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Editorial

Clinical evidence and the experience of illness in family medicine

The contributions in this issue of the Middle East Journal of Family Medicine examine childhood obesity, dementia assessment, restless legs syndrome, persistent symptoms following nasal trauma, and concerns about artificial intelligence and social media. They approach these subjects through clinical reviews, a retrospective cohort study, personal experience, and commentary. Reading them together calls for attention to both the evidence supporting a clinical explanation and the effects of illness on everyday life.

The retrospective cohort study from Qatar examines overweight and obesity among children and adolescents attending Primary Health Care Corporation health centres between January 2017 and July 2021. The authors report 160,209 participants aged 2–18 years, with obesity increasing from 5.6% in 2017 to 16.3% in 2021 and overweight increasing from 6.4% to 15.5%. These findings document a substantial increase within the population studied. However, the rise was already apparent before the pandemic. Although the authors discuss restrictions on activity, school closures, and changes in daily routines as possible contributors, the observational design does not establish how much of the increase was caused by COVID-19 preventive measures. Their proposal for coordinated prevention involving families, schools, and health services addresses a problem that preceded the restrictions and continued during them.

A. Abyad's review of neuroimaging in dementia examines what different imaging methods can contribute to diagnosis, prognosis, and treatment monitoring. Structural, functional, and molecular examinations answer different questions. The review stresses that an imaging abnormality must be interpreted alongside the cognitive presentation, functional impairment, disease course, and accompanying conditions. The presence of amyloid pathology, for example, does not establish that it explains every cognitive symptom. For family physicians involved in assessment and continuing care, the article offers a framework for understanding both the information a scan provides and the uncertainty that can remain after testing.

Nadiya Zainab Rizvi and Eman Azhari Bramble Adam examine restless legs syndrome from a primary care perspective. Their review describes the characteristic urge to move the legs, worsening during rest, relief with movement, and evening or night predominance. It also addresses conditions that can mimic the disorder, iron status, associated illnesses, and medicines that may aggravate symptoms. The discussion of augmentation, in which symptoms worsen during dopaminergic treatment, gives particular attention to the need to reassess a changing symptom pattern. Throughout the review, disrupted sleep and impaired daytime functioning provide the clinical context for diagnosis and management.

Ebtisam Elghblawi's personal narrative describes persistent nasal symptoms after an e-bike collision, septal fracture, and subsequent surgery. Nasal obstruction, secretions, crusting, and disturbed sleep are accompanied by frustration over unanswered questions and the absence of a satisfactory explanation. The author considers structural, mucosal, and neural mechanisms while acknowledging that the precise cause of her continuing symptoms remains uncertain. This individual account cannot establish a general mechanism or estimate the outcomes of nasal surgery. It does, however, describe in detail how prolonged symptoms and unsatisfactory communication can affect a patient's experience of care.

Lesley's contribution raises concerns about social media, artificial intelligence, and psychological harm. The supplied summary expresses particular concern about interactions between vulnerable people and AI systems, including experiences described as "AI psychosis." These concerns require careful examination of individual circumstances and the evidence behind proposed causal links. Reports of disturbing interactions should be distinguished from established diagnoses and from conclusions about how frequently harm occurs. In introducing this discussion, the journal provides space to examine questions that the full contribution will need to support with documented evidence.

Across these contributions, clinical interpretation remains a matter of matching conclusions to the evidence available. Population data can describe a trend without isolating its cause; an imaging result can identify pathology without explaining an entire clinical presentation; and a personal narrative can describe suffering while leaving its mechanism unresolved. Family medicine encounters each of these situations. Care depends on explaining what is known, acknowledging what remains uncertain, and continuing to attend to the patient's symptoms and daily functioning.

Warm regards,
Dr. Abdulrazak Abyad
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Trends in Overweight and Obesity Among Children and Adolescents in Qatar Before and During the COVID-19 Pandemic: A Retrospective Cohort Study

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Abstract

Background: Due to the COVID-19 pandemic lockdown, countries implemented health preventive measures, including travel bans, online schooling, restricted access to parks and beaches, and restrictions on all other gatherings. In Qatar, schools implemented virtual learning, families relied on online shopping, and for almost six months, children were mainly confined to their homes, leading to drastic lifestyle changes across society, especially among children and adolescents.

This study aimed to examine trends in the prevalence of overweight and obesity among children and adolescents attending Primary Health Care Corporation (PHCC) health centers in Qatar before and during the COVID-19 pandemic.

Methods: This retrospective cohort study used longitudinal electronic health record data from children and adolescents aged 2–18 years attending PHCC health centers in Qatar between 1 January 2017 and 31 July 2021. Participants entered the cohort when they first met the eligibility criteria and were followed longitudinally through subsequent years. Each participant was followed across subsequent years using their available BMI measurements. Overweight and obesity were classified according to WHO growth references, and trends were assessed using chi-square tests for trend. Analyses were performed using SPSS version 28.0.

Results: A total of 160,209 cases aged 2 to 18 years were followed from January 2017 to July 2021. Females were 77,904, representing 48.6%, and males were 82,305, representing 51.4%. In 2017, the overweight rate was 6.4%, while the obesity rate was 5.6%. In 2018, overweight was 8.1%, and obesity was 6.7%; in 2019, overweight was 11.0%, and obesity was 9.8%. In 2020, overweight was 16.6%, and obesity was 15.2%. In 2021, overweight was 15.5%, and obesity was 16.3%.

Conclusions: During the study period, obesity almost tripled, starting from 5.6% in 2017 to 16.3% in 2021. The overweight rate more than doubled, increasing from 6.4% in 2017 to 15.5% in 2021. This showed an increasing trend in obesity and overweight among children aged 2–18 years before the pandemic, with a further increase during the pandemic period. Males showed a significantly higher prevalence of obesity than females. Based on the study results, we recommend a national strategy for preventing, screening, and managing obesity and overweight involving families, schools, and the health sector.

Keywords: Obesity, Prevalence, COVID-19, Lockdown, Overweight

Introduction

Obesity and overweight are complex metabolic disorders caused by an imbalance between energy intake and energy expenditure, resulting in abnormal accumulation of body fat and weight gain that causes health impairment. They are a global health problem affecting both developed and developing countries and carry a substantial economic burden, as they involve not only the disease itself but also its health and socioeconomic complications. In the last 40 years, obesity has emerged as a health problem that also threatens children and adolescents, as the prevalence of obesity and overweight in childhood and adolescence has increased drastically from 4% in 1975 to over 18% in 2016 in children between 5 and 19 years old, according to WHO, meaning that over 340 million children and adolescents were obese or overweight that year. Moreover, in 2019, about 38.2 million children under the age of 5 years were overweight or obese, and almost half of them lived in Asia (1).

Obesity in adults is defined by body mass index (BMI), with higher numbers indicating more adipose tissue. Using BMI in the definition of obesity and overweight in children has its inaccuracies, as a higher number may indicate more muscle mass in the growing child, not more adipose tissue; despite this fact, in the absence of another easy, accurate way to assess obesity, BMI continues to be the essence of the obesity definition. In children and adolescents, gender-specific charts are used for BMI, weight, and weight-for-height. WHO defines obesity as greater than three standard deviations above the WHO Child Growth Standards median for weight-for-height in children under 5 years old and greater than two standard deviations above the WHO Growth Reference median for BMI for children from 5 to 19 years old (1).

Obesity is caused by increased energy intake, decreased energy consumption, or both. Unhealthy eating patterns, such as skipping breakfast, consuming high-calorie sweetened drinks, and eating highly saturated foods; lack of physical activity; and spending more time on screens and leading a highly sedentary lifestyle all contribute to an energy imbalance. Genetic, social, and environmental factors interact together to alter both body physiology and personal behavior, affecting energy intake and consumption that may lead to obesity and overweight (2-4).

Childhood obesity can affect children and adolescents' lives in various ways. Physically, as it is a proinflammatory state affecting all body systems, it may lead to hypertension, dyslipidemia, impaired glucose tolerance, type 2 diabetes, fatty liver disease, obstructive sleep apnea, asthma, menstrual abnormalities, and orthopedic problems like slipped capital femoral epiphysis and increased fractures. Psychosocially, it can lead to anxiety, depression, low self-esteem, being stigmatized and discriminated against, increased risk of bullying, and academic failure. Children and adolescents with obesity are also more likely to struggle with adult obesity and its complications (2-6).

International efforts have been made to prevent and treat obesity after recognizing obesity as a global health problem on both the state and international levels. For example, the "Global action plan on physical activity 2018–2030: more active people for a healthier world" was launched by the WHO to encourage healthy lifestyle changes worldwide (7).

The Global School-Based Student Health Survey-Qatar 2011 reported that most children and adolescents had poor eating habits and low levels of physical activity (8).

In Qatar, significant efforts are being made to reduce the risk factors associated with overweight and obesity by ensuring greater access to recreational facilities, such as neighborhood parks, and by promoting physical exercise and fitness through campaigns. Additionally, efforts emphasize promoting healthy eating and other healthy lifestyle choices. However, due to the COVID-19 pandemic, Qatar implemented preventive health measures similar to other countries, including a travel ban; the closure of schools, parks, wellness clubs, and beaches; and restrictions on gatherings. These measures led to virtual schooling and increased reliance on online shopping, with children and adolescents confined to their homes for at least 6 months from the start of the COVID-19 lockdown, resulting in drastic lifestyle changes across society, especially among children and adolescents.

This study aimed to examine trends in the prevalence of overweight and obesity among children and adolescents attending PHCC health centers in Qatar before and during the COVID-19 pandemic.

Methods

This was a retrospective cohort study conducted between 1 January 2017 and 31 July 2021.

Enrollment criteria: For the year 2017, all individuals aged 2 years up to 15 years during the year 2017 and who had at least one valid BMI measurement before the end of that year (together with at least one BMI from 2018 and another from 2019 if available) and at least one other BMI measurement after January 1, 2020, were included. For the year 2018, individuals who had not visited PHCC health centers during 2017 and who had completed 2 years up to 16 years during that year and had at least one valid BMI measurement before the end of that year (together with at least one BMI from the year 2019 if available), and at least one other BMI measurement after January 1, 2020, were included. For the year 2019, individuals who had not visited PHCC health centers during 2017 to 2018 and completed 2 years up to 17 years during that year and had at least one valid BMI measurement before the end of that year, and at least one other BMI measurement after January 1, 2020, were included.

Children and adolescents entered the cohort when they first met the eligibility criteria and were subsequently followed longitudinally through the remaining study period; each participant was followed across subsequent years using their available BMI measurements.

We obtained data from Cerner, the electronic health record system for PHCC, the primary health care provider covering all of Qatar through its widespread health centers. The data were de-identified and recorded during outpatient encounters. We used the WHO reference ranges for obesity and overweight (1).

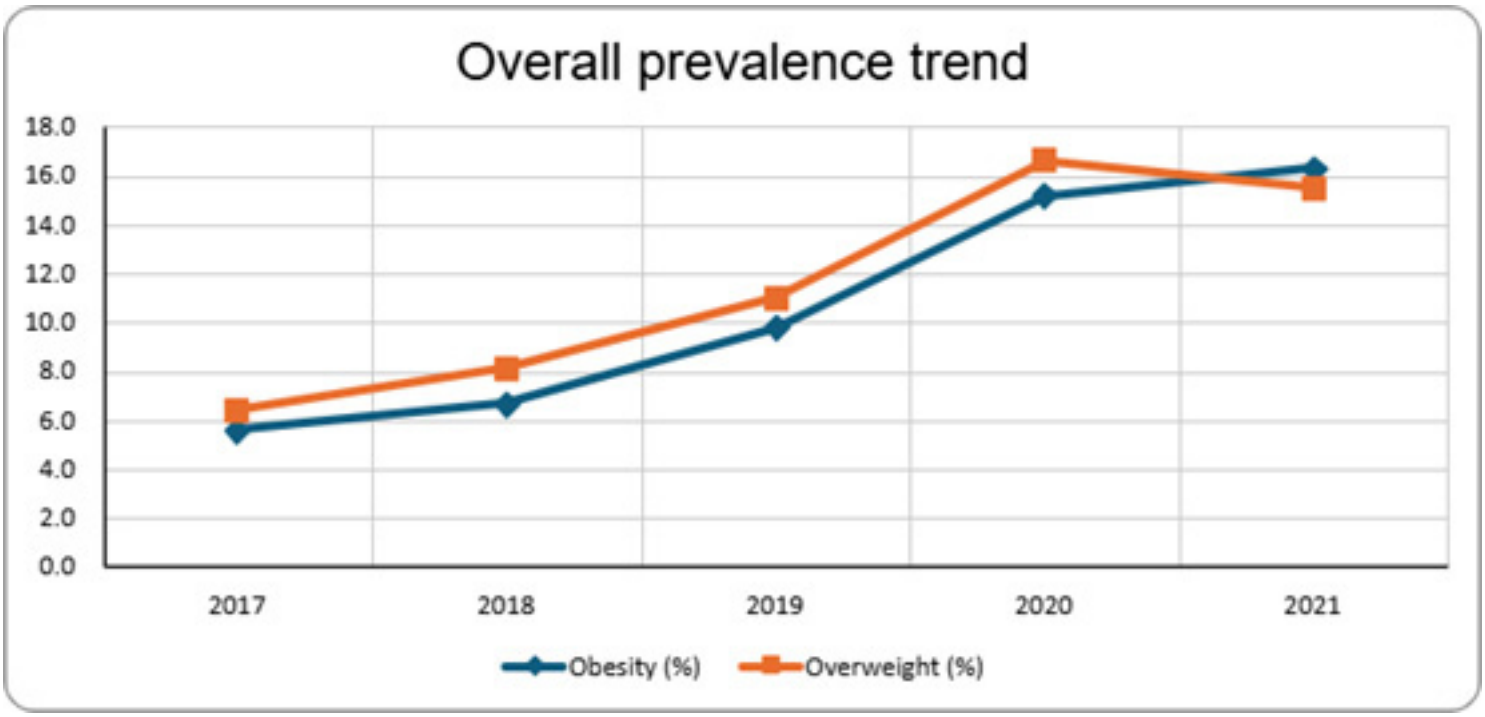
Statistical methods:
Frequencies with percentages were calculated for obesity and overweight according to the years (2017 to 2021). A chi-square test for trend analysis was performed to examine the trends in obesity and overweight by year and gender. A p-value of 0.05 (two-tailed) was considered a statistically significant level. SPSS 28.0 statistical package was used for analysis.

The study was reviewed and approved under the exempt category by PHCC Research Sub-Committee, Qatar (reference number: PHCC/DCR/2021/03/022; approval date: 6 June 2021). The study used participant data in accordance with the approved study scope, with confidentiality and data protection maintained throughout the study.

Results

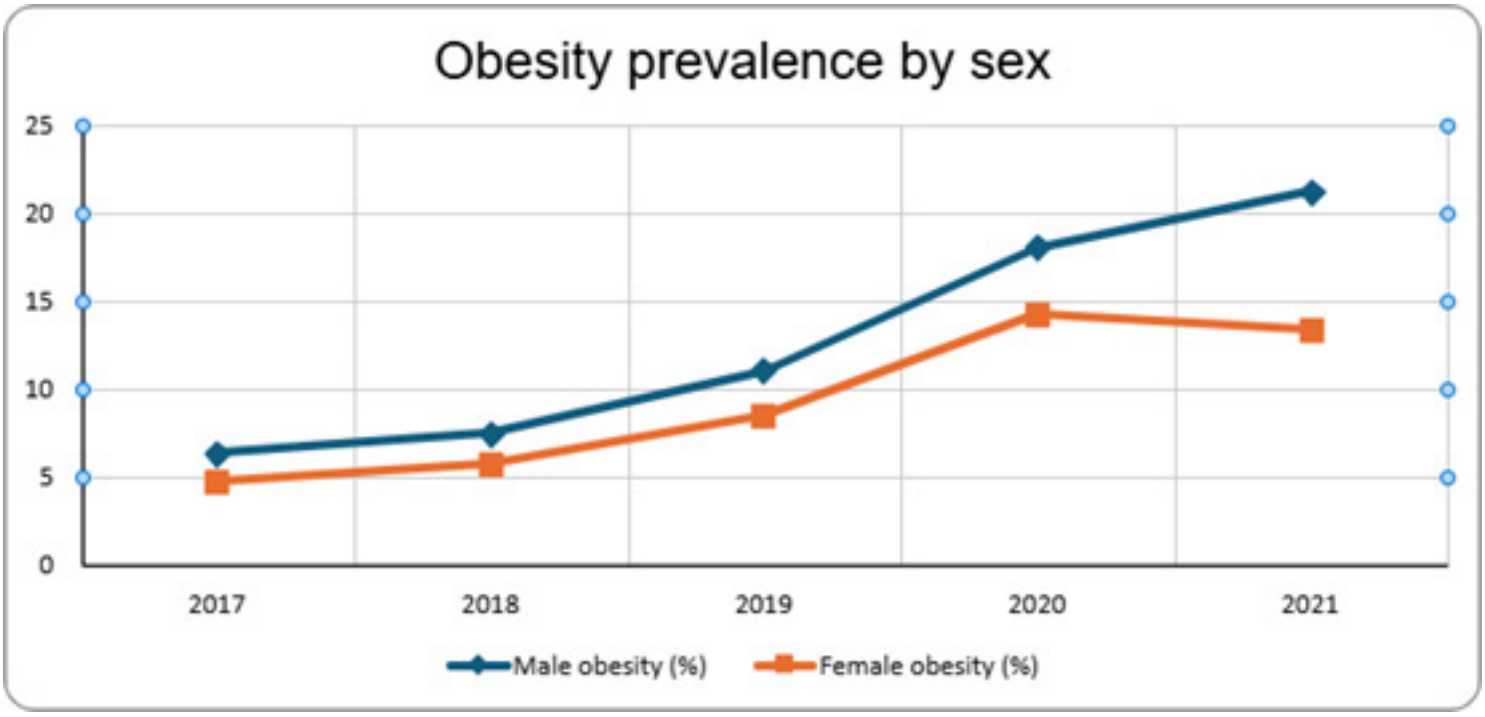
A total of 160,209 cases aged 2 to 18 years were followed from January 1, 2017, to July 31, 2021. Females were 77,904, representing 48.6%, and males were 82,305, representing 51.4%. In 2017, the overweight rate was 6.4%, while the obesity rate was 5.6%. In 2018, overweight was 8.1%, and obesity was 6.7%; in 2019, overweight was 11.0%, and obesity was 9.8%. In 2020, overweight was 16.6%, and obesity was 15.2%. In 2021, overweight was 15.5%, and obesity was 16.3%. Overweight and obesity rose from 2017 to 2020; obesity continued to increase, reaching 16.3% in 2021, while overweight decreased slightly to 15.5% in 2021, as shown in Figure 1.

