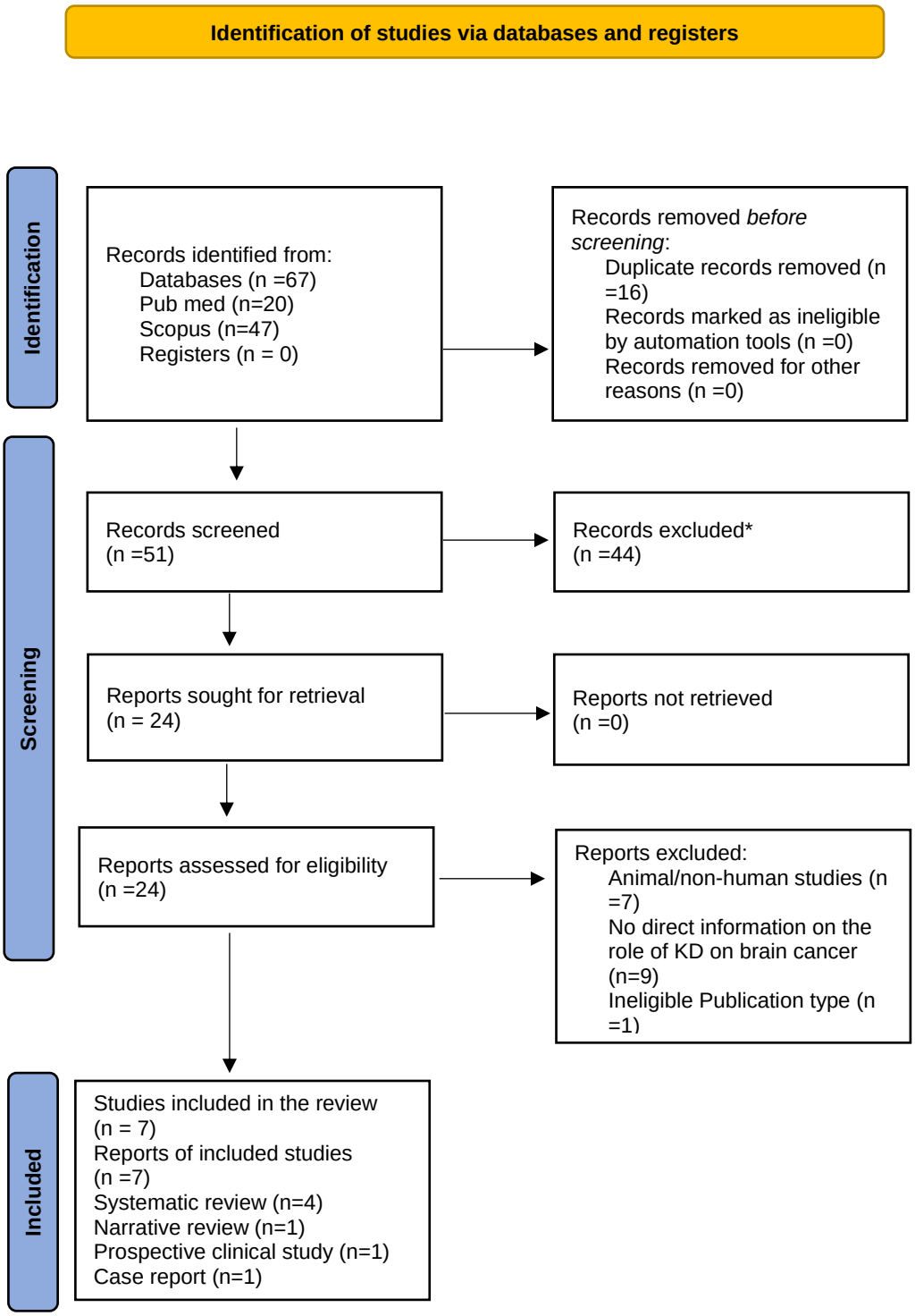


Table 2 provides the characteristics of the 7 studies included in this review. The selected studies include 1 prospective study, 1 critical review, 1 case report, and 4 systematic reviews. These studies were conducted across different countries (USA, India, Italy, Romania, Kazakhstan, Greece, Switzerland, Spain, Saudi Arabia…). Additionally, **Table 2** provides baseline characteristics (sex, age, and gender), the aim of the studies, and the main outcomes of the studies. Moreover, the table shows the feasibility of KD in the management of brain cancer.

Table 2: Characteristics of included papers

Author, Year	**Country**	**Setting**	**Study Design**	**Total Participants, Gender, sex, and Age.**	**Aim of the Study**	**Main Outcome**
Chelikam et al (2024).	USA, India, the Philippines, Pakistan, Romania, Kazakhstan, and more.	Hospitals and universities of the mentioned countries	Systematic Review	N =NR (40 studies>1300 neurological patients, Brain tumor=33) Age=NR (1-16 Y pediatric to >60Y elderly).	To evaluate the role of ketogenic diets and intermittent fasting in neurological diseases, cancers, and obesity.	KD and IF may provide neuroprotective benefits, support cancer treatment outcomes, and improve metabolic markers in obese type 2 diabetic patients; evidence supports that it improves QOL and safety, and feasibility.