Figure 1. Prevalence of overweight and obesity by year



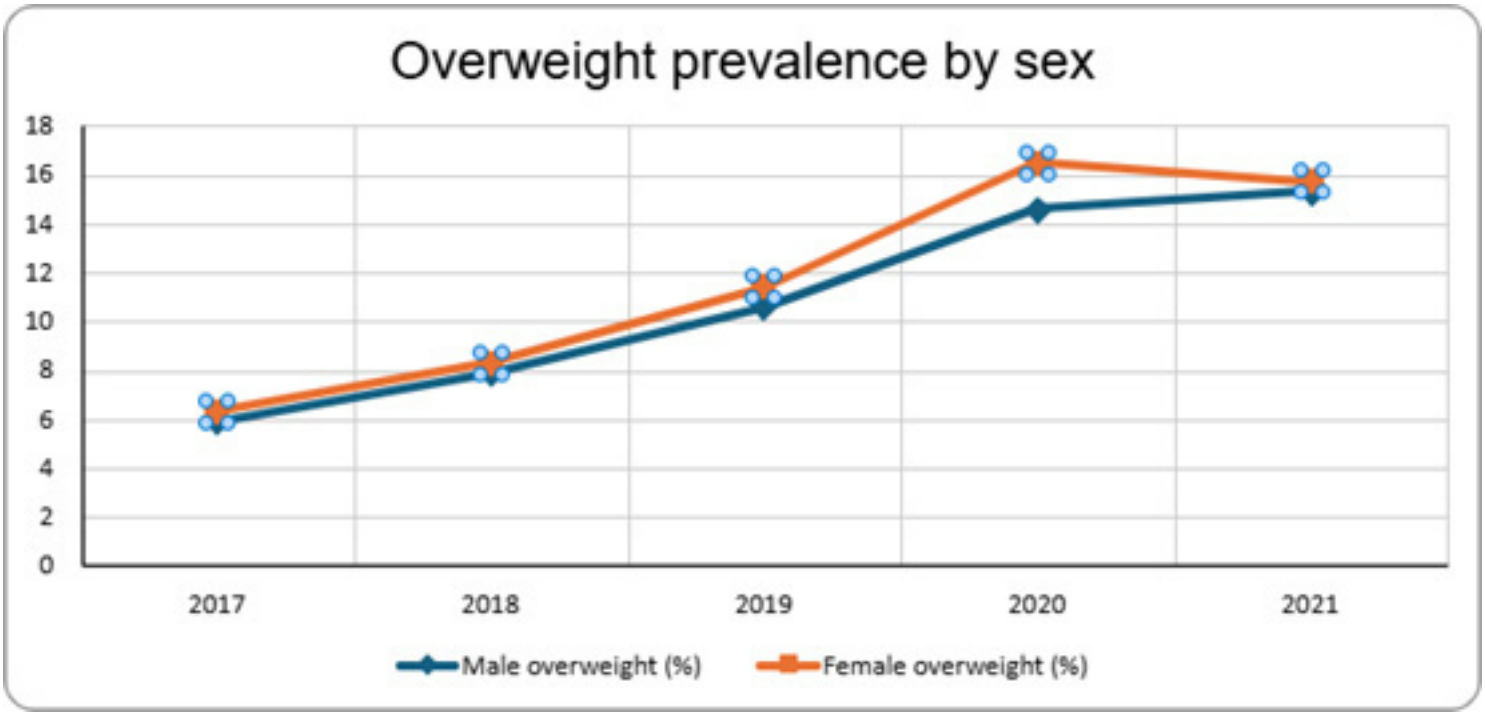
Obesity distribution among males and females was as follows: in 2017, obesity was 4.8% in females and 6.4% in males (p=0.001); in 2018, it was 5.8% in females and 7.5% in males (p=0.001). In 2019, it was 8.5% in females and 11.1% in males (p=0.001). In 2020, obesity was 14.3% among females and 18.1% among males (p=0.001); in 2021, it was 13.4% among females and 21.3% among males (p=0.001), as shown in Figure 2.

Figure 2. Prevalence of obesity by sex and year



Overweight distribution among males and females was as follows: in 2017, females 6.3%, males 5.9%; in 2018, females 8.3%, males 7.9% (p=0.001); in 2019, females 11.4%, males 10.6%; in 2020, females 16.5%, males 14.6% and in 2021 females 15.7%, males 15.3%. The trend was statistically significant, rising in both females and males, as illustrated in Figure 3.

Figure 3. Prevalence of overweight by sex and year



Discussion

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. It is a global health concern as the prevalence of obesity and overweight among children and adolescents has almost tripled since 1975. In 2016, over 340 million children and adolescents were obese or overweight worldwide (1).

A 2018 study by Al-Thani et al. in Qatar found that the prevalence of overweight and obesity was 44.8% and 40.4% among males and females, respectively, among school students aged 5–19 years (9).

In 2020, as COVID-19 spread globally, countries implemented preventive health measures that varied from one country to another. In Qatar, after the first announced COVID-19 cases on February 29, 2020, the lockdown started on March 11, 2020, and continued till September 2020. Then restrictions were gradually lifted in four phases, taking into account health risks and social and economic benefits. The first phase began on June 15, 2020; the second on July 1, 2020; and the third and fourth on August 1, 2020, and September 1, 2020, respectively. Online schooling began on March 10, 2020, and with phase 4, learning gradually returned to in-person learning until late 2021, when Qatar officially stopped using online learning as the primary mode of instruction (10-12).

This study aimed to examine trends in the prevalence of overweight and obesity among children and adolescents attending PHCC health centers in Qatar before and during the COVID-19 pandemic.

This retrospective cohort study included 160,209 children and adolescents who were registered and followed at PHCC health centers from January 1, 2017, to July 31, 2021. 77,904 (48.6%) were female, and 82,305 (51.4%) were male.

During the study period, obesity and overweight increased before the pandemic, with a further marked increase during the pandemic. Obesity almost tripled, from 5.6% in 2017 to 16.3% in 2021. Compared to 2019 (the pre-pandemic year), obesity rates continued to increase, from 9.8% in 2019 to 15.2% in 2020 and 16.3% in 2021.

At the beginning of the study, males were slightly more obese, 6.4% compared to 4.8% for females, and this pattern persisted throughout the study, reaching 21.3% in 2021, compared to only 13.4% for females. Obesity increased significantly for both males and females in 2020: males were 18.1%, and females were 14.3%, up from 11.1% in males and 8.5% in females in 2019. This significant male-female difference warrants further research into the sex-specific behavioral, environmental, and biological factors that may have contributed to this discrepancy.

The overweight rate more than doubled, rising from 6.4% in 2017 to 15.5% in 2021, with a more noticeable increase in 2020 to 16.6% compared to 11% in 2019. Overall, overweight was higher than obesity each year, except in 2021, when obesity was 16.3%, and overweight was 15.5%. Compared to obesity, the proportion of females with overweight was slightly higher than that of males with overweight over the years of the study.

The study results are consistent with previous studies. In one large cohort study conducted in the USA by Lange et al., 432,302 persons aged 2 to 19 years, with outpatient visits, showed that the rate of BMI increase almost doubled during the COVID-19 pandemic compared to the pre-pandemic period, and obesity also increased from 19.3% in August 2019 to 22.4% one year later. In a study by Woolford et al., youths aged 5 to 17 years gained more weight during the COVID-19 pandemic than before the pandemic. Furthermore, in another study by Jenssen et al., similar results were reported (13-15).

The rise in obesity began in the 1st year of the study and continued to increase throughout the study period. So, when the COVID-19 lockdown started, the rates of obesity had already drastically increased, and after the COVID-19 lockdown, obesity continued to increase. Overweight substantially increased from 2017 to 2020, but it decreased slightly to 15.5% from 16.6% in 2020.

Before the pandemic, obesity and overweight prevalence was high in Qatar, as reported in the study by Al-Thani et al. (9). Most children and adolescents had poor eating habits and low activity, as shown in the Global School-Based Student Health Survey-Qatar 2011. The survey reported that 55.4% of girls and 43.6% of boys spent three or more hours per day on sedentary activities during a typical day. Regarding physical activity, only 15% of survey participants were considered appropriately active (i.e., engaging in at least 60 minutes of activity per day for five or more days per week). Moreover, 62.5% of students (60% boys, 64.8% girls) drank carbonated soft drinks at least once per day in the past 30 days (8).

Before the pandemic, Qatar invested significant effort in preventing and treating obesity in its population by ensuring greater access to recreational facilities, such as neighborhood parks, and by promoting campaigns to encourage physical exercise and fitness, as well as healthy eating and other healthy lifestyle choices.

Many studies show that during the COVID-19 pandemic and after infection-prevention measures were implemented, children and adolescents' lifestyles changed dramatically, with decreased physical activity, increased sedentary time, longer hours at home, and shifts in eating patterns. In a study conducted by Dunton et al. in the USA, it was found that physical activity decreased and sedentary behavior increased during the early COVID-19 lockdown among children aged 5–13 years (16). Another large longitudinal study conducted by Xiang et al. in China, which included children and adolescents aged 6 to 17 years, showed a substantial decrease in physical activity and an increase in screen time during the COVID-19 pandemic among the study population (17). Also, in a study by Nicodemo et al. in Italy, maintaining a healthy lifestyle was difficult for these children despite enrollment in a Food-Education Program ((18). Indeed, children and adolescents developed eating habits during the COVID-19 period that were different from their previous habits. This was supported by a systematic review by Pourghazi et al., a literature review by Stavridou et al., and another literature review by Abbas et al. (19-21).

The increase in obesity among children and adolescents during COVID-19 raises concerns regarding the increased severity of COVID-19 infection in obese children and adolescents and the likelihood of progressing to adulthood obesity, especially if the behavior patterns that this population developed during the COVID-19 lockdown continue after returning to everyday life with no lockdown, and this needs to be investigated further after the COVID-19 preventive measures are lifted (22-23).

Conclusions

This study showed that the prevalence of obesity and overweight among children and adolescents attending PHCC health centers increased markedly during the COVID-19 pandemic period; however, an increasing trend was already present before the pandemic.

A national strategy for preventing, screening, and managing overweight and obesity, involving families, schools, the health sector, communities, and policymakers, is necessary to address the more serious health complications that may result if childhood obesity progresses to adulthood obesity.

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Conflict of interest
The authors declare no conflict of interest.

References

1. World Health Organization. Obesity and overweight [Internet]. Geneva: World Health Organization; 2021 Jun 9 [cited 2023 Feb 28]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
2. Güngör NK. Overweight and obesity in children and adolescents. J Clin Res Pediatr Endocrinol. 2014;6(3):129-43. doi:10.4274/Jcrpe.1471.
3. Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes and consequences. J Family Med Prim Care. 2015;4(2):187-92. doi:10.4103/2249-4863.154628.
4. Smith JD, Fu E, Kobayashi MA. Prevention and management of childhood obesity and its psychological and health comorbidities. Annu Rev Clin Psychol. 2020;16:351-78. doi:10.1146/annurev-clinpsy-100219-060201.
5. Shaban Mohamed MA, AbouKhatwa MM, Saifullah AA, Hareez Syahmi M, Mosaad M, Elrggal ME, et al. Risk factors, clinical consequences, prevention, and treatment of childhood obesity. Children (Basel). 2022;9(12):1975. doi:10.3390/children9121975.
6. Marcus C, Danielsson P, Hagman E. Pediatric obesity: long-term consequences and effect of weight loss. J Intern Med. 2022;292(6):870-91. doi:10.1111/joim.13547.
7. World Health Organization. Global action plan on physical activity 2018–2030: more active people for a healthier world [Internet]. Geneva: World Health Organization; 2018 [cited 2026 Oct 27]. Available from: https://www.who.int/publications/i/item/9789241514187
8. World Health Organization. Global School-Based Student Health Survey: Qatar 2011 country factsheet [Internet]. Geneva: World Health Organization; 2011 [cited 2023 Feb 28]. Available from: https://www.who.int/publications/m/item/2011-gshs-country-factsheet-qatar
9. Al-Thani M, Al-Thani A, Alyafei S, Al-Chetachi W, Khalifa SE, Ahmed A, et al. The prevalence and characteristics of overweight and obesity among students in Qatar. Public Health. 2018;160:143-9. doi:10.1016/j.puhe.2018.03.020.
10. Doha News Team. One year of COVID-19 in Qatar: a timeline [Internet]. Doha News; 2021 Mar 17 [cited 2025 Aug 19]. Available from: https://dohanews.co/one-year-of-covid-19-in-qatar-a-timeline/
11. Government Communications Office. Statement by the Supreme Committee for Crisis Management on phase four of the gradual lifting of coronavirus restrictions [Internet]. Doha: Government Communications Office; 2020 Aug 26 [cited 2025 Aug 19]. Available from: https://www.gco.gov.qa/en/media-centre/top-news/phase-4-statement/
12. Marhaba Qatar. What you need to know about the gradual lifting of COVID-19 restrictions [Internet]. Marhaba Qatar; 2021 May 26 [cited 2025 Aug 19]. Available from: https://marhaba.qa/what-you-need-to-know-qatar-gradual-lifting-of-covid19-restrictions/
13. Lange SJ, Kompaniyets L, Freedman DS, Kraus EM, Porter R, Blanck HM, et al. Longitudinal trends in body mass index before and during the COVID-19 pandemic among persons aged 2-19 years: United States, 2018-2020. MMWR Morb Mortal Wkly Rep. 2021;70(37):1278-83. doi:10.15585/mmwr.mm7037a3.
14. Woolford SJ, Sidell M, Li X, Else V, Young DR, Resnicow K, et al. Changes in body mass index among children and adolescents during the COVID-19 pandemic. JAMA. 2021;326(14):1434-6. doi:10.1001/jama.2021.15036.
15. Jenssen BP, Kelly MK, Powell M, Bouchelle Z, Mayne SL, Fiks AG. COVID-19 and changes in child obesity. Pediatrics. 2021;147(5):e2021050123. doi:10.1542/peds.2021-050123.
16. Dunton GF, Do B, Wang SD. Early effects of the COVID-19 pandemic on physical activity and sedentary behavior in children living in the U.S. BMC Public Health. 2020;20(1):1351. doi:10.1186/s12889-020-09429-3.
17. Xiang M, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. Prog Cardiovasc Dis. 2020;63(4):531-2. doi:10.1016/j.pcad.2020.04.013.
18. Nicodemo M, Spreghini MR, Manco M, Wietrzykowska Sforza R, Morino G. Childhood obesity and COVID-19 lockdown: remarks on eating habits of patients enrolled in a food-education program. Nutrients. 2021;13(2):383. doi:10.3390/nu13020383.
19. Pourghazi F, Eslami M, Ehsani A, Ejtahed HS, Qorbani M. Eating habits of children and adolescents during the COVID-19 era: a systematic review. Front Nutr. 2022;9:1004953. doi:10.3389/fnut.2022.1004953.
20. Stavridou A, Kapsali E, Panagouli E, Thirios A, Polychronis K, Bacopoulou F, et al. Obesity in children and adolescents during COVID-19 pandemic. Children (Basel). 2021;8(2):135. doi:10.3390/children8020135.
21. Abbas SA, Athar S, Jilani NZ. The impact of the COVID-19 pandemic on the physical and mental health of school-aged children. HCA Healthc J Med. 2023;4(3):223-8. doi:10.36518/2689-0216.1547.
22. Nogueira-de-Almeida CA, Del Ciampo LA, Ferraz IS, Del Ciampo IRL, Contini AA, Ued FDV. COVID-19 and obesity in childhood and adolescence: a clinical review. J Pediatr (Rio J). 2020;96(5):546-58. doi:10.1016/j.jped.2020.07.001.
23. Brambilla I, Delle Cave F, Guarracino C, De Filippo M, Votto M, Licari A, et al. Obesity and COVID-19 in children and adolescents: a double pandemic. Acta Biomed. 2022;93 Suppl 3:e2022195. doi:10.23750/abm.v93iS3.13075.

Neuroimaging in dementia

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Abstract

Neuroimaging contributes to dementia assessment by detecting structural lesions, characterizing neurodegenerative and vascular injury, identifying molecular pathology, and monitoring treatment safety. These functions require different acquisitions and support different levels of inference. Computed tomography remains useful when magnetic resonance imaging is unavailable, contraindicated, or poorly tolerated, whereas magnetic resonance imaging provides more complete assessment of regional atrophy, small vessel disease, diffusion restriction, and hemorrhagic lesions. Fluorodeoxyglucose positron emission tomography and perfusion single photon emission computed tomography characterize regional dysfunction; dopamine transporter imaging addresses nigrostriatal degeneration. Amyloid positron emission tomography identifies fibrillar amyloid burden, while tau positron emission tomography provides information about the distribution and severity of Alzheimer type tau aggregates. Neither a positive molecular scan nor an atrophy pattern independently establishes the cause of every cognitive symptom. The interpretation of imaging therefore requires integration with the cognitive phenotype, functional status, disease tempo, comorbidity, and the consequences of diagnostic uncertainty. This narrative review examines acquisition, interpretation, diagnostic criteria, differential diagnosis, tracer characteristics, quantification, and clinical algorithms. It also evaluates emerging biomarkers of synaptic density, neuroinflammation, astrocyte reactivity, microstructural injury, perfusion, blood–brain barrier dysfunction, susceptibility, and network organization. Particular attention is given to biological versus clinical definitions of Alzheimer disease, the limitations of early tau detection, and the distinction between amyloid clearance and clinical benefit. Imaging for antiamyloid therapy introduces an additional requirement: reproducible magnetic resonance surveillance for amyloid related imaging abnormalities. Future clinical adoption of emerging measures depends on analytical reproducibility, external validation, representative populations, and evidence that their use improves decisions or outcomes.

Keywords: dementia; magnetic resonance imaging; computed tomography; positron emission tomography; amyloid; tau; imaging biomarkers

Introduction

Dementia is a clinical syndrome defined by acquired cognitive impairment that interferes with independent function. It is not a single pathological entity. Alzheimer disease, Lewy body disease, frontotemporal lobar degeneration, cerebrovascular injury, and combinations of these processes can produce overlapping syndromes. Imaging contributes most effectively when the clinical question is explicit: exclusion of an alternative structural explanation, identification of the anatomical basis of a syndrome, assessment of a candidate pathology, estimation of progression risk, or evaluation of treatment safety. A scan that answers one question may leave the others unresolved. A structural magnetic resonance imaging examination can show hippocampal atrophy without identifying its protein substrate, and an amyloid scan can demonstrate plaques without proving that plaques explain the presenting syndrome (Dickerson et al., 2025; Jack et al., 2024).

The relation between imaging and diagnosis has changed with the development of molecular biomarkers and amyloid targeting treatments. Structural imaging was initially used predominantly to exclude mass lesions, hydrocephalus, and cerebrovascular disease. Contemporary practice also uses regional atrophy and metabolic patterns to support syndrome classification, amyloid testing to establish a treatment target, and serial magnetic resonance imaging to detect treatment associated edema and hemorrhagic injury. The 2024 Alzheimer's Association criteria and 2025 appropriate use criteria for amyloid and tau positron emission tomography formalize several of these applications, while retaining the need for clinical interpretation (Jack et al., 2024; Rabinovici, Knopman, et al., 2025).