				Gender=NR		
Kiryttopoulos et al (2025)	Greece	Hospitals and clinics in Thessaloniki	Prospective clinical study	N=18 F=8 M=10 Median Age=57.5 (Age range 34–75 Y)	To assess the effect of a Mediterranean-style ketogenic diet on survival in patients with GBM.	Patients with >6-month KD adherence had a 3-year survival rate of 66.7% vs. 8.3% in non-adherent; KD supported chemotherapy effectiveness and metabolic stability.
AlMutairi et al (2025)	Saudi Arabia, UK	Clinical Nutrition Department, King Faisal Specialist Hospital and Research Center, Riyadh.Children's Brain Tumor Research Center, Bio Discovery Institute, University of Nottingham, Nottingham NG7 2RD,	Systematic Review	N=11 pediatric patients F=5 M=6 Median Age=5.3(Age range 2.5-15.5 Y)	To evaluate the safety, feasibility, and effectiveness of KDs in children with brain tumors.	KD was safe and tolerable for children, with mild side effects; 6 patients had tumor reduction, 5 showed neurological improvement, but the evidence quality was limited.

Valerio, et al (2024)	USA, Italy, Spain.	Neurosurgery and oncology centers in the mentioned countries	Systematic Review	N=NR(>200 neurological brain tumor patients Age=NR Gender=NR	To evaluate the feasibility, safety, and potential efficacy KDs in managing glioblastoma and other gliomas.	KD shows anti-tumor potential and may improve survival in GBM, but human clinical data are inconsistent, highlighting the need for more robust trials.
PHILLIPS et al (2024).	New Zealand Waikato	Rotorua Hospitals	Case report	N=1 patient F=1 Age=64	To assess the feasibility and potential efficacy of a long-term, multimodal ketogenic metabolic therapy timed with standard GBM treatment.	Two years of stable disease with high quality of life during full KMT adherence, followed by slow tumor progression in year three after reduced adherence and increased life stress.
Pahwa, et al. (2023)	USA, Europe, and Asia	Hospitals and oncology centers in the mentioned countries	Systematic review	N=828 Adult patients Mean Age=43.3 years M=416 F=286 Remaining 126 patent gender was not mentioned	To evaluate clinical outcomes in glioma patients treated with nutritional adjuncts and/or antimetabolite drugs.	For newly diagnosed cases, a KD had the highest median OS of all the adjuncts (42.6 months) assessed in the review.
ThomopoulosTitomihelakis et al. (2025)	USA	Memorial Sloan Kettering Cancer Center and	Narrative review	N=NR Age=NR Gender=NR	To critically assess the role of KDs throughout the cancer continuum for neuroglioma	Found KD to be a feasible adjunct in treatment and survivorship, though evidence for prevention is limited.

		affiliated institutions			from a Medical Nutrition Therapy perspective.	Emphasized the vital role of RDNs in guiding patients safely and effectively through ketogenic interventions.

Table 3. Reported Effects of KD in Brain Cancer Patients.

Author (Year)	Tumor Response	Survival Outcomes	Metabolic Effects	Quality of Life (QOL)	Adverse Effects	Adherence to the KD intervention
Chelikam et al.(2024).	Mixed results were seen, but some reduction or stabilization	Not consistently reported.	Improved metabolic control (glucose, ketones) as a result of KD	Some studies noted improvement in cognitive function and metabolic health.	Mild or GI symptoms	The adherence varies depending on the condition of the patient and even though long-term adherence was challenging due to some effects, modified versions of the diet show better compliance in some cases.
Kiryttopoulos et al. (2025).	Tumor progression was controlled in the KD-adherent patient groups.	66.7% 3-year survival in adherents' vs 8.3% in non-adherents.	GKI less than 2 correlated with better outcomes.	Maintained good functional status and improvement.	Minor; manageable	A high adherence in 6/18 patients to the intervention showed better response.

AlMutairi et al. (2025)	Positive tumor response in 6/11 patients was seen.	Limited data reported.	Positive metabolic shifts from glucose to ketone bodies were observed.	5 out of 11 patients showed improvement in neurological function and overall improved QoL.	Mild GI symptoms	Adherence was generally high, especially with short-term interventions, and some patients discontinued due to disease progression or personal choice, not side. Modified versions (e.g., MCT-supplemented KD) improved compliance.
newValerio et al. (2024)	Some cases showed regression/stabilization	OS is extended up to 60 months in select cases	Improved insulin sensitivity, GKI reduction	Mixed; some benefit	Variable; mostly mild	Often poor without proper dietitian guidance.
Phillips et al. (2024)	2 years of tumor suppression; recurrence with reduced adherence.	Survived 3 years; passed in year 4	GKI ~1.6–2.0 represents tumor control; GKI 3.2+ represents progression	High QOL until relapse happens.	Mild: fatigue, cold intolerance	Very high in years 1–2; dropped in year 3, because of family matters.
Pahwa et al. (2023)	Not specified specifically, but	42.6 months (in new cases);	Not described in detail.	Not reported	Not reported	Not specified

	the paper showed KD had the highest median OS.					
Thomopoulos-Titomihelakis et al. (2025)	Some radiographic improvement; reduced edema	Not reported	Improved ketones, metabolic flexibility	Better energy, mood, seizure control	GI symptoms, weight loss, keto flu	Variable adherence was seen, and improved with Registered Dietitian Nutritionists (RDN) support

6.2 Reported Effects of KD in Brain Cancer Patients.

6.2.1 Tumor response and progression

Across studies, adherence to different types of KDs has been associated with slower tumor growth and progression. Of 18 GBM patients who adhered to a Mediterranean-style KD for more than 6 months, 6 had isocitrate dehydrogenase (IDH) wild-type GBM, which is associated with poor prognosis and slower progression (Kiryttopoulos et al., 2025). Among 11 pediatric patients, two patients showed 15% reduction in tumor size and six patients showed tumor stabilization (AlMutairi et al., 2025).