This review addresses computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and single photon emission computed tomography (SPECT), with particular emphasis on amyloid and tau ligands and emerging biomarkers. It treats diagnostic accuracy, prognosis, and clinical utility as separate evidentiary domains. Pathological validation supports an inference about tissue abnormalities; prospective prediction supports an inference about future outcomes; a change in clinician management does not by itself establish improved patient function or quality of life. This distinction is necessary when evaluating both established techniques and research methods.

Review approach and evidentiary scope

This paper is a narrative review, not a systematic review or meta-analysis. Its evidence base comprises peer reviewed diagnostic criteria, consensus procedure guidelines, imaging to autopsy studies, prospective cohorts, clinical trials, and methodological investigations. Priority is given to publications from 2020 onward; earlier studies are retained when they establish still used diagnostic criteria, tracer validation, quantification standards, or measurement methods. Literature retrieval used PubMed indexed records and Europe PMC metadata and abstracts, supplemented by accessible full texts and citation tracing. The review does not claim exhaustive retrieval, duplicate screening, or a formal risk of bias assessment.

Evidence is interpreted according to the population, reference standard, acquisition, and intended use. Studies of terminally ill participants with autopsy confirmation are particularly informative about tissue specificity but can over-represent advanced disease. Studies comparing clinically diagnosed Alzheimer dementia with healthy controls often provide a less demanding classification problem than the mixed and uncertain presentations encountered in memory clinics. Prognostic studies require a defined time horizon and an outcome that is not circularly determined by the index scan. These distinctions also inform the assessment of automated imaging systems (Borchert et al., 2023; Fleisher et al., 2020; Soleimani-Meigooni et al., 2020).

Clinical algorithms presented below are a synthesis of the cited recommendations and evidence. They are not a newly validated prediction rule. Treatment monitoring is discussed using published clinical trials and appropriate use recommendations; drug specific prescribing information and local protocols remain the operational authority for dosing and surveillance. This distinction is especially relevant when a published research protocol and subsequent clinical practice recommendations differ (Cummings et al., 2023; Rabinovici, Selkoe, et al., 2025).

Biological interpretation and diagnostic frameworks

Syndromes and pathology

Imaging should be interpreted across three related axes: cognitive functional stage, anatomical syndrome, and underlying disease. An amnestic syndrome may be associated with Alzheimer pathology, limbic predominant age related TDP-43 encephalopathy (LATE), hippocampal sclerosis, or combinations of these. A language led presentation may reflect Alzheimer pathology or frontotemporal lobar degeneration. The same proteinopathy can affect different networks and therefore produce different clinical phenotypes. Conversely, the same anatomical pattern can arise from more than one pathology (Gorno-Tempini et al., 2011; Nelson et al., 2019).

MRI atrophy and fluorodeoxyglucose (FDG) PET hypometabolism are downstream indicators of tissue injury and dysfunction. They are useful for assessing the distribution of disease but are not specific assays of amyloid, tau, TDP-43, or alpha-synuclein. This distinction explains why an Alzheimer compatible FDG pattern should be described as supportive of an etiological hypothesis rather than as direct evidence of Alzheimer protein deposition. The 2018 amyloid, tau, and neurodegeneration framework explicitly placed neurodegeneration measures in parentheses to indicate their lack of specificity to Alzheimer disease (Jack et al., 2018).

Alzheimer disease definitions

The 2024 Alzheimer's Association criteria define Alzheimer disease biologically and distinguish early changing Core 1 biomarkers from later changing Core 2 biomarkers. Amyloid PET is a Core 1 measure. Selected cerebrospinal fluid assays and sufficiently accurate blood assays also fall in this group. Tau PET belongs to Core 2 and provides information about aggregated tau distribution and biological stage. The distinction matters because soluble phosphorylated tau measures and tau PET do not represent interchangeable observations of the same temporal process (Jack et al., 2024).

Under these criteria, an abnormal validated Core 1 result can establish biological Alzheimer disease, but clinical stage remains separately assessed. Biological staging by PET ranges from amyloid positivity without measurable tau PET abnormality, through medial temporal tau involvement, to increasing neocortical tau burden. These PET stages are not equivalent to neuropathological Braak stages, because ligand sensitivity, spatial resolution, and thresholds limit detection. A negative tau PET study, particularly with a visual reading method optimized for advanced neocortical pathology, does not exclude earlier Alzheimer disease (Fleisher et al., 2020; Jack et al., 2024; Soleimani-Meigooni et al., 2020).

The International Working Group takes a different position on clinical nomenclature. Its 2021 recommendations require an appropriate clinical phenotype together with biomarker evidence, and its 2024 update retains Alzheimer disease as a clinical biological construct. Most cognitively unimpaired people with biomarker abnormalities are described as at risk, with more specific consideration of presymptomatic states when the biomarker profile indicates closer proximity to symptoms. The disagreement concerns how disease terminology should be applied clinically, not whether amyloid and tau can be measured before dementia develops (Dubois et al., 2021; Dubois et al., 2024).

The practical implication is that reports and research papers should identify the framework being used. "Amyloid positive," "biological Alzheimer disease under the 2024 criteria," and "dementia due to Alzheimer disease" are related but different statements. Reporting a molecular result without describing clinical status can obscure that distinction. Likewise, an apparently typical clinical syndrome should not be assumed to be biomarker confirmed when molecular testing has not been performed.

Table 1: Diagnostic frameworks and the role of imaging

Framework	Core diagnostic requirement	Imaging contribution and limit
Alzheimer's Association 2024	Biological Alzheimer disease may be established by a validated abnormal Core 1 biomarker. Clinical severity is assessed separately.	Amyloid PET is Core 1; tau PET is Core 2 and contributes to biological staging. MRI atrophy and FDG hypometabolism are nonspecific injury measures.
International Working Group 2021 and 2024	Clinical diagnosis combines an appropriate phenotype with biological evidence. Most biomarker positive cognitively unimpaired people are considered at risk.	Molecular imaging supports the clinical biological construct; positivity alone does not establish dementia.
DLB Consortium 2017	Dementia plus at least two core clinical features, or one core feature with an indicative biomarker, supports probable DLB. Biomarkers alone do not establish probable DLB.	Reduced striatal dopamine transporter uptake is indicative; occipital hypometabolism and relative medial temporal preservation are supportive.
Behavioural variant FTD 2011	Possible disease requires three of six specified clinical features. Probable disease adds functional decline and characteristic imaging.	Frontal or anterior temporal atrophy, hypometabolism, or hypoperfusion supports probable disease; it does not determine the protein substrate.
Primary progressive aphasia 2011	Progressive language led impairment is classified by variant specific language features.	An expected regional pattern supports an imaging supported variant; definite pathology requires pathological or genetic evidence.
VASCOG 2014	Objective cognitive disorder with evidence supporting a vascular etiology, interpreted through clinical course and lesion distribution.	MRI or CT establishes vascular injury; lesion burden alone does not prove causation or exclude Alzheimer copathology.
Boston criteria version 2.0	Probable CAA requires an eligible clinical presentation at age 50 or older and a specified combination of lobar hemorrhagic and white matter features, without deep hemorrhagic lesions or another cause.	Use the complete criteria. Multiple strictly lobar hemorrhagic lesions, or a lobar lesion plus a qualifying white matter feature, can support probable CAA.

Note. Sources: (Charidimou et al., 2022; Dubois et al., 2021; Dubois et al., 2024; Gorno-Tempini et al., 2011; Jack et al., 2024; McKeith et al., 2017; Rascovsky et al., 2011; Sachdev et al., 2014). Abbreviations: CAA, cerebral amyloid angiopathy; DLE

Structural imaging with computed tomography

Clinical indications and diagnostic yield

Noncontrast CT is an appropriate structural examination when MRI cannot be obtained or when rapid assessment of hemorrhage, mass effect, or another acute intracranial process is required. It can identify large infarcts, extensive white matter hypoattenuation, substantial regional atrophy, ventricular enlargement, subdural collections and intracranial masses. Its acquisition is short and less susceptible than a lengthy MRI protocol to intolerance or sustained motion. These advantages are relevant in patients with advanced cognitive impairment or substantial medical instability (Dickerson et al., 2025).

CT has lower soft tissue contrast than MRI for subtle regional atrophy and small vascular lesions. It does not provide the susceptibility sensitive assessment needed to characterize cerebral microbleeds and cortical superficial siderosis adequately. A CT examination that excludes a mass therefore does not answer the separate question of hemorrhagic small vessel burden. This limitation becomes clinically consequential when considering an amyloid targeting antibody: CT cannot replace the MRI examination required for baseline risk assessment and subsequent detection of amyloid related imaging abnormalities (ARIA) (Cummings et al., 2023; Duering et al., 2023; Rabinovici, Selkoe, et al., 2025).

Interpretation and limitations

Atrophy should be assessed for anatomical distribution, symmetry, and proportionality to age, while recognizing the limited specificity of each feature. Medial temporal volume loss, widening of the temporal horns, and posterior cortical volume loss may support a neurodegenerative syndrome, but the combination must be interpreted against the presenting deficits. Marked frontal or anterior temporal atrophy can suggest frontotemporal degeneration, whereas extensive infarction may establish a substantial vascular contribution. Neither finding excludes coexisting Alzheimer pathology (Rascovsky et al., 2011; Sachdev et al., 2014).

Ventricular enlargement requires distinction between tissue loss and a hydrocephalic configuration. An enlarged ventricular system accompanied by disproportionate sulcal changes can justify further assessment for normal pressure hydrocephalus when the clinical presentation is compatible. CT can raise this possibility, although MRI better characterizes associated tissue abnormalities and alternative diagnoses. The imaging finding alone does not establish shunt responsiveness (Nakajima et al., 2021).

The report should state the examination's limitations when the clinical question exceeds its capabilities. In a patient with progressive cognitive impairment and an unrevealing CT, MRI or molecular imaging may still be indicated because absence of a gross structural abnormality is not evidence against early neurodegeneration. Routine repetition of CT without a change in the clinical question offers little etiological clarification; subsequent imaging should address a defined unresolved problem (Dickerson et al., 2025).

Magnetic resonance imaging acquisition and analysis

Core sequences

A dementia MRI protocol should combine volumetric structural assessment with vascular and diffusion sensitive sequences. A three dimensional T1 weighted acquisition supports multiplanar inspection and volumetry. T2 weighted and fluid attenuated inversion recovery (FLAIR) images characterize white matter lesions, edema, lacunes, and other abnormalities. Diffusion weighted imaging with apparent diffusion coefficient maps detects restricted diffusion. A susceptibility sensitive sequence, either T2 star gradient echo or susceptibility weighted imaging, assesses hemorrhagic lesions. Sequence selection should follow the clinical question and local technical capabilities (Dickerson et al., 2025; Duering et al., 2023).

These acquisitions are complementary. A small lesion that appears bright on diffusion weighted imaging requires assessment on apparent diffusion coefficient maps to distinguish true restriction from T2 shine through. A susceptibility focus requires correlation with anatomy and other sequences to distinguish hemorrhagic products from vessels, calcification, or artifact. FLAIR hyperintensity should not automatically be labeled ischemic: distribution and associated findings can suggest inflammatory, demyelinating, infectious, or treatment related processes. An abbreviated examination can preserve diagnostic value if it retains the sequences necessary for the actual decision.

Contrast enhancement is not routinely required to characterize uncomplicated degenerative atrophy. It becomes relevant when a neoplastic, inflammatory, infectious, or meningeal process is suspected. Similarly, angiographic, venographic, perfusion, and vessel wall acquisitions should be added selectively rather than treated as mandatory components of every dementia examination. The technical aim is adequate coverage of the differential diagnosis without imposing acquisitions that the patient cannot tolerate or that will not inform management (Dickerson et al., 2025; Duering et al., 2023).

Visual assessment and quantitative morphometry

Visual assessment should describe medial temporal, posterior, frontal, and anterior temporal involvement, asymmetry, ventricular configuration, and vascular injury. Structured visual ratings can make observations more reproducible, but age, disease stage, and reader training affect their interpretation. An atrophy score should not be treated as a binary assay for Alzheimer disease. A relatively preserved hippocampus also does not exclude Alzheimer pathology in a posterior cortical or language led phenotype (Gorno-Tempini et al., 2011; Jack et al., 2018).

Automated morphometry estimates regional volumes, cortical thickness, and deviation from reference populations. These measures can reveal subtle anatomical differences and support longitudinal analysis, but they are vulnerable to segmentation errors, motion, acquisition differences, and inappropriate normative comparisons. Visual review of the source images and the segmentation is therefore part of interpretation. A numerically low hippocampal percentile is not sufficient evidence of a specific proteinopathy, and a normal percentile cannot override a convincing clinical progression.

Multisite work illustrates the need to separate biological differences from scanner effects. Fortin and colleagues showed that harmonization can reduce nonbiological variance in cortical thickness measurements, while large lifespan reference charts offer a framework for age dependent interpretation. Neither approach removes the need to validate measurements in the population and scanner configuration in which they will be used. Normative centiles summarize deviation from a reference distribution; they do not independently provide an etiological diagnosis (Bethlehem et al., 2022; Fortin et al., 2018).

Longitudinal measurement

Serial MRI can document progressive regional tissue loss, but the interpretation depends on acquisition consistency, scan interval, and measurement uncertainty. Scanner replacement, software updates, changes in sequence parameters, and head motion can produce apparent differences unrelated to progression. An observed volume change should exceed plausible technical variability before it is interpreted as an individual biological effect. Longitudinal pipelines should maintain registration and segmentation consistency while preserving sensitivity to genuine change (Fortin et al., 2018).

Treatment studies introduce additional complexity. A meta-analysis reported accelerated volume changes with several antiamyloid drug classes, including ventricular enlargement associated with ARIA inducing antibodies. The biological explanation and long term clinical implications of these changes are not fully resolved. Consequently, volume loss during treatment cannot simply be equated with the untreated rate of neuronal death, and MRI volume change is not an established stand alone surrogate for cognitive benefit or harm (Alves et al., 2023).

Structural patterns across dementia syndromes

Alzheimer phenotypes

Typical amnestic Alzheimer presentations frequently involve medial temporal structures and temporoparietal association regions. The relative contribution of hippocampal and neocortical abnormalities varies across patients. Young onset and atypical presentations can show disproportionate posterior cortical or language network involvement. Structural imaging is therefore interpreted against the dominant deficits: visuospatial dysfunction directs attention to posterior association regions, while language impairment requires careful analysis of perisylvian and temporal anatomy (Gorno-Tempini et al., 2011; Jack et al., 2018).

Atrophy is a measure of accumulated tissue injury and may be absent or subtle early in a molecularly positive individual. Conversely, pronounced hippocampal atrophy can occur without Alzheimer amyloid pathology. This is particularly relevant in advanced age, when LATE and hippocampal sclerosis may produce an amnestic syndrome. The appropriate inference from hippocampal atrophy is evidence of limbic injury, followed by an etiological assessment that considers molecular results, disease tempo, and competing explanations (Nelson et al., 2019; Wolk et al., 2025).

Frontotemporal degeneration and primary progressive aphasia

In behavioural variant frontotemporal dementia, frontal and anterior temporal abnormalities support the clinical syndrome. The revised consensus criteria distinguish possible disease based on clinical features from probable disease, which additionally requires functional decline and characteristic imaging. The imaging requirement increases etiological confidence but does not identify whether the underlying substrate is tau, TDP-43, or another pathology. An apparently normal early scan also requires consideration of disease stage and alternative psychiatric or neurological explanations (Rascovsky et al., 2011).

Primary progressive aphasia is initially a clinical diagnosis, with imaging supported classification based on the expected anatomical distribution. Nonfluent or agrammatic presentations commonly direct attention to left posterior frontal and insular regions; semantic presentations to anterior temporal regions; and logopenic presentations to left temporoparietal regions. The association between logopenic aphasia and Alzheimer pathology is useful for test selection but is not absolute. Molecular confirmation is particularly valuable when the pathology will determine treatment eligibility or research enrollment (Gorno-Tempini et al., 2011; Rabinovici, Knopman, et al., 2025).

Lewy body disease

Relative preservation of medial temporal structures can support dementia with Lewy bodies (DLB) compared with an amnestic Alzheimer presentation, but structural MRI is not an indicative biomarker under the DLB consensus criteria. Greater medial temporal atrophy may reflect concomitant Alzheimer pathology. The main structural contribution is assessment of vascular disease, other lesions, and the extent of tissue injury, while the syndrome is defined through clinical features and, when appropriate, dopaminergic or other indicative biomarkers (McKeith et al., 2017).

Prodromal DLB requires particular caution because clinical features and imaging abnormalities may be incomplete. The 2020 research criteria operationalize mild cognitive impairment with Lewy bodies, while recognizing insufficient evidence for equally formalized delirium onset and psychiatric onset categories. A later systematic review supported the clinical features and the potential utility of dopaminergic imaging, but emphasized limitations in the biomarker evidence. Dementia stage estimates of test sensitivity should therefore not be transferred directly to prodromal populations (Donaghy et al., 2023; McKeith et al., 2020).

LATE and non Alzheimer limbic injury

The inability to image TDP-43 directly limits the specificity of MRI in an older patient with an amnestic syndrome. LATE can produce marked medial temporal atrophy and coexist with Alzheimer pathology. Proposed clinical criteria use clinical characteristics and available biomarkers to identify suspected cases, but this is an inferential classification rather than direct visualization of TDP-43. A negative amyloid result may reduce the probability of Alzheimer disease while leaving several non Alzheimer causes of limbic degeneration unresolved (Nelson et al., 2019; Wolk et al., 2025).

A 2026 memory clinic investigation examined operationalized clinical LATE categories and found different trajectories between probable LATE, Alzheimer disease, and co-occurring categories. This provides evidence that multimodal profiles can identify clinically distinct groups, but it does not establish a pathology specific imaging assay. Classification performance in a specialist cohort also requires validation in other settings before the same operational definitions are used for individual prognostication (Groot et al., 2026).

Vascular injury and mixed dementia

Lesion characterization

MRI should document the type, location, and burden of cerebrovascular injury. Relevant findings include recent small subcortical infarcts, lacunes, white matter hyperintensities, enlarged perivascular spaces, cerebral microbleeds, cortical superficial siderosis, and larger cortical or subcortical infarcts. STRIVE-2 updates terminology and acquisition considerations and extends attention to quantitative measures of tissue injury. Standard terminology reduces ambiguity when comparing reports, research cohorts, and longitudinal examinations (Duering et al., 2023).

Lesion burden is not interchangeable with clinical attribution. A strategically located infarct can have disproportionate cognitive consequences, while extensive white matter abnormality may produce a gradual executive and processing speed syndrome. Temporal association with stroke, lesion distribution, cognitive phenotype, and functional consequences all inform whether vascular disease substantially contributes. The VASCOG criteria explicitly address a spectrum of mild and major vascular cognitive disorders and acknowledge frequent coexisting Alzheimer pathology (Sachdev et al., 2014).

Hemorrhagic small vessel disease

Strictly lobar hemorrhagic lesions and cortical superficial siderosis can support cerebral amyloid angiopathy (CAA), whereas deep hemorrhagic lesions suggest a different arteriopathy distribution. The Boston criteria version 2.0 combine clinical eligibility, hemorrhagic findings, selected white matter features, and exclusion of other causes. Their use requires the full set of conditions; finding a single lobar microbleed is insufficient to diagnose probable CAA. The criteria were developed and validated against neuropathological assessment in a multicentre study (Charidimou et al., 2022).

CAA is relevant both as a contributor to cognitive impairment and as a treatment safety consideration. Amyloid PET does not reliably distinguish vascular amyloid from parenchymal plaque amyloid at the individual level. A positive scan therefore cannot substitute for susceptibility sensitive MRI when estimating hemorrhagic risk. Conversely, the absence of visible hemorrhagic markers does not prove the absence of microscopic vascular amyloid. Treatment decisions must use the modality that measures the relevant safety concern (Charidimou et al., 2022; Cummings et al., 2023; Rabinovici, Selkoe, et al., 2025).

Quantitative vascular biomarkers

White matter hyperintensity volume captures only part of small vessel injury. Diffusion based measures can quantify abnormalities in normal appearing tissue and the aggregate effect of tract injury. Peak width of skeletonized mean diffusivity was developed as an automated measure associated with processing speed across several small vessel disease cohorts. It provides a useful example of a quantitative biomarker whose intended target is distributed vascular injury, not a specific dementia proteinopathy (Baykara et al., 2016).

STRIVE-2 places such measures within a broader research agenda that includes subvisible tissue injury, higher field imaging, and lesion symptom relationships. Translation requires reproducibility across scanners and acquisition schemes, appropriate handling of motion, and demonstration that the added measurement improves a relevant decision. A stronger association with a cognitive score does not automatically establish an advantage over conventional MRI for routine diagnosis or treatment selection (Duering et al., 2023).

Functional imaging with FDG PET

Physiological basis and acquisition

FDG PET measures the distribution of a glucose analogue whose transport and phosphorylation provide an index of regional glucose utilization. In dementia, the observed signal reflects regional neuronal and synaptic activity together with contributions from other metabolically active cells. It is a functional measure of tissue state rather than a direct count of neurons or synapses. Reduced uptake can precede readily visible atrophy, but this temporal advantage does not confer pathological specificity (Guedj et al., 2022).

Patient preparation and the uptake environment influence interpretation. Fasting status, blood glucose, medication exposure, sensory stimulation, and sedation should be documented. Hyperglycemia reduces tracer uptake and can alter image quality and regional contrast. Sedation can change cerebral metabolism and should be timed and administered according to a validated procedural protocol when necessary. A patient who is restless during acquisition may also have motion induced abnormalities that resemble focal hypometabolism or compromise registration (Guedj et al., 2022).

PET/CT provides attenuation correction and anatomical localization; the low dose CT used for correction is not necessarily a complete diagnostic structural examination. PET/MRI can combine metabolic information with structural and other MRI acquisitions, although attenuation correction and motion remain potential sources of error. In both configurations, the metabolic findings should be interpreted alongside an adequate structural study. A focal metabolic deficit adjacent to an infarct, tumor, or severe atrophy requires a different explanation from the same apparent pattern without a structural correlate (Guedj et al., 2022).

Patterns and differential diagnosis

The usual Alzheimer associated pattern includes temporoparietal, precuneus, and posterior cingulate hypometabolism, with extension depending on stage and phenotype. Frontal involvement may become more evident with progression, and asymmetry can accompany language or visuospatial presentations. The anatomical pattern should be compared with the cognitive syndrome rather than scored solely against a canonical template. FDG PET can support an Alzheimer hypothesis, but confirmation of amyloid pathology requires an appropriate molecular or fluid biomarker (Guedj et al., 2022; Rabinovici, Knopman, et al., 2025).

Frontotemporal degeneration often produces frontal, anterior cingulate, insular, or anterior temporal abnormalities, with the distribution determined by the clinical phenotype. Semantic and nonfluent aphasic syndromes have different expected patterns. Overlap with Alzheimer and psychiatric presentations limits the specificity of an isolated frontal reduction. The source images, structural findings, disease tempo, and clinical examination remain necessary to establish whether the metabolic result provides coherent evidence for a progressive neurodegenerative syndrome (Gorno-Tempini et al., 2011; Guedj et al., 2022; Rascovsky et al., 2011).

DLB can show occipital hypometabolism with relative preservation of posterior cingulate metabolism, the cingulate island sign. This pattern is supportive, not an indicative biomarker under the consensus criteria. It also overlaps with posterior cortical presentations and is influenced by concurrent Alzheimer pathology. The distinction between relative preservation and normal absolute metabolism is important: a region may appear preserved only because adjacent regions are more severely affected (Guedj et al., 2022; McKeith et al., 2017).

Quantification and uncertainty

Semiquantitative analysis compares regional uptake with a reference region or a normative database. Surface projection and statistical maps can help identify subtle patterns, but they depend on registration, smoothing, age matching, scanner characteristics, and the choice of normalization. A reference region affected by disease can distort the apparent distribution of abnormalities. Thresholded color maps should therefore be interpreted as aids to visual assessment rather than as independent diagnostic outputs (Guedj et al., 2022).

Partial volume effects are especially relevant in an atrophic brain because a PET voxel contains mixtures of gray matter, white matter, and cerebrospinal fluid. Apparent hypometabolism may partly reflect loss of tissue volume. Correction can improve estimation of tissue activity but introduces dependence on segmentation and registration and may amplify noise. The report should distinguish a robust distributed metabolic pattern from findings dominated by focal atrophy, technical limitations, or equivocal statistical deviations (Guedj et al., 2022).

A normal or nonspecific FDG study may reduce confidence in a currently active, widespread degenerative process, but its prognostic meaning depends on disease stage and follow-up horizon. It does not exclude molecular Alzheimer pathology or all future neurodegeneration. FDG PET is most useful when the unresolved question concerns the functional anatomy of a symptomatic syndrome and the result is expected to change the differential diagnosis or management.

SPECT and dopaminergic imaging

Cerebral perfusion SPECT

Perfusion SPECT commonly uses technetium labeled radiopharmaceuticals to estimate regional cerebral blood flow. Because perfusion and metabolism are coupled under many physiological conditions, regional patterns can resemble those on FDG PET. The biological quantities are nevertheless different, and vascular disease, altered transit, acquisition, and reconstruction can affect the relationship. Perfusion SPECT should therefore be interpreted as a perfusion measure with its own technical and clinical limitations (Guedj et al., 2022).

Where FDG PET is unavailable, perfusion SPECT can provide functional information in a clinically selected patient. Its interpretation requires attention to spatial resolution, attenuation and scatter correction, head positioning, and the normative database. Apparent posterior or frontal reductions are not intrinsically specific for a proteinopathy. Choosing between modalities should consider local expertise and the unresolved question, rather than assuming that every functional technique is interchangeable. The FDG procedure guideline also discusses perfusion SPECT as an alternative in selected circumstances, including problematic glycemic conditions (Guedj et al., 2022).

Dopamine transporter imaging

Dopamine transporter SPECT, typically with iodine-123 ioflupane, addresses presynaptic nigrostriatal integrity. It does not measure cerebral perfusion and should not be grouped with perfusion SPECT as if the tests answer the same question. Reduced striatal uptake is an indicative biomarker in the DLB consensus criteria, interpreted in conjunction with the clinical features. It supports a degenerative dopaminergic deficit but does not directly demonstrate alpha-synuclein (McKeith et al., 2017; Morbelli et al., 2020).

A reduced dopamine transporter signal is not specific to DLB among all neurodegenerative Parkinsonian disorders. Interpretation requires consideration of progressive supranuclear palsy, corticobasal degeneration, multiple system atrophy, and other causes of nigrostriatal degeneration. Structural lesions can also affect regional striatal appearance, and medications that interact with transporter binding require review. Procedural guidance emphasizes acquisition quality, age appropriate reference data, semiquantification, and the limitations of visual and quantitative assessments (Morbelli et al., 2020).

Cardiac iodine-123 metaiodobenzylguanidine scintigraphy assesses sympathetic cardiac innervation and is another indicative biomarker in the DLB criteria. Cardiac disease, diabetes, and medication effects can complicate interpretation. It is an extracerebral autonomic measure, not a brain perfusion examination. Polysomnographic confirmation of REM sleep without atonia supplies another diagnostic route and illustrates why an imaging result must be integrated with the full set of diagnostic evidence (McKeith et al., 2017).

Table 2: Comparison of structural and functional modalities

Modality	Principal measurement	Best matched question	Main limitation
Noncontrast CT	Gross anatomy and attenuation	Mass lesion, major infarction, hemorrhage, hydrocephalus; structural assessment when MRI is impractical	Limited small lesion and tissue contrast; inadequate for ARIA surveillance
Conventional MRI	Anatomy, tissue signal, diffusion, susceptibility	Regional injury, vascular disease, alternative diagnoses, treatment safety	Atrophy is not protein specific; motion and protocol affect sensitivity
FDG PET	Regional glucose analogue utilization	Functional pattern in a clinically uncertain progressive syndrome	Metabolic dysfunction is nonspecific; preparation and normalization matter
Perfusion SPECT	Regional tracer distribution related to blood flow	Functional assessment where appropriate and locally available	Perfusion is not metabolism; resolution and correction influence interpretation
Dopamine transporter SPECT	Presynaptic striatal transporter availability	Evidence of nigrostriatal degeneration in suspected DLB	Abnormal in other degenerative Parkinsonian disorders; no direct synuclein measurement
Amyloid PET	Fibrillar amyloid retention	Presence of target pathology and selected treatment decisions	Positivity does not assign all symptoms to Alzheimer disease
Tau PET	Ligand dependent aggregated tau retention	Alzheimer tau distribution, biological stage, selected prognosis	Limited early sensitivity and variable binding across tau conformations

Note. Sources: (Dickerson et al., 2025; Duering et al., 2023; Guedj et al., 2022; Morbelli et al., 2020; Rabinovici, Knopman, et al., 2025; Soleimani-Meigooni et al., 2020). ARIA, amyloid related imaging abnormalities.

Amyloid PET tracers and interpretation

Molecular target and established ligands

Amyloid PET detects aggregated fibrillar amyloid with sufficient density to generate a measurable retention pattern. Carbon-11 Pittsburgh compound B (PiB) established the feasibility of in vivo amyloid imaging and remains a research reference ligand. Its short radioactive half-life limits distribution compared with fluorine-18 labeled agents. Florbetapir, florbetaben, and flutemetamol are established fluorine-18 amyloid tracers with imaging to pathology validation. Their acquisition protocols and visual interpretation rules are ligand specific (Clark et al., 2012; Curtis et al., 2015; Klunk et al., 2004; Sabri et al., 2015).

The ligands differ in kinetics, nonspecific retention, imaging windows, and reading procedures. These differences mean that an uptake ratio cannot be transferred uncritically from one tracer to another. The broad clinical inference is common: a positive cortical retention pattern supports a clinically meaningful burden of amyloid deposition. It does not identify soluble oligomer concentration, establish a complete neuropathological diagnosis by itself, or determine how much of an individual's disability is attributable to Alzheimer disease (Rabinovici, Knopman, et al., 2025).

Imaging to autopsy validation

In a prospective florbetapir study, sensitivity for moderate to frequent neuritic plaques was 92% and specificity was 100% among participants with autopsy within two years of imaging. The corresponding confidence intervals were 78%–98% and 80%–100%, respectively, reflecting the limited sample. These values validate detection of a defined pathological category in the studied population; they should not be presented as universal sensitivity and specificity for the clinical syndrome of Alzheimer dementia (Clark et al., 2012).

Florbetaben validation included 74 deceased participants with matched imaging and tissue assessment. The reported subject level sensitivity was 97.9% and specificity 88.9% for the defined neuritic plaque classification. Flutemetamol validation similarly demonstrated an association between visual scan interpretation and neuritic plaque density in an end of life population. Reader variation and differences between subject level and regional tissue matched analyses require attention when comparing results across ligands (Curtis et al., 2015; Sabri et al., 2015).

Autopsy studies provide a strong reference standard but have selection and temporal limitations. Terminally ill volunteers differ from typical patients with mild cognitive impairment, and pathology can progress between imaging and death. The reference category also matters: none or sparse versus moderate or frequent neuritic plaques is not the same comparison as presence versus absence of every microscopic amyloid deposit. A negative PET result is therefore compatible with low density pathology below the detection threshold (Clark et al., 2012; Jack et al., 2024).

Visual reading and technical pitfalls

A negative amyloid scan typically retains gray white matter contrast, with prominent nonspecific white matter signal. A positive scan shows cortical retention that reduces this contrast in characteristic regions. Tracer specific training is required because region selection and positivity rules differ. Atrophy, motion, low count statistics, and misregistration can blur the cortical boundary. Correlation with MRI or CT is helpful when cortical thinning makes the anatomical assignment of uptake uncertain (Rabinovici, Knopman, et al., 2025).

Borderline scans should not be forced into unwarranted certainty. Quantification can support review, but a result near a threshold requires consideration of technical quality and the purpose of testing. A second trained read, review of the reference region, or an independent biomarker may be appropriate when the result will determine a consequential treatment decision. The uncertainty should be reflected in the report and in the subsequent clinical explanation (Jack et al., 2024; Rabinovici, Knopman, et al., 2025).

Centiloid quantification

The Centiloid system was developed to place amyloid PET results on a common scale anchored by young controls and typical Alzheimer participants. It is a calibrated measurement scale, not a percentage of neurons affected or a percentage of maximum possible amyloid. Values may fall below zero or above 100. Valid conversion depends on the tracer and processing pipeline, including region definitions, reference tissue, registration, and scanner characteristics (Klunk et al., 2015).

Florbetapir to Centiloid conversion illustrates this dependence. Navitsky and colleagues derived a conversion for a specified analytical method and identified a pathology based discrimination threshold in their validation data. Applying that equation to a different pipeline without validation would defeat the purpose of standardization. Similarly, a threshold chosen to detect early amyloid accumulation need not equal one used for visual positivity or treatment completion (Navitsky et al., 2018).

Longitudinal quantification is useful for measuring target engagement in treatment trials, but changes in cerebral blood flow, reference region behaviour, scanner performance, and partial volume can influence standardized uptake value ratios. A numerical decline is most persuasive when acquisition and analysis are consistent and the magnitude exceeds expected measurement variability. Standardization supports comparison; it does not eliminate the need for quality control.

Clinical role and clinical utility

Amyloid PET is valuable when Alzheimer pathology is a meaningful diagnostic possibility and knowing amyloid status is expected to change management. Examples include early onset or atypical presentations, unresolved mixed syndromes, and confirmation of a target before amyloid directed treatment. The updated appropriate use criteria assess amyloid and tau PET separately across 17 clinical scenarios. They do not support an indiscriminate molecular imaging sequence for every patient with a cognitive complaint (Rabinovici, Knopman, et al., 2025).

The IDEAS study found changes in a composite management outcome in 60.2% of patients with mild cognitive impairment and 63.5% of patients with dementia after amyloid PET. Because the design lacked a randomized control group, these results establish association with management change rather than a causal improvement in patient outcomes. The AMYPAD-DPMS randomized trial addressed a different outcome: early PET increased the proportion receiving a high confidence etiological diagnosis at three months compared with later imaging. Diagnostic confidence remains distinct from preserved cognition, reduced institutionalization, or improved quality of life (Altomare et al., 2023; Rabinovici et al., 2019).

Tau PET tracers and biological staging

Tau conformations and ligand specificity

Tau aggregates differ in isoform composition, conformation, and anatomical distribution across diseases. Alzheimer disease contains paired helical filament tau with both three repeat and four repeat isoforms, while progressive supranuclear palsy and corticobasal degeneration have predominantly four repeat pathology. A ligand that recognizes Alzheimer type tau cannot be assumed to bind all tauopathies with comparable affinity. This molecular constraint limits the use of an Alzheimer validated tracer as a general diagnostic assay for frontotemporal degeneration (Brendel et al., 2020; Soleimani-Meigooni et al., 2020; Tagai et al., 2021).

The Braak neuropathological scheme describes a characteristic progression of neurofibrillary changes from transentorhinal through limbic to widespread isocortical regions. PET can estimate a related regional distribution, but its spatial resolution and detection threshold prevent exact substitution for histological staging. A PET based stage should therefore be identified as such. In particular, microscopic early medial temporal pathology can be present when a clinical visual read remains negative (Braak & Braak, 1991; Jack et al., 2024).

Flortaucipir

Flortaucipir is the most extensively established clinical tau ligand in the evidence reviewed here. An imaging to autopsy study demonstrated high sensitivity for advanced Alzheimer type tau pathology, with reader dependent specificity. The validation target included Braak V–VI disease, not uniformly sensitive detection of early transentorhinal tangles. The study's advanced age and terminal illness population also limits direct transfer of performance estimates to younger patients or those with subtle impairment (Fleisher et al., 2020).

A separate PET to autopsy series found good correspondence with advanced Alzheimer tau pathology but inconsistent correspondence in non Alzheimer tauopathies and limited detection of earlier Braak stages. This supports a restricted inference: an appropriate neocortical flortaucipir pattern can provide strong evidence of Alzheimer type tau burden, while a negative result does not exclude early Alzheimer disease and a subcortical signal does not establish progressive supranuclear palsy or corticobasal degeneration (Soleimani-Meigooni et al., 2020).

Off target retention can occur in structures adjacent to regions of interest, including choroid plexus and subcortical structures. Spillover can complicate medial temporal quantification, particularly in small or atrophic structures. Clinical visual interpretation and research regional quantification may also apply different positivity definitions. A study described as tau negative under a validated visual method may nevertheless contain quantitative medial temporal signal; these observations should not be treated as contradictory without examining the methods (Rabinovici, Knopman, et al., 2025).

RO948 and MK 6240

RO948 and MK-6240 are research ligands developed to improve measurement of Alzheimer type tau. In the BioFINDER-2 diagnostic study, RO948 discriminated Alzheimer dementia from non Alzheimer neurodegenerative disorders with high area under the receiver operating characteristic curve. The findings support its diagnostic potential, but the result depends on the studied populations, region definitions, and reference diagnoses. It does not establish equal performance in all prodromal or mixed pathology presentations (Leuzy et al., 2020).