6.2.2 Metabolic effect

In pediatric patients, 21% reduction in fluorodeoxyglucose (FDG) uptake was seen in two patients, indicating decreased metabolic activity (AlMutairi et al., 2025). Similar results were seen in a 64-year-old woman with IDH-wild GBM type, where the MRI revealed no radiological progression, and the patient maintained a low glucose ketone index (GKI) as a result of a KD as an intervention, reflecting metabolic shift (Philips et al., 2024).

6.3 Impact on Survival Outcomes

Several studies have shown that KD improved survival outcomes of brain cancer patients. For example, Valerio et al.(2024) reported that KD has improved survival outcomes of patients; in fact, in some cases, it has been shown that 60-month survival outcomes, which are greater than the normal standard of care, leading researchers to state KD as “A valid non-pharmacological approach in the treatment of brain tumors”. In agreement, Pahwa, Bhavya, et al (2023) found that the KD had the highest median Overall survival of all the adjuncts (42.6 months) in newly diagnosed glioma patients. Likewise, Phillips et al (2024) reported a better outcome of a 64-year-old patient who passed away at 38 months following relaxation of the diet due to emotional stress, significantly surpassing the typical survival expectancy for GBM. Similarly, Kiryttopoulos et al (2025) have shown that patients who strictly followed the KD intervention had a 3-year survival rate of 66.7% whereas in non-adherent patients, it was 8.3%. However, these outcomes may vary depending on adherence to KD, grade of the cancer, age, and overall health status.

6.4 Safety, Tolerability, and Compliance

In multiple studies, KD was reported to be safe and generally well-tolerated with mild, manageable side effects. AlMutairi et al. (2025) observed symptoms like vomiting, lipid imbalance, and constipation in 11 pediatric patients. These side effects were resolved with dietary adjustments, and as a result of the KD intervention, 5 patients showed improvement in neurological skills. Chelikam et al. (2024) similarly found that KD, with intermittent fasting, was tolerated with mild gastrointestinal discomfort, and KD provides neuroprotection and plays a role in improving cancer outcomes, and low glucose is an emerging marker of better prognosis. Likewise, a study by Phillips et al. (2024), Kiryttopoulos et al. (2025), and Thomopoulos Titomihelakis et al. (2025) has found KD to be feasible as an adjunct to standard treatment, though strict adherence appears to be crucial for sustained benefits. Across these studies, medical supervision was emphasized as essential, with Registered Dietitian Nutritionists (RDNs) playing a vital role in supporting adherence and ensuring safe implementation.

6.5 Summary of Findings

The included studies suggest that when KDs are used as an adjunct to standard cancer therapies, they may contribute to tumor stabilization, improved quality of life, and enhanced neurological function. The selective approach was shaped by the "News of the Week" internship experience, which focused on identifying and translating recent human-based scientific findings into accessible information for the general public.

The number of included studies is limited, which reflects the strict inclusion criteria: only human studies published within the last two years were considered. Despite the abundance of relevant animal and in vitro research, these were excluded to maintain clinical applicability and consistency with the goals of this thesis. The included studies suggest that when KDs are used as an adjunct to standard cancer therapies, they may contribute to tumor stabilization, improved quality of life, and enhanced neurological function. Key factors influencing outcomes included strict adherence to the diet, baseline patient status, and active metabolic monitoring (e.g., glucose-ketone index). While reported adverse effects were generally mild and manageable, rare complications were

noted.These findings underscore the potential feasibility, and therapeutic complementarity of ketogenic dietary interventions. However, implementation should be conducted under the supervision of qualified clinicians and dietitians. Further clinical research, particularly randomized controlled trials, is needed to confirm long-term efficacy, optimize dietary protocols, and define patient subgroups most likely to benefit.

Table 4 provides a structured summary of the human studies reviewed in this work that investigated the effects of the ketogenic diet in brain cancer patients. The table outlines key study characteristics, including the authors and publication year, the number of studies or patients involved, the type of ketogenic dietary intervention, the cancer types examined, the principal findings, and the reported limitations. Overall, the summarized studies suggest that the ketogenic diet is generally safe and feasible as an adjunct to standard therapies, with potential metabolic and clinical benefits. However, the evidence remains limited due to small sample sizes, heterogeneity in dietary protocols, short follow-up durations, and variability in study design.

Table 4. Summary of Reviewed Human Studies on KD in Brain Cancer

Author (Year)	**Number of Cancer Studies/ Patients**	**Diet Type(s)**	**Cancer Type(s)**	**Main Findings**	**Limitations**
Chelikama et al. (2024).	10 studies (human, cancer-focused)	Intermittent Fasting, Classical KD, Modified Atkins.	Glioblastoma, breast, head & neck, rectal, other solid tumors.	KD/IF improved metabolic health,QOL, tumor response; enhanced chemo/radiation tolerance; most effective in glioblastoma	No pooled total patient number, no meta-analysis performed, Short duration of intervention, Small sample sizes, no standardized KD protocols, and limited survival data.