Early MK-6240 kinetic work compared simplified uptake ratios with full kinetic modeling and identified an acquisition interval in which the measures were robust. This illustrates why tracer validation includes more than visual similarity to expected disease anatomy. Delivery, clearance, binding reversibility, reference tissue assumptions, and scan timing determine whether a regional value is an interpretable estimate of specific retention. Extracerebral or meningeal signal and spillover also require review with research tau ligands (Pascoal et al., 2018; Rabinovici, Knopman, et al., 2025).

PI 2620 and PM PBB3

PI-2620 has been investigated in progressive supranuclear palsy, including a multicentre study that found elevated binding in expected subcortical targets and reported discrimination from control groups. This is evidence of biomarker potential, not a definitive individual level assay for all four repeat tauopathies. The interpretation of low level subcortical retention requires careful consideration

of kinetics, control selection, and the degree of neuropathological corroboration (Brendel et al., 2020).

PM-PBB3, also known as APN-1607, has been studied for imaging a broader range of tau deposits. Experimental and clinical work reported retention patterns in Alzheimer disease and non Alzheimer tauopathies, with neuropathological support in selected cases. These findings justify further validation but do not make all positive uptake in a clinically suspected tauopathy pathology specific. The need for wider autopsy confirmation, standardized acquisition, and independent replication remains material (Tagai et al., 2021).

Prognosis and treatment stratification

Tau burden is more closely related to clinical expression than amyloid burden in many Alzheimer cohorts. A multicohort study found that baseline tau PET predicted subsequent cognitive change and provided stronger prognostic associations than the compared amyloid PET and MRI measures. This supports tau PET as a prognostic marker at the group level and as a potential aid to counseling, while leaving uncertainty about calibrated individual trajectories, competing pathology, and the influence of cognitive reserve (Ossenkoppele et al., 2021).

Among cognitively unimpaired participants, combined amyloid and tau positivity was associated with increased short term risk of cognitive decline and progression to mild cognitive impairment. Risk differed by tau distribution. These findings do not imply inevitable dementia within a fixed interval for every positive individual: hazard ratios describe relative rates in a cohort, and absolute risk depends on age, follow-up, competing mortality, and the population studied (Ossenkoppele et al., 2022).

Tau PET can also support trial stratification. TRAILBLAZER-ALZ 2 incorporated tau PET to characterize participants and analyze treatment effects by baseline pathology. That research role should not be confused with a universal requirement for clinical eligibility. Published donanemab appropriate use recommendations state that tau PET is not required for eligibility, while amyloid confirmation and MRI assessment remain necessary components of the clinical pathway (Rabinovici, Selkoe, et al., 2025; Sims et al., 2023).

Table 3: Amyloid and tau tracers and evidentiary boundaries

Tracer	Target and established evidence	Interpretive boundary
Carbon 11 PiB	Fibrillar amyloid; foundational human amyloid imaging and quantification reference	Short half-life constrains distribution; research reference rather than a universal clinical acquisition standard
Fluorine 18 florbetapir	Amyloid; prospective imaging to autopsy validation	Tracer specific visual rules and calibrated quantification are required
Fluorine 18 florbetaben	Amyloid; phase 3 imaging to histopathology validation	Regional and subject level accuracy estimates answer different questions
Fluorine 18 flutemetamol	Amyloid; phase 3 comparison with neuritic plaque density	End of life validation does not directly establish prognosis in mild cognitive impairment
Fluorine 18 flortaucipir	Alzheimer type tau; autopsy validation strongest for advanced pathology	Negative clinical visual read does not exclude early tau; off target retention requires review
Fluorine 18 RO948	Alzheimer type tau; strong discrimination in a specialist cohort	Research cohort performance requires independent clinical validation
Fluorine 18 MK 6240	Alzheimer type tau; kinetic and quantitative validation	Scan timing, modeling, and extracerebral signal influence measurement
Fluorine 18 PI 2620	Tau ligand studied in Alzheimer disease and four repeat tauopathies	PSP cohort findings do not establish universal pathology specific individual classification
Fluorine 18 PM PBB3	Broader tau binding investigated with experimental and selected pathological corroboration	Further standardized and independent validation is necessary

Note. Sources: (Brendel et al., 2020; Clark et al., 2012; Curtis et al., 2015; Fleisher et al., 2020; Klunk et al., 2004; Leuzy et al., 2020; Pascoal et al., 2018; Sabri et al., 2015; Soleimani-Meigooni et al., 2020; Tagai et al., 2021). PSP, progressive supranuclear palsy. Entries distinguish validation evidence from research potential and do not constitute a global regulatory status list.

Table 4: Clinical algorithm for etiological imaging

Decision point	Imaging action	Consequence
Establish syndrome and tempo	Select structural imaging after clinical and cognitive assessment; expand urgently for rapid or focal presentations	Identify a defined differential diagnosis and actionable structural causes
Obtain structural baseline	MRI with T1, T2 or FLAIR, diffusion and susceptibility sensitive sequences; CT if MRI is impractical	Characterize atrophy, vascular injury, hemorrhage and alternative lesions
Resolve uncertain functional anatomy	Consider FDG PET; perfusion SPECT may be an alternative in selected settings	Assess whether the regional pattern supports the suspected degenerative syndrome
Evaluate suspected DLB	Consider dopamine transporter imaging when the result would change diagnostic confidence	Interpret with core features and alternative causes of dopaminergic loss
Establish Alzheimer pathology when consequential	Use an appropriately validated fluid biomarker or amyloid PET within a specialist pathway	Clarify etiology or confirm a treatment target; avoid redundant confirmation without a reason
Refine selected stage or prognosis questions	Consider tau PET after defining the decision and expected incremental value	Integrate tau distribution with clinical stage and competing pathology
Investigate discordance	Review technical quality, thresholds, biomarker timing and mixed pathology; use an independent test selectively	Explain disagreement before repeating or expanding testing
Disclose integrated result	Combine clinical phenotype, structural injury and molecular findings	State diagnosis, contribution of each process, uncertainty and management consequences

Note. Clinical synthesis based on (Dickerson et al., 2025; Guedj et al., 2022; Jack et al., 2024; Morbelli et al., 2020; Rabinovici, Knopman, et al., 2025). This sequence is not a validated prediction rule or a requirement to perform every test.

Integrated clinical algorithms

Initial evaluation and test selection
The initial assessment establishes whether there is objective cognitive decline, whether independence is impaired, and which cognitive behavioural syndrome is present. The clinical evaluation also identifies delirium, medication effects, psychiatric illness, sleep disturbance, sensory impairment, and systemic contributors that can affect both symptoms and test interpretation. Structural imaging follows as part of an etiological assessment, with MRI preferred when feasible and CT used when MRI is impractical or unavailable (Dickerson et al., 2025).

The next test should address the uncertainty that remains after structural imaging. FDG PET is useful when the question concerns the distributed functional pattern of a progressive syndrome. Dopamine transporter imaging is useful when a DLB hypothesis remains uncertain and demonstration of nigrostriatal degeneration would change diagnostic confidence. Amyloid testing addresses whether Alzheimer pathology is present, while tau PET can refine biological stage or the likelihood that Alzheimer pathology substantially contributes to symptoms. These questions may overlap, but the tests should not be ordered as an automatic panel (Guedj et al., 2022; Morbelli et al., 2020; Rabinovici, Knopman, et al., 2025).

Discordant multimodal findings
Discordance is often biologically informative. Amyloid positivity with limited tau burden and a strongly non-Alzheimer phenotype may indicate coincident amyloid deposition. Marked hippocampal atrophy with negative amyloid testing can prompt consideration of LATE, hippocampal sclerosis, vascular injury, or another limbic process. A convincing Alzheimer clinical phenotype with a negative molecular result requires review of scan quality, threshold effects, alternative assays, and alternative diagnoses before any conclusion that the test is erroneous (Dubois et al., 2021; Jack et al., 2024; Wolk et al., 2025). The interpretation should distinguish a technical disagreement from a biological one. Motion, segmentation failure, an abnormal reference region, or inappropriate application of a threshold can generate an apparent discrepancy. When each measurement is technically credible, different biomarker timing and mixed pathology may explain the findings. Repeating several tests without first specifying the mechanism of disagreement can increase complexity without resolving the clinical question.

A practical multimodal conclusion states the syndrome, the observed abnormalities, their likely contribution, and the remaining uncertainty. For example, an amnestic dementia with amyloid positivity, extensive neocortical tau, and concordant temporoparietal injury provides a different degree of etiological support from isolated amyloid positivity in a patient with hallucinations, fluctuations, and reduced striatal dopamine transporter uptake. Both patients can have amyloid pathology, but the explanatory role of that pathology differs (Jack et al., 2024; McKeith et al., 2017).

Rapid progression and alternative structural explanations
Rapid or subacute cognitive decline requires an expanded differential diagnosis. Diffusion abnormalities, enhancement, edema, seizures, mass effect, and inflammatory or infectious patterns may redirect the investigation away from a routine degenerative pathway. The diagnostic value of MRI in this setting derives from its ability to identify a different mechanism and guide targeted clinical and laboratory testing. A dementia label should not delay the evaluation of an acute or potentially treatable process (Dickerson et al., 2025; Guedj et al., 2022).

Normal pressure hydrocephalus provides a different example of a potentially actionable imaging pattern. Disproportionately enlarged subarachnoid space hydrocephalus includes ventricular enlargement with characteristic sulcal disproportion. The finding is interpreted alongside gait and other clinical features and followed by appropriate specialist assessment. Imaging supports the pathway; it does not establish that every cognitive symptom will improve with cerebrospinal fluid diversion, particularly when neurodegenerative comorbidity is present (Nakajima et al., 2021).

Imaging in amyloid directed treatment

Confirmation and baseline risk assessment
Amyloid directed treatment requires confirmation of the target pathology in an appropriately selected clinical population. In the lecanemab phase 3 trial, participants had early Alzheimer disease with amyloid evidence by PET or cerebrospinal fluid testing. The donanemab trial incorporated both amyloid and tau imaging in its eligibility and analysis strategy. The imaging result must be integrated with clinical stage and other eligibility conditions; demonstration of amyloid is not sufficient to establish that treatment is appropriate (Sims et al., 2023; van Dyck et al., 2023).

Baseline MRI identifies hemorrhagic and vascular findings relevant to safety and provides a comparator for subsequent scans. Susceptibility sensitive imaging establishes the pre-existing microbleed and superficial siderosis burden, while FLAIR and diffusion imaging assist with edema, infarction, and alternative diagnoses. Published appropriate use recommendations specify exclusions and surveillance requirements for each agent. These are drug specific recommendations, and a threshold used in one protocol should not be generalized to every amyloid directed therapy (Cummings et al., 2023; Rabinovici, Selkoe, et al., 2025).

The donanemab recommendations, for example, advise excluding patients with more than four cerebral microbleeds, cortical superficial siderosis, or a major

vascular contribution to cognitive impairment. They also specify baseline MRI timing and additional monitoring for higher risk individuals. These criteria concern the studied treatment pathway; they are not diagnostic criteria for dementia or a universal definition of acceptable vascular burden (Rabinovici, Selkoe, et al., 2025).

ARIA detection and management implications

ARIA-E comprises edema or sulcal effusion, generally assessed on FLAIR. ARIA-H comprises hemorrhagic abnormalities including new microhemorrhages and superficial siderosis, assessed using susceptibility sensitive imaging. The two can occur together. MRI interpretation requires comparison with baseline because pre-existing lesions and treatment emergent lesions have different implications. A consistent acquisition technique is important when counting small susceptibility foci (Cummings et al., 2023; Rabinovici, Selkoe, et al., 2025; Salloway et al., 2022).

ARIA can be asymptomatic or associated with headache, confusion, visual symptoms, seizures, focal deficits, or other neurological changes. Published aducanumab safety analyses demonstrated that many events occurred early in treatment and that APOE epsilon 4 status influenced risk. These findings inform the broader understanding of ARIA but should not be used as a substitute for agent specific incidence estimates. Severity assessment combines radiographic extent and clinical symptoms (Salloway et al., 2022).

New neurological symptoms during treatment require prompt evaluation rather than reliance on the date of the next scheduled scan. FLAIR and susceptibility findings should be interpreted with diffusion imaging and the clinical presentation because infarction, hemorrhage, and other acute conditions may overlap. Decisions to continue, pause, or discontinue treatment depend on the agent's protocol, symptoms, radiographic severity, and evolution. CT can identify major acute hemorrhage but cannot reliably exclude the full ARIA spectrum (Cummings et al., 2023; Rabinovici, Selkoe, et al., 2025).

Target engagement and clinical response

Lecanemab and donanemab trials demonstrated substantial amyloid reduction together with statistically significant slowing of decline on clinical outcomes. The clinical effect should be described as reduced decline over the studied interval, not restoration of normal cognition. Amyloid clearance is a pharmacodynamic measure, while clinical benefit is assessed through cognition and function. Their association does not make the magnitude of PET reduction a direct individual measure of treatment success (Sims et al., 2023; van Dyck et al., 2023).

Repeat amyloid PET can have a treatment specific role, including consideration of treatment completion in a donanemab pathway. This is different from serial imaging to track untreated dementia severity. Tau PET, MRI atrophy, and fluid biomarkers may contribute to research on downstream effects, but changes in these measures require independent validation as surrogates for patient outcomes. Treatment decisions should not be inferred from an imaging biomarker's change without an established clinical interpretation (Alves et al., 2023; Rabinovici, Selkoe, et al., 2025).

Emerging MRI biomarkers

Diffusion microstructure

Diffusion MRI estimates water displacement within tissue and is sensitive to changes in white matter and gray matter microstructure. Conventional diffusion tensor measures, including fractional anisotropy and mean diffusivity, are influenced by axonal organization, extracellular water, crossing fibers, and partial volume. A reduced fractional anisotropy value is therefore not a histological diagnosis of demyelination or axonal loss. Its biological interpretation depends on anatomy, model assumptions, and complementary measurements (Bergamino et al., 2021).

Free water models separate an extracellular isotropic compartment from tissue related diffusion. In an Alzheimer study using OASIS-3 data, free water correction changed the pattern and consistency of several diffusion measures, demonstrating that extracellular water can materially influence conventional tensor estimates. The approach improves characterization of the measured signal but does not uniquely identify the cellular mechanism producing an abnormal compartment fraction. Model stability and acquisition sufficiency remain necessary for individual interpretation (Bergamino et al., 2021).

Neurite orientation dispersion and density imaging and related multicompartment methods attempt to characterize tissue complexity more specifically than a single tensor. A systematic review and meta-analysis of in vivo microstructural abnormalities in mild cognitive impairment and Alzheimer disease illustrates the breadth of diffusion investigations. Group differences support biological sensitivity, but cross-study heterogeneity and overlapping causes of microstructural injury limit direct diagnostic thresholds. Advanced diffusion currently complements research characterization more readily than it supplies a stand alone clinical etiological assay (Duering et al., 2023; Zhong et al., 2023).

Arterial spin labeling

Arterial spin labeling (ASL) uses magnetically labeled arterial blood water as an endogenous tracer to estimate perfusion without ionizing radiation or an injected contrast agent. It can be incorporated into MRI and offers a route to repeated physiological measurements. Consensus implementation recommendations favour standardized labeling, background suppression, acquisition, and cerebral blood flow calculation, because signal intensity alone does not provide a reliable comparable perfusion value (Alsop et al., 2015).

Table 5:: Clinical algorithm for imaging during amyloid directed therapy

Stage	Required imaging question	Interpretive action
Before treatment	Is target pathology established, and is MRI adequate for baseline risk assessment?	Confirm amyloid by the accepted pathway; assess microbleeds, siderosis, infarction, white matter disease and other exclusions
Scheduled surveillance	Is there new ARIA-E or ARIA-H compared with baseline?	Use the agent specific surveillance schedule and a reproducible MRI protocol
New neurological symptoms	Could ARIA, stroke, hemorrhage or another acute process explain symptoms?	Arrange prompt clinical assessment and appropriate imaging; do not await the next routine surveillance scan
ARIA identified	What are the clinical and radiographic severity and temporal evolution?	Communicate directly with the treatment team; apply the agent specific continuation, suspension or discontinuation rules
Follow-up after an event	Has edema resolved, and are hemorrhagic findings stable or progressive?	Compare FLAIR and susceptibility imaging with baseline and intervening scans before treatment decisions
Target engagement or completion	Would repeat amyloid quantification change the treatment plan?	Use only an established treatment specific pathway; distinguish plaque reduction from cognitive response

Note. Clinical synthesis based on (Cummings et al., 2023; Rabinovici, Selkoe, et al., 2025; Salloway et al., 2022; Sims et al., 2023; van Dyck et al., 2023). Published appropriate use recommendations inform this table; current drug specific

ASL is sensitive to labeling efficiency, arterial transit time, postlabeling delay, motion, and partial volume. Delayed arrival of blood can resemble low perfusion if the acquisition does not account for transit effects. These issues are especially relevant in older patients with vascular disease. A posterior perfusion deficit may be compatible with an Alzheimer associated pattern but is not a direct amyloid or tau measure, and its incremental diagnostic value depends on comparison with structural and other available biomarkers (Alsop et al., 2015).

Functional connectivity

Resting state functional MRI estimates temporal associations in blood oxygenation dependent signals. Alzheimer disease research has examined default mode and medial temporal network abnormalities, including both reduced and increased connectivity. Longitudinal work showed related changes in posterior medial and anterior temporal hippocampal networks associated with cognitive decline. Such findings indicate that network dysfunction is not adequately represented by a single model of uniformly reduced connectivity (Dautricourt et al., 2021).

The blood oxygenation signal depends on neurovascular coupling as well as neuronal activity. Head motion, vigilance, respiratory effects, vascular disease, preprocessing, and global signal treatment can alter connectivity estimates. An apparent increase may reflect compensation, disinhibition, altered network segregation, or methodological effects; the interpretation requires direct evidence rather than an automatic compensatory label. Clinical adoption requires reliable individual estimates and demonstrated value beyond standard assessment.

Susceptibility and tissue composition

Quantitative susceptibility mapping estimates local magnetic susceptibility and has been used to study tissue iron related changes. An AIBL study found that higher regional susceptibility was associated with faster cognitive deterioration among amyloid positive participants. This supports investigation of susceptibility as a modifier of risk, but it does not make the measure specific to iron concentration or establish a causal effect of iron on decline (Ayton et al., 2017).

Susceptibility is influenced by several tissue constituents, orientation, acquisition, and reconstruction. Hemorrhagic products and myelin also affect the signal, and regional values depend on the chosen reference. Susceptibility mapping should therefore be distinguished from conventional microbleed detection, even though both use susceptibility sensitive information. Its potential contribution is quantitative tissue characterization; validation must address reproducibility and the specificity of the proposed interpretation.

Spectroscopy and metabolic MRI

Proton magnetic resonance spectroscopy assesses metabolites such as N-acetylaspartate, myo-inositol, choline containing compounds, and creatine. Changes may provide information about neuronal metabolism and glial related processes, but metabolite concentrations and ratios are influenced by tissue composition, acquisition, spectral fitting, and the stability of the denominator. A metabolite ratio is not automatically a quantitative measure of one cell population.

A 2025 hybrid three dimensional spectroscopic imaging and amyloid PET study examined 174 participants and reported regional relationships between amyloid, lower N-acetylaspartate, and higher myo-inositol. The work supports the value of spatially matched metabolic and molecular measurements. Improved classification within a study, however, requires external validation before the combined protocol can be treated as a clinical diagnostic standard. Research on functional spectroscopy of lactate similarly remains limited by measurement and biological interpretation challenges (Shirbandi et al., 2023; Zhang et al., 2025).

Blood brain barrier imaging

Dynamic contrast enhanced MRI can estimate contrast transfer related to blood–brain barrier permeability. In a human study of APOE epsilon 4 carriers, hippocampal and medial temporal barrier dysfunction was associated with genotype and cognitive impairment, while cerebrospinal fluid evidence of pericyte injury predicted subsequent decline. The findings support a vascular pathway that is not simply reducible to measured amyloid and tau burden (Montagne et al., 2020).

Low level leakage measurements are technically demanding. Temporal resolution, acquisition duration, arterial input estimation, baseline relaxation measurements, vascular volume, and pharmacokinetic modeling influence the result. Contrast exposure also changes feasibility for repeated measurement. A group level association with cognitive impairment does not yet define a clinically transferable threshold or establish whether measuring permeability improves an individual diagnostic decision. The main current contribution is mechanistic characterization and research stratification.

Emerging molecular imaging biomarkers

Synaptic density

Synaptic vesicle glycoprotein 2A (SV2A) PET provides a molecular approach to estimating a presynaptic protein associated with synaptic density. Carbon-11 UCB-J studies have shown reduced binding in medial temporal and neocortical regions in early Alzheimer disease. In one study, regional reductions persisted after correction for volume loss and were more extensive than the observed gray matter volume differences. This indicates sensitivity to information that is not fully captured by morphometry (Mecca et al., 2020).

SV2A binding is not a literal count of all functional synapses. The signal depends on protein availability, tracer delivery, modeling, and potentially medications occupying the target. Synapse type and function also cannot be inferred from a single regional binding value. These considerations

are important when proposing SV2A PET as a treatment response biomarker: a change in target availability requires interpretation before it can be equated with synapse gain or loss.

A 2025 study compared cerebrospinal fluid SV2A with UCB-J PET in a small early Alzheimer and control sample and found correspondence between the measures within the Alzheimer group. The study illustrates how imaging can validate the spatial and biological interpretation of fluid markers. It also shows why different "synaptic" biofluid proteins should not be assumed to index the same process; several other measured proteins did not show the same relationship with PET (Mecca et al., 2025).

Microglial and other inflammatory targets

Translocator protein (TSPO) PET has been used to study inflammatory responses in Alzheimer disease. The biological signal is broader than a unique detrimental microglial state, and binding is affected by tracer properties and, for several ligands, TSPO genotype. Appropriate interpretation therefore requires careful participant characterization and kinetic analysis. A high signal should not automatically be labeled evidence that inflammation is causing faster clinical decline.

Longitudinal DPA-714 work reported different relationships between baseline binding, subsequent binding change, and clinical progression. Higher initial binding was associated with a more favorable course, whereas increasing signal over follow-up was associated with worsening. These observations argue against a single monotonic interpretation of TSPO binding across all patients. A later multimodal study found spatial relationships among microglial activation, tau propagation, and amyloid, supporting interaction among these processes without proving that a particular PET signal identifies a uniquely causal cell state (Hamelin et al., 2018; Pascoal et al., 2021).

New inflammatory targets may eventually provide more selective information than TSPO, but clinical translation requires demonstration of target specificity, brain penetration, adequate specific binding, test retest reliability, and pathological or biological validation. The evaluation should distinguish expression of a target from a full cellular phenotype. A tracer can accurately measure a protein while still supporting only limited inference about whether the underlying response is protective, harmful, or stage dependent.

Astrocyte reactivity

Astrocyte related PET research includes targets such as monoamine oxidase B and other proteins associated with reactive states. Target expression is not restricted to a single pathological interpretation, and cellular specificity must be demonstrated rather than assumed. Fluid and imaging combinations can help test whether astrocyte related processes modify the relationship between amyloid and tau.

Bellaver and colleagues studied more than 1,000 cognitively unimpaired individuals across three cohorts and found that astrocyte reactivity, assessed with a fluid marker, modified the association between amyloid and tau measures. Tau PET provided information about downstream regional accumulation. The study supports a multimodal model of interacting pathology; it is not direct validation of an astrocyte specific PET ligand. Keeping those roles separate prevents a fluid defined biological association from being misreported as tracer validation (Bellaver et al., 2023).

Unmet proteinopathy targets

The reviewed clinical pathways still lack an established broadly available PET assay for TDP-43 or alpha-synuclein comparable with established Alzheimer amyloid imaging. Dopamine transporter imaging identifies a functional consequence of nigrostriatal degeneration, and clinical LATE criteria infer a likely underlying process from phenotype and other biomarkers. Neither directly visualizes the relevant protein aggregate (McKeith et al., 2017; Morbelli et al., 2020; Wolk et al., 2025).

This limitation affects mixed pathology assessment. An amyloid negative result can exclude a substantial Alzheimer plaque burden while leaving uncertainty among several non Alzheimer disorders. Development of a new ligand requires more than an anatomically plausible retention pattern in a clinically diagnosed cohort. Binding should be established in tissue, specificity tested against competing aggregates and off target substrates, and in vivo performance confirmed with independent biological or neuropathological evidence.

Table 6: Emerging biomarkers and requirements for translation

Measure	Biological information	Main validation requirement
Advanced diffusion MRI	Microstructure, extracellular water and tract injury	Model robustness, multisite reproducibility and specificity of interpretation
ASL perfusion MRI	Regional cerebral blood flow	Control of transit time, labeling and partial volume effects
Resting state functional MRI	Network organization through hemodynamic correlations	Motion control, neurovascular confounding and reliable individual prediction
Quantitative susceptibility mapping	Tissue susceptibility influenced by iron and other constituents	Reconstruction standardization and separation of competing tissue effects
MR spectroscopy	Regional metabolite concentrations or ratios	Spectral quality, tissue correction and externally validated incremental value
Dynamic contrast enhanced MRI	Barrier transfer and vascular permeability estimates	Reliable low leakage measurement and clinically interpretable thresholds
SV2A PET	Presynaptic protein availability associated with synaptic density	Target occupancy review, kinetic reliability and outcome validation
TSPO PET	Inflammation related protein expression	Genotype and cellular specificity, modeling, and stage dependent interpretation
Astrocyte related imaging	Selected proteins associated with astrocyte biology	Direct target and cellular validation; separation from fluid defined associations
AI and normative modeling	Patterns and deviation from reference anatomy or combined measurements	Independent, representative validation; calibration and clinical decision benefit

Note. Sources: (Alsop et al., 2015; Ayton et al., 2017; Bellaver et al., 2023; Bergamino et al., 2021; Bethlehem et al., 2022; Borchert et al., 2023; Dautricourt et al., 2021; Hamelin et al., 2018; Mecca et al., 2020; Montagne et al., 2020; Pascoal et al., 2021; Zhang et al., 2025; Zhong et al., 2023).

Multimodal integration and blood biomarkers

Blood based biomarkers can alter the sequence and frequency of imaging without eliminating its distinct spatial and safety functions. A prospective clinical study found high diagnostic accuracy for plasma percentage phosphorylated tau 217 and an amyloid probability score in symptomatic primary and secondary care populations. These results support blood testing as a potentially efficient route to assessing Alzheimer pathology when the assay and intended population are appropriately validated (Palmqvist et al., 2024).

The relation to imaging is conditional. A sufficiently accurate assay may establish a biological category under a specified framework, while PET remains useful for resolving equivocal or discordant findings and quantifying spatial pathology. MRI remains necessary for structural causes, vascular injury, and ARIA assessment because blood testing does not supply an anatomical map of hemorrhage or edema. Tau PET also provides regional staging information that cannot be reconstructed directly from a single blood concentration (Jack et al., 2024; Rabinovici, Knopman, et al., 2025).

A two threshold blood testing strategy can separate clearly low and high probability results from an intermediate zone that requires further evaluation. Its performance depends on prevalence, assay calibration, and comorbid influences. The downstream pathway should specify which result warrants PET or cerebrospinal fluid confirmation and why. Combining multiple correlated biomarkers without a defined decision rule can increase apparent certainty while adding little independent information.

For a multimodal model, incremental value should be measured against the best feasible existing pathway. Adding PET to a weak clinical comparator may appear beneficial even when the same gain could be achieved with a more complete clinical assessment or an accessible validated fluid assay. Conversely, a blood assay may be efficient for amyloid classification while leaving a major unresolved question about the anatomical distribution of tau, vascular comorbidity, or treatment safety. The value of each modality is determined by the decision it improves (Dickerson et al., 2025; Palmqvist et al., 2024; Rabinovici, Knopman, et al., 2025).

Artificial intelligence and quantitative implementation

Clinical questions and validation

Machine learning systems can estimate diagnosis, progression, regional abnormality, and patterns of heterogeneity from structural and molecular imaging. These are different tasks and require different reference standards. A classifier trained to distinguish Alzheimer dementia from healthy controls does not establish performance for differentiating Alzheimer disease from DLB, LATE, depression, or mixed vascular disease in a memory clinic. The intended population and decision should be defined before choosing a performance metric.

A systematic review of 255 neuroimaging artificial intelligence studies found heavy dependence on the Alzheimer's Disease Neuroimaging Initiative and limited independent validation. This concentration creates a risk that reported performance reflects features of a selected research sample, acquisition environment, or diagnostic labeling procedure. External validation should therefore include other institutions, scanner configurations, demographic groups, disease severities, and clinically relevant alternatives (Borchert et al., 2023).

Data leakage can occur when repeated scans from one participant appear in both training and test sets, preprocessing uses information from the full dataset, or feature selection is performed before partitioning. A high area under the curve does not resolve these design problems. Prospective evaluation should also assess calibration, failure modes, missing data, and the consequences of acting on false positive and false negative predictions.

Harmonization and normative interpretation

Harmonization methods aim to reduce scanner dependent variation while retaining biological differences. Their validity depends on the study design: if diagnostic groups and sites are strongly confounded, separating site from disease is difficult. The method and its parameters should be fitted within the training data in predictive studies and assessed on independent data. A statistical correction cannot replace an adequate acquisition and quality assurance protocol (Borchert et al., 2023; Fortin et al., 2018).

Normative brain charts provide age related centiles, but their clinical application requires an appropriate reference population and uncertainty estimates. The large lifespan dataset assembled by Bethlehem and colleagues demonstrates the scale needed to model anatomical variation, while also acknowledging uneven population representation. A low centile indicates an unusual measurement relative to that reference; it does not state whether the cause is developmental, vascular, degenerative, or technical (Bethlehem et al., 2022).

Deployment and accountability

A clinically deployed imaging system should make its input requirements, intended use, and failure conditions explicit. Segmentation overlays should be available for review, and numerical results should be traceable to a processing version. Quality assurance should detect motion, incomplete coverage, unexpected anatomy, and out of distribution inputs. An algorithm that cannot produce a dependable output should identify that failure rather than issue an apparently precise diagnostic probability.

Monitoring after deployment is necessary because scanner software, referral patterns, and population characteristics change. Performance should be evaluated through decisions and outcomes as well as discrimination metrics. The immediate clinical responsibility remains interpretation of the complete case, including symptoms and competing pathology. Automation can improve consistency and throughput, but its value requires evidence that its use improves the actual diagnostic pathway (Borchert et al., 2023).

Reporting standards and clinical communication

A useful imaging report distinguishes observations from etiological interpretation. The technical section identifies the modality, tracer where relevant, acquisition limitations, and comparison studies. The findings describe regional anatomy or uptake, vascular lesions, and incidental abnormalities. The conclusion states what the findings support, what they do not resolve, and whether an additional test could answer a specific remaining question. This structure avoids converting a compatible pattern into an unsupported pathological diagnosis (Guedj et al., 2022; Morbelli et al., 2020; Rabinovici, Knopman, et al., 2025).

For molecular imaging, the result should be expressed using the validated reading method, with quantification identified as supplementary or as part of an explicitly validated analysis. If a Centiloid value is reported, the analytical pipeline and its relevant interpretation should be clear. For tau PET, the distinction between an approved visual classification and research regional staging should be stated. For treatment surveillance, new lesions and change from baseline require explicit comparison, together with the imaging severity assessment used by the treatment team.

Disclosure should connect the result to the original question. A positive amyloid scan means amyloid pathology is present above the relevant detection threshold; it does not provide an exact date of future decline or establish that all symptoms arise from that pathology. A negative scan may narrow the differential diagnosis without identifying the alternative. The specialist should explain how the result changes diagnostic confidence, treatment options, and the need for further evaluation (Dubois et al., 2024; Rabinovici, Knopman, et al., 2025).

Limitations of the evidence and priorities for research

The evidence base is uneven across modalities and disease stages. Amyloid ligands have substantial pathological validation, whereas several emerging targets are supported by smaller mechanistic studies. Clinical tau PET has a stronger basis for advanced Alzheimer type pathology than for early microscopic disease or all non Alzheimer tau conformations. MRI and FDG patterns are widely used but remain biologically nonspecific. These differences should determine the strength of the language used in diagnosis and research conclusions (Clark et al., 2012; Fleisher et al., 2020; Soleimani-Meigooni et al., 2020).

Mixed pathology is a central limitation of single target interpretation. Multiple processes can contribute to one clinical syndrome, and the availability of an assay for one process can bias attention toward it. Greater neocortical tau burden can strengthen an Alzheimer attribution, while vascular MRI and dopaminergic imaging may demonstrate additional mechanisms. The absence of established direct assays for other common proteinopathies leaves a residual uncertainty that should not be concealed by a positive Alzheimer biomarker (Jack et al., 2024; McKeith et al., 2017; Nelson et al., 2019).

Research priorities include imaging to autopsy validation across disease stages, prospective studies with representative clinical populations, reproducible quantification, and comparisons against realistic diagnostic pathways. Emerging biomarkers should be evaluated for incremental prognosis and treatment response, not only separation of cases from controls. Therapeutic studies should distinguish target engagement, safety markers, and validated clinical outcomes. For imaging driven management pathways, randomized or otherwise, well controlled outcome studies are needed to determine whether greater diagnostic certainty translates into benefit for patients and care partners (Altomare et al., 2023; Borchert et al., 2023; Rabinovici et al., 2019).

Conclusion

Neuroimaging in dementia is most informative when each modality is matched to a specific inference. CT and MRI identify structural disease and injury; functional imaging characterizes regional dysfunction; amyloid and tau PET assess defined molecular targets with different temporal and pathological sensitivities. Clinical interpretation requires an explicit diagnostic framework and recognition of mixed pathology. In amyloid directed treatment, MRI also has a separate safety function that molecular or blood biomarkers cannot replace. Emerging techniques broaden measurement of synapses, glial responses, microstructure, perfusion, barrier integrity, and network function, but their clinical use requires reproducible individual measurements and evidence of added decision value.

References

Alsop, D. C., Detre, J. A., Golay, X., Günther, M., Hendrikse, J., Hernandez-Garcia, L., Lu, H., MacIntosh, B. J., Parkes, L. M., Smits, M., van Osch, M. J., Wang, D. J., Wong, E. C., & Zaharchuk, G. (2015). Recommended implementation of arterial spin-labeled perfusion MRI for clinical applications: A consensus of the ISMRM perfusion study group and the European consortium for ASL in dementia. Magnetic Resonance in Medicine, 73(1), 102-116. https://doi.org/10.1002/mrm.25197

Altomare, D., Barkhof, F., Caprioglio, C., Collij, L. E., Scheltens, P., Lopes Alves, I., Bouwman, F., Berkhof, J., van Maurik, I. S., Garibotto, V., Moro, C., Delrieu, J., Payoux, P., Saint-Aubert, L., Hitzel, A., Molinuevo, J. L., Grau-Rivera, O., Gispert, J. D., Drzezga, A., … Amyloid Imaging to Prevent Alzheimer's Disease (AMYPAD) Consortium (2023). Clinical effect of early vs late amyloid positron emission tomography in memory clinic patients: The AMYPAD-DPMS randomized clinical trial. JAMA Neurology, 80(6), 548-557. https://doi.org/10.1001/jamaneurol.2023.0997

Alves, F., Kalinowski, P., & Ayton, S. (2023). Accelerated brain volume loss caused by anti-β-amyloid drugs: A systematic review and meta-analysis. Neurology, 100(20), e2114-e2124. https://doi.org/10.1212/wnl.0000000000207156

Ayton, S., Fazlollahi, A., Bourgeat, P., Raniga, P., Ng, A., Lim, Y. Y., Diouf, I., Farquharson, S., Fripp, J., Ames, D., Doecke, J., Desmond, P., Ordidge, R., Masters, C. L., Rowe, C. C., Maruff, P., Villemagne, V. L., Australian Imaging Biomarkers and Lifestyle (AIBL) Research Group, Salvado, O., & Bush, A. I. (2017). Cerebral quantitative susceptibility mapping predicts amyloid-β-related cognitive decline. Brain, 140(8), 2112-2119. https://doi.org/10.1093/brain/awx137

Baykara, E., Gesierich, B., Adam, R., Tuladhar, A. M., Biesbroek, J. M., Koek, H. L., Ropele, S., Jouvent, E., Alzheimer's Disease Neuroimaging Initiative, Chabriat, H., Ertl-Wagner, B., Ewers, M., Schmidt, R., de Leeuw, F. E., Biessels, G. J., Dichgans, M., & Duering, M. (2016). A novel imaging marker for small vessel disease based on skeletonization of white matter tracts and diffusion histograms. Annals of Neurology, 80(4), 581-592. https://doi.org/10.1002/ana.24758

Bellaver, B., Povala, G., Ferreira, P. C. L., Ferrari-Souza, J. P., Leffa, D. T., Lussier, F. Z., Benedet, A. L., Ashton, N. J., Triana-Baltzer, G., Kolb, H. C., Tissot, C., Therriault, J., Servaes, S., Stevenson, J., Rahmouni, N., Lopez, O. L., Tudorascu, D. L., Villemagne, V. L., Ikonomovic, M. D., … Pascoal, T. A. (2023). Astrocyte reactivity influences amyloid-β effects on tau pathology in preclinical Alzheimer's disease. Nature Medicine, 29(7), 1775-1781. https://doi.org/10.1038/s41591-023-02380-x

Bergamino, M., Walsh, R. R., & Stokes, A. M. (2021). Free-water diffusion tensor imaging improves the accuracy and sensitivity of white matter analysis in Alzheimer's disease. Scientific Reports, 11(1), 6990. https://doi.org/10.1038/s41598-021-86505-7