Kiryttopoulos et al. (2025)	18 GBM patients (6 adhered to KD >6 months)	Mediterranean KD(2:1–2.5:1), MCT-supplemented KD.	Glioblastoma Multiforme (GBM).	KD adherence ≥6 months associated with 66.7% 3-year survival vs. 8.3% in non-adherents (p=0.0114); stable GKI, improved metabolic control.	Small sample, non-randomized, adherence problems, only focuses on glycolysis, no targeting of glutaminolysis.
AlMutairi et al. (2025)	8 publications / 11 pediatric patients	Classic KD, Modified Atkins, Low-carb with MCT oil	DIPG, astrocytoma, glioblastoma, medulloblastoma.	KD was well-tolerated, showed positive tumor response in 6/11 patients, improved neurological function in 5, and enhanced QOL and growth. And 3 negative responses were also reported.	Small sample size, heterogeneity in diet protocols, short duration, and mostly no meta-analysis possible.

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Valerio et al. (2024)	23 studies (13 prospective, 3 retrospective, 7 case reports/series)	Classic KD, Modified Atkins, MCT-KD, fasting protocols	Glioblastoma (adult & pediatric).	KD is generally safe; some studies reported improved OS (up to 60 months); mixed results on tumor response; best as an adjunct to standard care.	High heterogeneity in diet types, sample sizes, and study designs; poor adherence in some trials; inconsistent survival benefit
Phillips et al. (2024)	1 patient (female, IDH-wildtype GBM)	Multimodal KMT: TRKD + prolonged fasts.	Glioblastoma Multiforme (GBM).	Timed KMT (GKI ~1.6–2.0)with standard care correlated with 2 years of tumor suppression; KMT relaxation linked to recurrence; mild side effects.	Case study only; no generalizability; stress and dexamethasone may have influenced outcomes; glutamine not directly targeted

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Pahwa,et al.(2023)	22 studies / 828 patients	KD, low-copper diet, others.	Glioma (newly diagnosed and recurrent).	KD showed the highest median OS: 42.6 mo (new) and 10 mo (recurrent).	Includes multiple diet types; survival difference not statistically significant
Thomopoulos, Titomihelakis et al.(2025)	8 human studies summarized	Classical KD, Modified Atkins, KD + IF.	Glioma (GBM, astrocytoma, oligodendroglioma).	KD improved metabolic markers, QOL, and seizure control in some; emphasized the RDN role.	Narrative format; limited data specificity

Abbreviations:KD = Ketogenic Diet; **GBM** = Glioblastoma Multiforme; **IF** = Intermittent Fasting; **GKI** = Glucose–Ketone Index; **OS** = Overall Survival; **QOL** = Quality of Life; **MCT** = Medium-Chain Triglycerides; **TRKD** = Time-Restricted Ketogenic Diet; **RDN** = Registered Dietitian Nutritionist; **GI** = Gastrointestinal, **NR**=Not Reported.

6.6 Result of “News of the week project”

The final result of the News of the week consists of 2 original papers, namely Ketogenic metabolic therapy in conjunction with standard treatment for glioblastoma: A case report, and Successful application of dietary ketogenic metabolic therapy in patients with glioblastoma: a clinical study published in the year 2023 - 2025. These papers were summarized in a maximum of 500 to 550 words and structured in a format that contains sections like the title with the DOI and author's name, background of the study, main finding, implications on patients, and News of the week. The result contains a small number of studies for the following reasons: strict timeline, inclusion criteria, and exclusion criteria listed in the previous section of this thesis. In both studies, it has been shown that adherence to the diet has a significant influence on the outcome of the patients, there are few manageable side effects, and it is a feasible and generally well-tolerated dietary intervention. Additionally, the result shows integrating the KD as an adjunct intervention to brain cancer treatment, but not an independent treatment. This work shows promising insight about how News of the week helps communicate with the public by translating complex scientific findings in simple words on the https://lifestylemedicine.it/ platform on a weekly basis.

Figure 15: Structure of "News of the week".

Title: Ketogenic metabolic therapy in conjunction with standard treatment for glioblastoma: A case report.
https://doi.org/10.3892/ol.2024.14363
Author: Matthew C L Phillips 1, Ziad Thotathil 2, Prashanth Hari Dass 3, Fouzia Ziad 4, Ben G Moon 5
Publication Date: March 6, 2024,(Accepted)
Journal Name: Oncology Letters
DOI: 10.3892/ol.2024.14363
Background:
Glioblastoma (GBM) is an aggressive brain cancer, which exhibits metabolic alteration, such as the Warburg effect, where it heavily depends on glucose fermentation instead of oxidative phosphorylation for energy. This paper is a case report exploring the use of ketogenic metabolic therapy (KMT) alongside the standard treatments, surgical resection, temozolomide, and radiotherapy, to improve patients' outcome.
Main Findings:
The patient, a 64-year-old woman with IDH-wildtype GBM, followed an intensive multi-modal KMT that included prolonged fasting and a strict ketogenic diet alongside standard treatment. During the first two years, she maintained a low Glucose Ketone Index (GKI), which coincided with complete clinical improvement, a healthy body-mass index, quality of life, and the absence of visible tumor progression on MRI scans the patient lived for 38 months, much longer than the typical 12-15 months.
Practical Implications on Patients:
Strict adherence to the diet may help improve GBM treatment outcomes by keeping a low Glucose Ketone Index (GKI) .However, sticking to such a strict diet over time can be tough, especially during emotionally difficult moments, which might reduce its effectiveness.
News of the Week:
"Harnessing the Ketogenic Diet has been shown to lower glucose ketone index, leading to Better Glioblastoma Outcomes .A three year case-study".

As seen above in the box the structure and content of News of the Week includes: - Title, Author, Publication date Journal name, DOI, Background, Main finding, Practical implication on patients, and news of the week.

7. DISCUSSION

There are various risk factors predisposing a person to brain cancer, mainly 1. Non-modifiable risk factors and 2. Environmental and lifestyle factors. Current treatment options include surgical removal of the tumor and radiation, often accompanied by neurotoxic effects. However, this project of recent literature from 2023–2025 demonstrated growing evidence supporting KD as a safe and feasible metabolic intervention that may complement standard treatments by shifting glycolysis to ketone body usage and improving patient outcomes. Our "News of the week" project was used to communicate with the public about the effect of KD on brain cancer.

Across the included studies, the ketogenic diet is positively correlated with brain tumor control and patients' outcomes. The survival outcome varies depending on the patient subtype group, age, IDH mutation status, disease stage, relaxation of the diet, and tumor location. In pediatric populations, AlMutairi et al. (2025) found KD to be both safe and well-tolerated, with neurological improvement in nearly half of the participants. Nevertheless, side effects commonly known as "Keto flu", such as fatigue, headache, dizziness, nausea, vomiting, constipation, low exercise tolerance, GIT disturbance, happen. These are typically manageable; various strategies have been explored to mitigate these side effects and improve adherence; for example, Philips et al. (2024) combined the Mediterranean diet with KD, resulting in better tolerability and safer outcomes. However, these effects must be interpreted cautiously, as patient selection, concurrent therapies, and varying definitions of adherence may have contributed to the observed benefits. Nonetheless, the consistency of favorable outcomes across studies strengthens the rationale for further investigation of ketogenic strategies as adjunctive treatments in neuro-oncology. However, before initiating KD, it is crucial to assess the patient's clinical and nutritional status, ketone levels, and potential metabolic complications. Tailoring the intervention appropriately to ensure patient safety. And it should be implemented under careful medical supervision.

Although the improvements are modest, as mentioned by various authors of the studies, the variability of the results makes it difficult to measure patients' responses

quantitatively. But these results are still clinically significant given the aggressive nature of brain tumors, where there is limited efficacy of current treatments.

While our findings focused exclusively on human clinical studies, several excluded papers provide valuable mechanistic insights that contextualize these findings. For example, a recent preclinical study by Fan et al. (2023), on human cells, has demonstrated that the ketone body 3-hydroxybutyrate (3-HBA) exerts antitumor effects by inhibiting proliferative signaling pathways, such as the Raf/MEK/ERK pathway, and downregulating immune evasion markers, including programmed death ligand 1 (PD-L1). These findings highlight that KD is not merely a dietary intervention but a promising metabolic strategy that fundamentally alters tumor biology. Another study by Clontz (2023) highlighted the translational gap between the tumor suppression observed in preclinical murine models and the more variable clinical outcomes in glioblastoma patients, showing the challenge of translating preclinical studies to a clinical setting. The review compared multiple human trials with ongoing preclinical models, evaluating the efficacy, safety, and tolerability of ketogenic dietary interventions in glioblastoma multiforme (GBM). Although animal studies consistently showed promising antitumor effects, human trials often yielded mixed results, influenced largely by patient adherence and individual metabolic variability. Another study by Makuku et al. (2023) focusing on preclinical models reviewed evidence suggesting that KD may enhance neuroblastoma treatment by modulating tumor metabolism, impacting brain tumor progression, and improving responses to chemo-immunotherapy. Similarly, a recent review by Cecchi et al. (2023) offers valuable mechanistic insights. Their work highlights potential antitumor effects of KD through epigenetic modulation and reduction of oxidative stress in gliomas, providing biological plausibility for the clinical benefits observed in this thesis. As stated by Liu et al. (2024), given the variability in individual microbiome composition, a personalized approach may be necessary, and future research should explore how these microbial and metabolic changes influence systemic responses and treatment efficacy. Despite growing evidence of the effect of KD on Brain tumors, there remains a significant need for robust clinical data and well-controlled trials to definitively establish the efficacy and safety of KD in brain tumor management, and these underscore important biological mechanisms that merit further investigation in clinical settings (Clontz, 2023). Emerging studies show KD interacts with glutamine metabolism in addition to

glucose metabolism. Duraj et al. (2024) proposed a combined approach targeting both critical fuels that help tumor growth in glioblastoma and other types of brain tumors. The approach advocates for combined dietary strategies, fasting, and metabolic inhibitors. Evaluating therapeutic progress and monitoring compliance by using biomarkers such as the glucose-ketone index (GKI) and the ketone uptake rate (ketosis).

Ongoing clinical trials highlight the role of KD in brain tumors. For example, NCT05708352 ("Phase 2 Study of the KD vs. Standard Diet Guidance for Patients with Glioblastoma in Combination with Standard-of-care Treatment") started in 2023, ends in 2029, and another trial, NCT03451799 ("KD in Combination with Standard-of-care Radiation and Temozolomide for Patients with Glioblastoma"). These were started in 2023 and are still ongoing active trials, which will be helpful to understand which subgroup will benefit from KD intervention.