Bethlehem, R. A. I., Seidlitz, J., White, S. R., Vogel, J. W., Anderson, K. M., Adamson, C., Adler, S., Alexopoulos, G. S., Anagnostou, E., Areces-Gonzalez, A., Astle, D. E., Auyeung, B., Ayub, M., Bae, J., Ball, G., Baron-Cohen, S., Beare, R., Bedford, S. A., Benegal, V., … Alexander-Bloch, A. F. (2022). Brain charts for the human lifespan. Nature, 604(7906), 525-533. https://doi.org/10.1038/s41586-022-04554-y

Borchert, R. J., Azevedo, T., Badhwar, A., Bernal, J., Betts, M., Bruffaerts, R., Burkhart, M. C., Dewachter, I., Gellersen, H. M., Low, A., Lourida, I., Machado, L., Madan, C. R., Malpetti, M., Mejia, J., Michopoulou, S., Muñoz-Neira, C., Pepys, J., Peres, M., … Rittman, T. (2023). Artificial intelligence for diagnostic and prognostic neuroimaging in dementia: A systematic review. Alzheimer's & Dementia, 19(12), 5885-5904. https://doi.org/10.1002/alz.13412

Braak, H., & Braak, E. (1991). Neuropathological stageing of Alzheimer-related changes. Acta Neuropathologica, 82(4), 239-259. https://doi.org/10.1007/bf00308809

Brendel, M., Barthel, H., van Eimeren, T., Marek, K., Beyer, L., Song, M., Palleis, C., Gehmeyr, M., Fietzek, U., Respondek, G., Sauerbeck, J., Nitschmann, A., Zach, C., Hammes, J., Barbe, M. T., Onur, O., Jessen, F., Saur, D., Schroeter, M. L., … Sabri, O. (2020). Assessment of 18F-PI-2620 as a biomarker in progressive supranuclear palsy. JAMA Neurology, 77(11), 1408-1419. https://doi.org/10.1001/jamaneurol.2020.2526

Charidimou, A., Boulouis, G., Frosch, M. P., Baron, J. C., Pasi, M., Albucher, J. F., Banerjee, G., Barbato, C., Bonneville, F., Brandner, S., Calviere, L., Caparros, F., Casolla, B., Cordonnier, C., Delisle, M. B., Deramecourt, V., Dichgans, M., Gokcal, E., Herms, J., … Greenberg, S. M. (2022). The Boston criteria version 2.0 for cerebral amyloid angiopathy: a multicentre, retrospective, MRI-neuropathology diagnostic accuracy study. The Lancet Neurology, 21(8), 714-725. https://doi.org/10.1016/s1474-4422(22)00208-3

Clark, C. M., Pontecorvo, M. J., Beach, T. G., Bedell, B. J., Coleman, R. E., Doraiswamy, P. M., Fleisher, A. S., Reiman, E. M., Sabbagh, M. N., Sadowsky, C. H., Schneider, J. A., Arora, A., Carpenter, A. P., Flitter, M. L., Joshi, A. D., Krautkramer, M. J., Lu, M., Mintun, M. A., Skovronsky, D. M., & AV-45-A16 Study Group (2012). Cerebral PET with florbetapir compared with neuropathology at autopsy for detection of neuritic amyloid-β plaques: a prospective cohort study. The Lancet Neurology, 11(8), 669-678. https://doi.org/10.1016/s1474-4422(12)70142-4

Cummings, J., Apostolova, L., Rabinovici, G. D., Atri, A., Aisen, P., Greenberg, S., Hendrix, S., Selkoe, D., Weiner, M., Petersen, R. C., & Salloway, S. (2023). Lecanemab: Appropriate use recommendations. The Journal of Prevention of Alzheimer's Disease, 10(3), 362-377. https://doi.org/10.14283/jpad.2023.30

Curtis, C., Gamez, J. E., Singh, U., Sadowsky, C. H., Villena, T., Sabbagh, M. N., Beach, T. G., Duara, R., Fleisher, A. S., Frey, K. A., Walker, Z., Hunjan, A., Holmes, C., Escovar, Y. M., Vera, C. X., Agronin, M. E., Ross, J., Bozoki, A., Akinola, M., … Salloway, S. (2015). Phase 3 trial of flutemetamol labeled with radioactive fluorine 18 imaging and neuritic plaque density. JAMA Neurology, 72(3), 287-294. https://doi.org/10.1001/jamaneurol.2014.4144

Dautricourt, S., de Flores, R., Landeau, B., Poisnel, G., Vanhoutte, M., Delcroix, N., Eustache, F., Vivien, D., de la Sayette, V., & Chételat, G. (2021). Longitudinal changes in hippocampal network connectivity in Alzheimer's disease. Annals of Neurology, 90(3), 391-406. https://doi.org/10.1002/ana.26168

Dickerson, B. C., Atri, A., Clevenger, C., Karlawish, J., Knopman, D., Lin, P. J., Norman, M., Onyike, C., Sano, M., Scanland, S., & Carrillo, M. (2025). The Alzheimer's Association clinical practice guideline for the Diagnostic Evaluation, Testing, Counseling, and Disclosure of Suspected Alzheimer's Disease and Related Disorders (DETeCD-ADRD): Executive summary of recommendations for specialty care. Alzheimer's & Dementia, 21(1), e14337. https://doi.org/10.1002/alz.14337

Donaghy, P. C., Carrarini, C., Ferreira, D., Habich, A., Aarsland, D., Babiloni, C., Bayram, E., Kane, J. P., Lewis, S. J., Pilotto, A., Thomas, A. J., Bonanni, L., & Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment Lewy Body Dementias Prodromal Working Group (2023). Research diagnostic criteria for mild cognitive impairment with Lewy bodies: A systematic review and meta-analysis. Alzheimer's & Dementia, 19(7), 3186-3202. https://doi.org/10.1002/alz.13105

Dubois, B., Villain, N., Frisoni, G. B., Rabinovici, G. D., Sabbagh, M., Cappa, S., Bejanin, A., Bombois, S., Epelbaum, S., Teichmann, M., Habert, M. O., Nordberg, A., Blennow, K., Galasko, D., Stern, Y., Rowe, C. C., Salloway, S., Schneider, L. S., Cummings, J. L., & Feldman, H. H. (2021). Clinical diagnosis of Alzheimer's disease: recommendations of the International Working Group. The Lancet Neurology, 20(6), 484-496. https://doi.org/10.1016/s1474-4422(21)00066-1

Dubois, B., Villain, N., Schneider, L., Fox, N., Campbell, N., Galasko, D., Kivipelto, M., Jessen, F., Hanseeuw, B., Boada, M., Barkhof, F., Nordberg, A., Froelich, L., Waldemar, G., Frederiksen, K. S., Padovani, A., Planche, V., Rowe, C., Bejanin, A., … Frisoni, G. B. (2024). Alzheimer disease as a clinical-biological construct-an international working group recommendation. JAMA Neurology, 81(12), 1304-1311. https://doi.org/10.1001/jamaneurol.2024.3770

Duering, M., Biessels, G. J., Brodtmann, A., Chen, C., Cordonnier, C., de Leeuw, F. E., Debette, S., Frayne, R., Jouvent, E., Rost, N. S., Ter Telgte, A., Al-Shahi Salman, R., Backes, W. H., Bae, H. J., Brown, R., Chabriat, H., De Luca, A., deCarli, C., Dewenter, A., … Wardlaw, J. M. (2023). Neuroimaging standards for research into small vessel disease-advances since 2013. The Lancet Neurology, 22(7), 602-618. https://doi.org/10.1016/s1474-4422(23)00131-x

Fleisher, A. S., Pontecorvo, M. J., Devous, M. D., Lu, M., Arora, A. K., Truocchio, S. P., Aldea, P., Flitter, M., Locascio, T., Devine, M., Siderowf, A., Beach, T. G., Montine, T. J., Serrano, G. E., Curtis, C., Perrin, A., Salloway, S., Daniel, M., Wellman, C., … A16 Study Investigators (2020). Positron emission tomography imaging with [18F]flortaucipir and postmortem assessment of Alzheimer disease neuropathologic changes. JAMA Neurology, 77(7), 829-839. https://doi.org/10.1001/jamaneurol.2020.0528

Fortin, J. P., Cullen, N., Sheline, Y. I., Taylor, W. D., Aselcioglu, I., Cook, P. A., Adams, P., Cooper, C., Fava, M., McGrath, P. J., McInnis, M., Phillips, M. L., Trivedi, M. H., Weissman, M. M., & Shinohara, R. T. (2018). Harmonization of cortical thickness measurements across scanners and sites. NeuroImage, 167, 104-120. https://doi.org/10.1016/j.neuroimage.2017.11.024

Gorno-Tempini, M. L., Hillis, A. E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S. F., Ogar, J. M., Rohrer, J. D., Black, S., Boeve, B. F., Manes, F., Dronkers, N. F., Vandenberghe, R., Rascovsky, K., Patterson, K., Miller, B. L., Knopman, D. S., Hodges, J. R., Mesulam, M. M., & Grossman, M. (2011). Classification of primary progressive aphasia and its variants. Neurology, 76(11), 1006-1014. https://doi.org/10.1212/wnl.0b013e31821103e6

Groot, C., Calandri, I. L., Bader, I., Bocancea, D. I., de Bruin, H., Carrigan, M., Collij, L. E., Duits, F. H., Kamps, S., de Koning, L. A., Lemstra, A. W., Mastenbroek, S. E., Rikken, R. M., van Tol, B. G. J., Vermeiren, M. R., Wesseling, A., Xia, Y., Teunissen, C. E., van de Giessen, E., … Ossenkoppele, R. (2026). Characterizing individuals fulfilling clinical criteria for limbic-predominant age-related TDP-43 encephalopathy in a tertiary memory clinic. Neurology, 106(9), e214810. https://doi.org/10.1212/wnl.0000000000214810

Guedj, E., Varrone, A., Boellaard, R., Albert, N. L., Barthel, H., van Berckel, B., Brendel, M., Cecchin, D., Ekmekcioglu, O., Garibotto, V., Lammertsma, A. A., Law, I., Peñuelas, I., Semah, F., Traub-Weidinger, T., van de Giessen, E., Van Weehaeghe, D., & Morbelli, S. (2022). EANM procedure guidelines for brain PET imaging using [18F]FDG, version 3. European Journal of Nuclear Medicine and Molecular Imaging, 49(2), 632-651. https://doi.org/10.1007/s00259-021-05603-w

Hamelin, L., Lagarde, J., Dorothée, G., Potier, M. C., Corlier, F., Kuhnast, B., Caillé, F., Dubois, B., Fillon, L., Chupin, M., Bottlaender, M., & Sarazin, M. (2018). Distinct dynamic profiles of microglial activation are associated with progression of Alzheimer's disease. Brain, 141(6), 1855-1870. https://doi.org/10.1093/brain/awy079

Jack, C. R., Andrews, J. S., Beach, T. G., Buracchio, T., Dunn, B., Graf, A., Hansson, O., Ho, C., Jagust, W., McDade, E., Molinuevo, J. L., Okonkwo, O. C., Pani, L., Rafii, M. S., Scheltens, P., Siemers, E., Snyder, H. M., Sperling, R., Teunissen, C. E., & Carrillo, M. C. (2024). Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimer's & Dementia, 20(8), 5143-5169. https://doi.org/10.1002/alz.13859

Jack, C. R., Bennett, D. A., Blennow, K., Carrillo, M. C., Dunn, B., Haeberlein, S. B., Holtzman, D. M., Jagust, W., Jessen, F., Karlawish, J., Liu, E., Molinuevo, J. L., Montine, T., Phelps, C., Rankin, K. P., Rowe, C. C., Scheltens, P., Siemers, E., Snyder, H. M., … Contributors (2018). NIA-AA research framework: Toward a biological definition of Alzheimer's disease. Alzheimer's & Dementia, 14(4), 535-562. https://doi.org/10.1016/j.jalz.2018.02.018

Klunk, W. E., Engler, H., Nordberg, A., Wang, Y., Blomqvist, G., Holt, D. P., Bergström, M., Savitcheva, I., Huang, G. F., Estrada, S., Ausén, B., Debnath, M. L., Barletta, J., Price, J. C., Sandell, J., Lopresti, B. J., Wall, A., Koivisto, P., Antoni, G., … Långström, B. (2004). Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. Annals of Neurology, 55(3), 306-319. https://doi.org/10.1002/ana.20009

Klunk, W. E., Koeppe, R. A., Price, J. C., Benzinger, T. L., Devous, M. D., Jagust, W. J., Johnson, K. A., Mathis, C. A., Minhas, D., Pontecorvo, M. J., Rowe, C. C., Skovronsky, D. M., & Mintun, M. A. (2015). The Centiloid Project: standardizing quantitative amyloid plaque estimation by PET. Alzheimer's & Dementia, 11(1), 1-15.e1-4. https://doi.org/10.1016/j.jalz.2014.07.003

Leuzy, A., Smith, R., Ossenkoppele, R., Santillo, A., Borroni, E., Klein, G., Ohlsson, T., Jögi, J., Palmqvist, S., Mattsson-Carlgren, N., Strandberg, O., Stomrud, E., & Hansson, O. (2020). Diagnostic performance of RO948 F 18 tau positron emission tomography in the differentiation of Alzheimer disease from other neurodegenerative disorders. JAMA Neurology, 77(8), 955-965. https://doi.org/10.1001/jamaneurol.2020.0989

McKeith, I. G., Boeve, B. F., Dickson, D. W., Halliday, G., Taylor, J. P., Weintraub, D., Aarsland, D., Galvin, J., Attems, J., Ballard, C. G., Bayston, A., Beach, T. G., Blanc, F., Bohnen, N., Bonanni, L., Bras, J., Brundin, P., Burn, D., Chen-Plotkin, A., … Kosaka, K. (2017). Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology, 89(1), 88-100. https://doi.org/10.1212/wnl.0000000000004058

McKeith, I. G., Ferman, T. J., Thomas, A. J., Blanc, F., Boeve, B. F., Fujishiro, H., Kantarci, K., Muscio, C., O'Brien, J. T., Postuma, R. B., Aarsland, D., Ballard, C., Bonanni, L., Donaghy, P., Emre, M., Galvin, J. E., Galasko, D., Goldman, J. G., Gomperts, S. N., … prodromal DLB Diagnostic Study Group (2020). Research criteria for the diagnosis of prodromal dementia with Lewy bodies. Neurology, 94(17), 743-755. https://doi.org/10.1212/wnl.0000000000009323

Mecca, A. P., Ashton, N. J., Chen, M. K., O'Dell, R. S., Toyonaga, T., Zhao, W., Young, J. J., Salardini, E., Bates, K. A., Ra, J., Goodcase, S., Silva-Rudberg, J. A., Nabulsi, N. B., Brinkmalm, A., Kvartsberg, H., Schöll, M., Nilsson, J., Arnsten, A. F. T., Huang, Y., … van Dyck, C. H. (2025). Cerebrospinal fluid and brain positron emission tomography measures of synaptic vesicle glycoprotein 2A: Biomarkers of synaptic density in Alzheimer's disease. Alzheimer's & Dementia, 21(6), e70344. https://doi.org/10.1002/alz.70344

Mecca, A. P., Chen, M. K., O'Dell, R. S., Naganawa, M., Toyonaga, T., Godek, T. A., Harris, J. E., Bartlett, H. H., Zhao, W., Nabulsi, N. B., Wyk, B. C. V., Varma, P., Arnsten, A. F. T., Huang, Y., Carson, R. E., & van Dyck, C. H. (2020). In vivo measurement of widespread synaptic loss in Alzheimer's disease with SV2A PET. Alzheimer's & Dementia, 16(7), 974-982. https://doi.org/10.1002/alz.12097

Montagne, A., Nation, D. A., Sagare, A. P., Barisano, G., Sweeney, M. D., Chakhoyan, A., Pachicano, M., Joe, E., Nelson, A. R., D'Orazio, L. M., Buennagel, D. P., Harrington, M. G., Benzinger, T. L. S., Fagan, A. M., Ringman, J. M., Schneider, L. S., Morris, J. C., Reiman, E. M., Caselli, R. J., … Zlokovic, B. V. (2020). APOE4 leads to blood-brain barrier dysfunction predicting cognitive decline. Nature, 581(7806), 71-76. https://doi.org/10.1038/s41586-020-2247-3

Morbelli, S., Esposito, G., Arbizu, J., Barthel, H., Boellaard, R., Bohnen, N. I., Brooks, D. J., Darcourt, J., Dickson, J. C., Douglas, D., Drzezga, A., Dubroff, J., Ekmekcioglu, O., Garibotto, V., Herscovitch, P., Kuo, P., Lammertsma, A., Pappata, S., Peñuelas, I., … Law, I. (2020). EANM practice guideline/SNMMI procedure standard for dopaminergic imaging in Parkinsonian syndromes 1.0. European Journal of Nuclear Medicine and Molecular Imaging, 47(8), 1885-1912. https://doi.org/10.1007/s00259-020-04817-8

Nakajima, M., Yamada, S., Miyajima, M., Ishii, K., Kuriyama, N., Kazui, H., Kanemoto, H., Suehiro, T., Yoshiyama, K., Kameda, M., Kajimoto, Y., Mase, M., Murai, H., Kita, D., Kimura, T., Samejima, N., Tokuda, T., Kaijima, M., Akiba, C., … research committee of idiopathic normal pressure hydrocephalus (2021). Guidelines for management of idiopathic normal pressure hydrocephalus (third edition): Endorsed by the Japanese Society of Normal Pressure Hydrocephalus. Neurologia Medico-Chirurgica, 61(2), 63-97. https://doi.org/10.2176/nmc.st.2020-0292

Navitsky, M., Joshi, A. D., Kennedy, I., Klunk, W. E., Rowe, C. C., Wong, D. F., Pontecorvo, M. J., Mintun, M. A., & Devous, M. D. (2018). Standardization of amyloid quantitation with florbetapir standardized uptake value ratios to the Centiloid scale. Alzheimer's & Dementia, 14(12), 1565-1571. https://doi.org/10.1016/j.jalz.2018.06.1353

Nelson, P. T., Dickson, D. W., Trojanowski, J. Q., Jack, C. R., Boyle, P. A., Arfanakis, K., Rademakers, R., Alafuzoff, I., Attems, J., Brayne, C., Coyle-Gilchrist, I. T. S., Chui, H. C., Fardo, D. W., Flanagan, M. E., Halliday, G., Hokkanen, S. R. K., Hunter, S., Jicha, G. A., Katsumata, Y., … Schneider, J. A. (2019). Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report. Brain, 142(6), 1503-1527. https://doi.org/10.1093/brain/awz099