8. LIMITATION

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9. FUTURE DIRECTION

8. LIMITATION

The three years' time frame, inclusion and exclusion criteria, which are guided by the News of the week for this review, limited the number of studies and the findings demonstrated in the thesis. Even though they show valuable and promising outcomes, there is a need for more randomized controlled trials. KD was not compared with other diets for brain tumors, except for one study that combined the Mediterranean diet with KD for enhancing tolerance. Only a single study discussed emotional stress affecting adherence to the KD diet and leading to relaxation of the diet, and finally affecting progression. Only publications in the English language were included and additionally there is a limited study on how emotional, psychological, or socioeconomic factors influence adherence to the diet.

9. FUTURE DIRECTION

Future research should focus on implementing large-scale randomized control trials to gain more insight into which patient population will respond positively to KD intervention and to build personalized treatment protocols that integrate KD with standard treatments. Since the mechanism of KD is shifting the metabolic pathway from glycolysis to utilizing ketone bodies, further exploration into metabolic and behavioral factors that impact the outcome of brain cancer patients should be encouraged. In addition, more efforts should be made to advocate public health initiatives that focus on prevention, early diagnosis, and equitable availability of integrative care through evidence-based policymaking. And projects like "News of the Week" enhance the generalizability of findings to the broader population by translating scientific updates into multiple languages, this approach could improve public engagement and accessibility to reliable health information.

10. CONCLUSION

This project explored the potential of KD as a complementary therapeutic plan in brain cancer management alongside standard care. Our findings suggest that KD may contribute to the reduction of tumor progression, enhance overall survival rates, reduce neuro-inflammation, and improve overall quality of life. Mechanistically, KD appears to sensitize tumor cells by restricting glucose availability and promoting ketone-based energy metabolism. Although generally safe and well-tolerated, its effectiveness varies depending on tumor grade, patient adherence, patient mutation status, age, and individual metabolic responses. While the KD shows promise as a non-invasive and supportive intervention, it should be viewed as a complementary approach and not a replacement for standard care, and an interdisciplinary collaboration between oncologists, dietitians, neuroscientists, and microbiome researchers is essential to fully elucidate the role of KD in brain cancer treatment and translate findings into real-world clinical practice. Incorporating KD within a broader lifestyle medicine framework may offer an adjunctive strategy to improve survival and quality of life in patients with brain tumors.

In conclusion, this work underscores the significance of information platforms like the "News of the Week" project that posts topics related to lifestyle medicine in healthcare, oncology, and advocating for integrative approaches that include dietary interventions, physical activity, stress management, and social connection. This will help the public to understand that integrating lifestyle alongside standard care may empower patients and contribute to more personalized and integrative health care.

11. ACKNOWLEDGMENT

To my supervisor, Professor Alice Masini, and co-supervisor, Dr. Rabia Bibi, I would like to express my sincere gratitude for being the best teacher I have ever known, patiently guiding me from the very basics to helping me to build a strong academic foundation. I cannot thank you enough for my learning, growth, and confidence as a student. Lastly, but not least, I would like to thank God, family, and colleagues for the encouragement, support, and perseverance to complete this project.

12. REFERENCES

1. World Health Organization. (2024 December 23). Non-communicable diseases (NCDs).

https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

2. International Diabetes Federation. (2021).IDF Diabetes Atlas (10th ed.).https://diabetesatlas.org/atlas-reports/

3. International Diabetes Federation. (2024, November 15). New estimates show that over 800 million people are living with diabetes. https://idf.org/news/new-diabetes-estimates/

4. World Health Organization.(2024 ,June 9) .Obesity, and overweight . https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

5. GBD 2019 Risk Factor Collaborators. "Global Burden of 87 Risk Factors in 204 Countries and Territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019". Lancet. 2020; 396:1223–1249.

6. American College of Lifestyle Medicine. (n.d.). American College of Lifestyle Medicine. https://lifestylemedicine.org/

7. Fallows, E. S. (2023). Lifestyle medicine: a cultural shift in medicine that can drive integration of care. Future Healthcare Journal, 10(3), 226–231. https://doi.org/10.7861/fhj.2023-0094

8. Mirsky, J., & Artz, K. (2023). Lifestyle Medicine Shared Medical Appointments: A proposed framework for high-value chronic disease care. Healthcare (Amsterdam, Netherlands), 11(4), 100723. https://doi.org/10.1016/j.hjdsi.2023.100723

9. China Kadoorie Biobank Collaborative Group (2023). Healthy lifestyle and life expectancy free of major chronic diseases at age 40 in China. Nature human behavior, 7(9), 1542–1550. disease, 18, E33. https://doi.org/10.5888/pcd18.210055

10. Neuhouser M. L. (2019). The importance of healthy dietary patterns in chronic disease prevention. Nutrition research (New York, N.Y.), 70, 3–6. https://doi.org/10.1016/j.nutres.2018.06.002

11. Melanson KJ. Nutrition Review: Relationships of Nutrition With Depression and Anxiety. American Journal of Lifestyle Medicine. 2007;1(3):171-174. doi:10.1177/1559827607299725

12. Fedorchenko, Y., Zimba, O., Sagtaganov, Z., & Yessirkepov, M. (2024). Enhancing chronic disease management through physical activity and pedometry-based health monitoring. Rheumatology international, 44(12), 2737–2743. https://doi.org/10.1007/s00296-024-05738-7

13. Centers for Disease Control and Prevention. (n.d). About physical activity. https://www.cdc.gov/physical-activity/php/index.html

14. Meltzer LJ, Moreno JP, Johnston CA. Sleep Is Not for Slackers. American Journal of Lifestyle Medicine. 2014;8(6):380-382. Doi:10.1177/1559827614545314

15. Goldstein, A. N., & Walker, M. P. (2014). The role of sleep in emotional brain function. Annual review of clinical psychology, 10, 679–708. https://doi.org/10.1146/annurev-clinpsy-032813-153716

16. Watson NF, Badr MS, Belenky G, Bliwise DL, Buxton OM, Buysse D, Dinges DF, Gangwisch J, Grandner MA, Kushida C, Malhotra RK, Martin JL, Patel SR, Quan SF, Tasali E. Recommended amount of sleep for a healthy adult: a joint consensus statement of American Academy of Sleep Medicine and Sleep Research Society. J Clin Sleep Med 2015;11(6):591–592.

17. Xiao Tan, Colin D. Chapman, Jonathan Cedernaes, Christian Benedict, Association between long sleep duration and increased risk of obesity and type 2 diabetes: A review of possible mechanisms, https://doi.org/10.1016/j.smrv.2017.11.001.

18. American Psychological Association n.(2024). Stress in America: The state of our nation. https://www.apa.org/news/press/releases/stress

19. Harvard T.H. Chan School of Public Health. (2021).Stress and health.

https://nutritionsource.hsph.harvard.edu/stress-and-health

20. American Heart Association. (2020). Smoking and cardiovascular disease. https://www.heart.org

21. World Health Organization.(2021).Alcohol. https://www.who.int/news-room/fact-sheets/detail/alcohol

22. US Department of Health and Human Services. Social connection (n.d.).

https://www.hhs.gov/surgeongeneral/reports-and-publications/index.html

23._Rook, K. S., & Charles, S. T. (2017). Close social ties and health in later life: Strengths and vulnerabilities. The American psychologist, 72(6), 567–577. https://doi.org/10.1037/amp0000104

24. Liu, X., Cheng, L.C., Gao, TY. et al. The burden of brain and central nervous system cancers in Asia from 1990 to 2019 and its predicted level in the next twenty-five years. BMC Public Health 23, 2522 (2023). https://doi.org/10.1186/s12889-023-17467-w

25.CancerResearch UK risk of Brain Cancer. https://www.cancerresearchuk.org/about-cancer/brain-tumours/risks-causes

26.https://odphp.health.gov/news/202206/lessening-cancer-risks-healthy-living-preventive-measures-and-public-health-practice

27. Michaelson, N. M., Watsula, A., Bakare-Okpala, A., Mohamadpour, M., Chukwueke, U. N., & Budhu, J. A. (2023). Disparities in Neuro-Oncology. Current neurology and neuroscience reports, 23(12), 81 5–825. https://doi.org/10.1007/s11910-023-01314-x

28. CDC. (2022). National Health Strategies and Cancer Prevention. https://www.cdc.gov/public-health-gateway/php/communications-resources/national-health-initiatives-strategies-action-plans.html

29. Healthline. (2024). Types of brain cancer. https://www.healthline.com/health/brain-tumor/types-of-brain-cancer.

30. MayoClinic (2024). Brain tumor symptoms and causes

https://www.mayoclinic.org/diseases-conditions/brain-tumor/symptoms-causes/syc-203500844

31 .GBM Research (2025).Brain Tumor Awareness Month Report.

https://www.gbmresearch.org/brain-tumor-awareness-month-2025

32. Harvard Health. (2024). Brain tumor overview.

https://www.health.harvard.edu/a_to_z/brain-tumor-overview-a-to-z

33 .Mayfield Clinic.(2024). Brain tumor treatment options.

https://mayfieldclinic.com/pe-braintumor.htm

34 . https://www.cancerresearchuk.org/about-cancer/brain-tumours

35.https://www.cancer.org/cancer/types/brain-spinal-cord-tumors-adults/causes-risks-prevention.html

36.Ostrom, Q. T., Adel Fahmideh, M., Cote, D. J., Muskens, I. S., Schraw, J. M., Scheurer, M. E., & Bondy, M. L. (2019). Risk factors for childhood and adult primary brain tumors. Neuro-oncology, 21(11), 1357–1375. https://doi.org/10.1093/neuonc/noz123

37. Schaff, L. R., & Mellinghoff, I. K. (2023). Glioblastoma and Other Primary Brain Malignancies in Adults: A Review. JAMA, 329(7), 574–587. https://doi.org/10.1001/jama.2023.0023

38. https://cbtrus.org/

39. National Brain Tumor Association https://braintumor.org/

40. Pan, Sai Yi MD; Ugnat, Anne-Marie PhD; Mao, Yang PhD. The Canadian Cancer Registries Epidemiology Research Group. Occupational Risk Factors for Brain Cancer in Canada. Journal of Occupational and Environmental Medicine 47(7):p 704-717, July 2005. | DOI: 10.1097/01.jom.0000165747.95801.c5

41. Vienne-Jumeau, A., Tafani, C., & Ricard, D. (2019). Environmental risk factors of primary brain tumors: A review. Revue neurologique, 175(10), 664-678.

42. Wheless J. W. (2008). History of the ketogenic diet. Epilepsia, 49 Suppl 8, 3–5. https://doi.org/10.1111/j.1528-1167.2008.01821.x).

43. Atkins, R. C. (1972). Dr. Atkins' diet revolution.

44. Weber, D. D., Aminazdeh-Gohari, S., & Kofler, B. (2018). Ketogenic diet in cancer therapy. Aging, 10(2), 164–165. https://doi.org/10.18632/aging.101382

45 .Rusek, M., Pluta, R., Ułamek-Kozioł, M., & Czuczwar, S. J. (2019). Ketogenic Diet in Alzheimer's Disease. International journal of molecular sciences, 20(16), 3892. https://doi.org/10.3390/ijms20163892

46. International Agency for Research on Cancer. (2022). Global Cancer Observatory (GLOBOCAN 2022): Brain and CNS cancers. World Health Organization. https://gco.iarc.fr/

47. Onyije, F. M., Dolatkhah, R., Olsson, A., Bouaoun, L., Deltour, I., Erdmann, F., Bonaventure, A., Scheurer, M. E., Clavel, J., & Schüz, J. (2024). Risk factors for childhood brain tumors: A systematic review and meta-analysis of observational studies from 1976 to 2022. Cancer Epidemiology, 88, 102510. https://doi.org/10.1016/j.canep.2023.102510

48. Dal Bello, S., Valdemarin, F., Martinuzzi, D., Filippi, F., Gigli, G. L., & Valente, M. (2022). Ketogenic Diet in the Treatment of Gliomas and Glioblastomas. Nutrients, 14(18), 3851. https://doi.org/10.3390/nu14183851)

49.Valerio, J., Borro, M., Proietti, E., Pisciotta, L., Olarinde, I. O., Fernandez Gomez, M., & Alvarez Pinzon, A. M. (2024). Systematic Review and Clinical Insights: The Role of the Ketogenic Diet in Managing Glioblastoma in Cancer Neuroscience. Journal of personalized medicine, 14(9), 929. https://doi.org/10.3390/jpm14090929

50. Pahwa, B., Leskinen, S., Didia, E., Huda, S., & D'Amico, R. S. (2023). Role of nutritional adjuncts in the management of gliomas: A systematic review of literature. Clinical neurology and neurosurgery, 231, 107853. https://doi.org/10.1016/j.clineuro.2023.107853

51. AlMutairi, H., McCullough, F., McCullough, Ghemlas, I., AlHarbi, M., Grundy, R., & Dandapani, M. (2025). Safety, Feasibility, and Effectiveness of Ketogenic Diet in Pediatric Patients with Brain Tumors: A Systematic Review. Journal of nutrition and metabolism, 2025, 7935879. https://doi.org/10.1155/jnme/7935879

52. Phillips, M. C. L., Thotathil, Z., Dass, P. H., Zaid, F., & Moon, B. G. (2024). Ketogenic metabolic therapy in conjunction with standard treatment for glioblastoma: A case report. Oncology letters, 27(5), 230. https://doi.org/10.3892/ol.2024.14363

53. Thomopoulos-Titomihelakis, K. D., Sachs, H., McCann, R., Zhang, Q., Kurnit, S., De Juan, G. C., & Rushing, A. (2025). Critical Review of Ketogenic Diet throughout the Cancer Continuum for Neuroglioma: Insights from a Medical Nutrition Therapy (MNT) Perspective. Current nutrition reports, 14(1), 24. https://doi.org/10.1007/s13668-025-00609-4

54. Kiryttopoulos, A., Evangeliou, A. E., Katsanika, I., Boukovinas, I., Foroglou, N., Zoonosis, B., Cheva, A., Nikolopoulos, V., Zaramboukas, T., Duraj, T., Seyfried, T. N., & Spilioti, M. (2025). Successful application of dietary ketogenic metabolic therapy in patients with glioblastoma: a clinical study. Frontiers in nutrition, 11, 1489812. https://doi.org/10.3389/fnut.2024.1489812

55. Chelikama, N., Akella, S. A., Lakhanpal, M. R., Lahori, S., Singh, A., Zafar, S., Shivashankar, P. G., Manjani, L., Ilyassov, R., Ali, A. I., Marandi, R., Gujarathi, R., Manjani, D., Adiga, A., & Patel, U. (2024). Role of ketogenic diets and intermittent fasting in neurologic diseases, cancers, and obesity: A systematic review of human studies. Journal of Endocrinology and Metabolism, 14(3), 103–127. https://doi.org/10.14740/jem944https://doi.org/10.1038/s41562-023-01624-7 Life expectancy increases free from NCD chronic disease when avoiding risky factors.

56. Fan, W. T., Liu, X. F., & Liang, R. C. (2023). Raf/MEK/ERK Signaling Pathway Is Involved in the Inhibition of Glioma Cell Proliferation and Invasion in the Ketogenic Microenvironment. Current medical science, 43(4), 759–767. https://doi.org/10.1007/s11596-023-2724-7

57. Clontz A. D. (2023). Ketogenic therapies for glioblastoma: Understanding the limitations in transitioning from mice to patients. Frontiers in nutrition, 10, 1110291. https://doi.org/10.3389/fnut.2023.1110291

58. Makuku, R., Far, Z. S., Khalili, N., Moyo, A., Razi, S., Keshavarz-Fathi, M., Mahmoudi, M., & Rezaei, N. (2023). The Role of Ketogenic Diet in the Treatment of Neuroblastoma. Integrative Cancer Therapies. https://doi.org/10.1177/15347354221150787

59.Santangelo, A., Corsello, A., Spolidoro, G. C. I., Trovato, C. M., Agostoni, C., Orsini, A., Milani, G. P., & Peroni, D. G. (2023). The Influence of Ketogenic Diet on Gut Microbiota: Potential Benefits, Risks and Indications. Nutrients, 15(17), 3680.https://doi.org/10.3390/nu15173680