Ossenkoppele, R., Pichet Binette, A., Groot, C., Smith, R., Strandberg, O., Palmqvist, S., Stomrud, E., Tideman, P., Ohlsson, T., Jögi, J., Johnson, K., Sperling, R., Dore, V., Masters, C. L., Rowe, C., Visser, D., van Berckel, B. N. M., van der Flier, W. M., Baker, S., … Hansson, O. (2022). Amyloid and tau PET-positive cognitively unimpaired individuals are at high risk for future cognitive decline. Nature Medicine, 28(11), 2381-2387. https://doi.org/10.1038/s41591-022-02049-x

Ossenkoppele, R., Smith, R., Mattsson-Carlgren, N., Groot, C., Leuzy, A., Strandberg, O., Palmqvist, S., Olsson, T., Jögi, J., Stormrud, E., Cho, H., Ryu, Y. H., Choi, J. Y., Boxer, A. L., Gorno-Tempini, M. L., Miller, B. L., Soleimani-Meigooni, D., Iaccarino, L., La Joie, R., … Hansson, O. (2021). Accuracy of tau positron emission tomography as a prognostic marker in preclinical and prodromal Alzheimer disease: A head-to-head comparison against amyloid positron emission tomography and magnetic resonance imaging. JAMA Neurology, 78(8), 961-971. https://doi.org/10.1001/jamaneurol.2021.1858

Palmqvist, S., Tideman, P., Mattsson-Carlgren, N., Schindler, S. E., Smith, R., Ossenkoppele, R., Calling, S., West, T., Monane, M., Verghese, P. B., Braunstein, J. B., Blennow, K., Janelidze, S., Stomrud, E., Salvadó, G., & Hansson, O. (2024). Blood biomarkers to detect Alzheimer disease in primary care and secondary care. JAMA, 332(15), 1245-1257. https://doi.org/10.1001/jama.2024.13855

Pascoal, T. A., Benedet, A. L., Ashton, N. J., Kang, M. S., Therriault, J., Chamoun, M., Savard, M., Lussier, F. Z., Tissot, C., Karikari, T. K., Ottoy, J., Mathotaarachchi, S., Stevenson, J., Massarweh, G., Schöll, M., de Leon, M. J., Soucy, J. P., Edison, P., Blennow, K., … Rosa-Neto, P. (2021). Microglial activation and tau propagate jointly across Braak stages. Nature Medicine, 27(9), 1592-1599. https://doi.org/10.1038/s41591-021-01456-w

Pascoal, T. A., Shin, M., Kang, M. S., Chamoun, M., Chartrand, D., Mathotaarachchi, S., Bennacef, I., Therriault, J., Ng, K. P., Hopewell, R., Bouhachi, R., Hsiao, H. H., Benedet, A. L., Soucy, J. P., Massarweh, G., Gauthier, S., & Rosa-Neto, P. (2018). In vivo quantification of neurofibrillary tangles with [18F]MK-6240. Alzheimer's Research & Therapy, 10(1), 74. https://doi.org/10.1186/s13195-018-0402-y

Rabinovici, G. D., Gatsonis, C., Apgar, C., Chaudhary, K., Gareen, I., Hanna, L., Hendrix, J., Hillner, B. E., Olson, C., Lesman-Segev, O. H., Romanoff, J., Siegel, B. A., Whitmer, R. A., & Carrillo, M. C. (2019). Association of amyloid positron emission tomography with subsequent change in clinical management among Medicare beneficiaries with mild cognitive impairment or dementia. JAMA, 321(13), 1286-1294. https://doi.org/10.1001/jama.2019.2000

Rabinovici, G. D., Knopman, D. S., Arbizu, J., Benzinger, T. L. S., Donohoe, K. J., Hansson, O., Herscovitch, P., Kuo, P. H., Lingler, J. H., Minoshima, S., Murray, M. E., Price, J. C., Salloway, S. P., Weber, C. J., Carrillo, M. C., & Johnson, K. A. (2025). Updated appropriate use criteria for amyloid and tau PET: A report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. Alzheimer's & Dementia, 21(1), e14338. https://doi.org/10.1002/alz.14338

Rabinovici, G. D., Selkoe, D. J., Schindler, S. E., Aisen, P., Apostolova, L. G., Atri, A., Greenberg, S. M., Hendrix, S. B., Petersen, R. C., Weiner, M., Salloway, S., & Cummings, J. (2025). Donanemab: Appropriate use recommendations. The Journal of Prevention of Alzheimer's Disease, 12(5), 100150. https://doi.org/10.1016/j.tjpad.2025.100150

Rascovsky, K., Hodges, J. R., Knopman, D., Mendez, M. F., Kramer, J. H., Neuhaus, J., van Swieten, J. C., Seelaar, H., Dopper, E. G., Onyike, C. U., Hillis, A. E., Josephs, K. A., Boeve, B. F., Kertesz, A., Seeley, W. W., Rankin, K. P., Johnson, J. K., Gorno-Tempini, M. L., Rosen, H., … Miller, B. L. (2011). Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain, 134(Pt 9), 2456-2477. https://doi.org/10.1093/brain/awr179

Sabri, O., Sabbagh, M. N., Seibyl, J., Barthel, H., Akatsu, H., Ouchi, Y., Senda, K., Murayama, S., Ishii, K., Takao, M., Beach, T. G., Rowe, C. C., Leverenz, J. B., Ghetti, B., Ironside, J. W., Catafau, A. M., Stephens, A. W., Mueller, A., Koglin, N., … Florbetaben Phase 3 Study Group (2015). Florbetaben PET imaging to detect amyloid beta plaques in Alzheimer's disease: phase 3 study. Alzheimer's & Dementia, 11(8), 964-974. https://doi.org/10.1016/j.jalz.2015.02.004

Sachdev, P., Kalaria, R., O'Brien, J., Skoog, I., Alladi, S., Black, S. E., Blacker, D., Blazer, D. G., Chen, C., Chui, H., Ganguli, M., Jellinger, K., Jeste, D. V., Pasquier, F., Paulsen, J., Prins, N., Rockwood, K., Roman, G., Scheltens, P., & Internationlal Society for Vascular Behavioral and Cognitive Disorders (2014). Diagnostic criteria for vascular cognitive disorders: a VASCOG statement. Alzheimer Disease & Associated Disorders, 28(3), 206-218. https://doi.org/10.1097/wad.0000000000000034

Salloway, S., Chalkias, S., Barkhof, F., Burkett, P., Barakos, J., Purcell, D., Suhy, J., Forrestal, F., Tian, Y., Umans, K., Wang, G., Singhal, P., Budd Haeberlein, S., & Smirnakis, K. (2022). Amyloid-related imaging abnormalities in 2 phase 3 studies evaluating aducanumab in patients with early Alzheimer disease. JAMA Neurology, 79(1), 13-21. https://doi.org/10.1001/jamaneurol.2021.4161

Shirbandi, K., Rikhtegar, R., Khalafi, M., Mirza Aghazadeh Attari, M., Rahmani, F., Javanmardi, P., Iraji, S., Babaei Aghdam, Z., & Rezaei Rashnoudi, A. M. (2023). Functional magnetic resonance spectroscopy of lactate in Alzheimer disease: A comprehensive review of Alzheimer disease pathology and the role of lactate. Topics in Magnetic Resonance Imaging, 32(2), 15-26. https://doi.org/10.1097/rmr.0000000000000303

Sims, J. R., Zimmer, J. A., Evans, C. D., Lu, M., Ardayfio, P., Sparks, J., Wessels, A. M., Shcherbinin, S., Wang, H., Monkul Nery, E. S., Collins, E. C., Solomon, P., Salloway, S., Apostolova, L. G., Hansson, O., Ritchie, C., Brooks, D. A., Mintun, M., Skovronsky, D. M., & TRAILBLAZER-ALZ 2 Investigators (2023). Donanemab in early symptomatic Alzheimer disease: The TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA, 330(6), 512-527. https://doi.org/10.1001/jama.2023.13239

Soleimani-Meigooni, D. N., Iaccarino, L., La Joie, R., Baker, S., Bourakova, V., Boxer, A. L., Edwards, L., Eser, R., Gorno-Tempini, M. L., Jagust, W. J., Janabi, M., Kramer, J. H., Lesman-Segev, O. H., Mellinger, T., Miller, B. L., Pham, J., Rosen, H. J., Spina, S., Seeley, W. W., … Rabinovici, G. D. (2020). 18F-flortaucipir PET to autopsy comparisons in Alzheimer's disease and other neurodegenerative diseases. Brain, 143(11), 3477-3494. https://doi.org/10.1093/brain/awaa276

Tagai, K., Ono, M., Kubota, M., Kitamura, S., Takahata, K., Seki, C., Takado, Y., Shinotoh, H., Sano, Y., Yamamoto, Y., Matsuoka, K., Takuwa, H., Shimojo, M., Takahashi, M., Kawamura, K., Kikuchi, T., Okada, M., Akiyama, H., Suzuki, H., … Shimada, H. (2021). High-contrast in vivo imaging of tau pathologies in Alzheimer's and non-Alzheimer's disease tauopathies. Neuron, 109(1), 42-58.e8. https://doi.org/10.1016/j.neuron.2020.09.042

van Dyck, C. H., Swanson, C. J., Aisen, P., Bateman, R. J., Chen, C., Gee, M., Kanekiyo, M., Li, D., Reyderman, L., Cohen, S., Froelich, L., Katayama, S., Sabbagh, M., Vellas, B., Watson, D., Dhadda, S., Irizarry, M., Kramer, L. D., & Iwatsubo, T. (2023). Lecanemab in early Alzheimer's disease. The New England Journal of Medicine, 388(1), 9-21. https://doi.org/10.1056/nejmoa2212948

Wolk, D. A., Nelson, P. T., Apostolova, L., Arfanakis, K., Boyle, P. A., Carlsson, C. M., Corriveau-Lecavalier, N., Dacks, P., Dickerson, B. C., Domoto-Reilly, K., Dugger, B. N., Edelmayer, R., Fardo, D. W., Grothe, M. J., Hohman, T. J., Irwin, D. J., Jicha, G. A., Jones, D. T., Kawas, C. H., … Schneider, J. A. (2025). Clinical criteria for limbic-predominant age-related TDP-43 encephalopathy. Alzheimer's & Dementia, 21(1), e14202. https://doi.org/10.1002/alz.14202

Zhang, M., Hu, J., Zhang, Y., Meng, Z., Zhao, Y., Li, Y., Jin, W., Qian, X. H., Wang, L., Ye, G., Jiang, X. F., Li, Y. D., Ye, J., Tang, H., Liu, J., Nachev, P., Liang, Z. P., Li, B., & Li, Y. (2025). Associations between Aβ deposition and neurometabolic alterations in Alzheimer's disease: Insights from hybrid 3D MRSI-PET imaging. Alzheimer's & Dementia, 21(6), e70332. https://doi.org/10.1002/alz.70332

Zhong, S., Lou, J., Ma, K., Shu, Z., Chen, L., Li, C., Ye, Q., Zhou, L., Shen, Y., Ye, X., & Zhang, J. (2023). Disentangling in-vivo microstructural changes of white and gray matter in mild cognitive impairment and Alzheimer's disease: a systematic review and meta-analysis. Brain Imaging and Behavior, 17(6), 764-777. https://doi.org/10.1007/s11682-023-00805-2

Restless Legs Syndrome: A Comprehensive Review for Primary Care Physicians

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Abstract

Restless Legs Syndrome (RLS), also known as Willis-Ekbom disease, is a common chronic neurological sensorimotor disorder characterized by an overwhelming urge to move the legs, usually accompanied by unpleasant sensory symptoms. The disorder affects sleep quality, daytime functioning, mental health, and overall quality of life. RLS is frequently encountered in primary care yet remains significantly underdiagnosed and undertreated. Primary care physicians play an important role in the detection, evaluation, and management of RLS. This review provides an evidence-based overview of epidemiology, pathophysiology, diagnosis, differential diagnosis, and current management strategies relevant to primary care.

Keywords: Restless Legs Syndrome; Willis-Ekbom Disease; Primary Care; Iron Deficiency; Alpha-2-Delta Ligands; Dopamine Agonists; Augmentation

Introduction

Restless Legs Syndrome (RLS) is a neurological disorder characterized by an irresistible urge to move the limbs, predominantly the legs, associated with unpleasant sensations that worsen during periods of rest and improve with movement. Symptoms typically become more prominent during the evening and night-time hours (1).

RLS is fundamentally a sensorimotor neurological condition. The disorder may present as either primary (idiopathic) or secondary to various medical conditions including iron deficiency, pregnancy, chronic kidney disease (CKD) and peripheral neuropathy (2).

RLS can cause major sleep disruption. These patients also commonly experience fatigue, impaired concentration, mood disturbances, reduced productivity, and cardiovascular consequences related to chronic sleep deprivation (3,4). Recognition of RLS in primary care is therefore essential for improving patient outcomes and reducing disease burden.

Epidemiology

RLS is among the most common neurological disorders encountered in outpatient practice. Population studies estimate that the overall prevalence is 5–10% of adults (3,5).

RLS occurs in both sexes but is approximately twice as common in women. The prevalence increases progressively with age, although symptoms may begin during childhood or adolescence (5).

Risk Factors

Several factors are associated with increased risk (Table 1).

Table 1: Risk factors for RLS

Modifiable risk factors	Non-modifiable risk factors
Iron deficiency / low ferritin levels	Increasing age
Excessive caffeine intake	Female sex
Alcohol consumption	Family history of RLS
Smoking / tobacco use	Genetic predisposition
Sleep deprivation or poor sleep hygiene	Inherited (primary) RLS
Obesity	Pregnancy (especially third trimester)
Physical inactivity	Certain underlying neurological predispositions
Certain medications (e.g., antidepressants, antihistamines, antipsychotics, dopamine antagonists)	
Poorly controlled diabetes mellitus	
Peripheral neuropathy due to treatable causes	
CKD (especially if poorly managed)	
Vitamin and mineral deficiencies (iron, folate, etc.)	

Pathophysiology

The pathogenesis of RLS is multifactorial and incompletely understood. Current evidence implicates a combination of iron dysregulation, dopaminergic dysfunction, and genetic susceptibility (6).

Brain Iron Deficiency
Iron plays a crucial role in dopamine synthesis and dopamine receptor function. Studies demonstrate reduced iron concentrations within the substantia nigra and other brain regions involved in motor control (7). Importantly, patients may have normal serum haemoglobin levels while exhibiting reduced brain iron stores (8).

Dopaminergic Dysfunction
The effectiveness of dopamine agonists and alterations in dopamine metabolism support a central role for dopaminergic dysfunction. Abnormalities involve reduced dopamine receptor activity, altered circadian dopamine regulation, and dysfunctional nigrostriatal pathways. Symptoms typically worsen in the evening, coinciding with physiological reductions in dopaminergic activity.

Genetic Factors
Approximately 40–60% of patients with early-onset disease report a family history of RLS. Familial RLS usually presents earlier and tends to follow a more chronic course.

Clinical Features

Patients commonly describe:
- An irresistible urge to move the legs
- Restlessness
- Crawling sensations
- Tingling
- Pulling sensations
- Burning discomfort
- Itching deep within the legs
- Electric shock-like sensations

The sensations are difficult for patients to describe and are often referred to as occurring “inside the legs.” Symptoms demonstrate four characteristic features.

1 Occurrence during Rest
Symptoms appear or worsen during:
- Sitting
- Lying down
- Long-distance travel
- Sedentary activities

2 Relief with Movement
Patients experience temporary improvement through:
- Walking
- Stretching
- Leg movements
- Pacing
- Massaging affected limbs

3 Circadian Pattern
Symptoms are:
- Minimal during the morning
- Progressive throughout the day
- Maximal during the evening and night-time

4 Recurrent Nature
Symptoms occur repeatedly and may become chronic.

Diagnostic Criteria

The International Restless Legs Syndrome Study Group (IRLSSG) defines five essential diagnostic criteria (1) (Table 2).

Table 2: IRLSSG essential diagnostic criteria for RLS (1)

Criterion	Description
1	An urge to move the legs, usually accompanied by uncomfortable sensations
2	Symptoms begin or worsen during periods of rest or inactivity
3	Symptoms are partially or completely relieved by movement
3	Symptoms are worse in the evening or at night than during the day
5	Symptoms cannot be explained solely by another medical or behavioural condition

Clinical Evaluation in Primary Care

A detailed history remains the cornerstone of diagnosis (9).

Medication Review
Numerous medications can worsen RLS symptoms (10).

Common offenders include:
- **Antidepressants:** fluoxetine, sertraline, escitalopram, venlafaxine
- **Antihistamines:** diphenhydramine, chlorpheniramine
- **Dopamine antagonists:** metoclopramide, prochlorperazine
- **Antipsychotic medications:** risperidone, olanzapine, haloperidol

Physical Examination
Physical examination is usually normal in primary RLS. The primary purpose of examination is to identify secondary causes.

Investigations
Although RLS is a clinical diagnosis, laboratory testing helps identify secondary causes.

Iron studies:
- Serum ferritin
- Transferrin saturation
- Serum iron
- Total iron-binding capacity

Current guidelines recommend evaluation of iron status in all patients (11–13).

Additional laboratory tests:
• Complete blood count
• Renal function tests
• Liver function tests
• Thyroid-stimulating hormone
• Fasting blood glucose or HbA1c
• Vitamin B12
• Folate
• Magnesium (selected patients)

Causes of Secondary RLS

Iron Deficiency
The most common reversible cause (13).

Pregnancy
Occurs in approximately 10–30% of pregnancies (14,15).
Characteristics:
- Most common during the third trimester
- Associated with reduced iron stores
- Usually resolves postpartum

Chronic Kidney Disease
RLS affects up to one-third of dialysis patients (2).

Neurological Diseases
- Peripheral neuropathy
- Parkinson disease
- Multiple sclerosis
- Spinal cord disorders

Differential diagnosis

- Nocturnal leg cramps
- Akathisia
- Peripheral neuropathy
- Peripheral vascular disease
- Positional leg discomfort

Management

Treatment Goals
Management aims to:
- Reduce symptom severity
- Improve sleep quality
- Enhance daytime functioning
- Improve health-related quality of life
- Prevent treatment-related complications

Non-Pharmacological Management
Recommended for all patients. Lifestyle modification includes:
• **Sleep hygiene:** fixed bedtime routines, a regular sleep schedule, minimal screen time before bed, and a quiet sleep environment.
• **Exercise:** moderate regular exercise improves symptoms. Patients should avoid excessive strenuous exercise and late-night vigorous workouts.
• **Avoiding triggering substances**: reduction or avoidance of caffeine, nicotine, and alcohol.
• **Symptomatic relief measures:** walking, stretching, leg massage, warm baths, heating pads, and cold compresses.

Iron Therapy
Oral iron: Recommended when ferritin is below normal or in the low-normal range (11,13). Typical regimen:

- Ferrous sulfate providing 65 mg elemental iron
- Combined with vitamin C to enhance absorption

Intravenous iron: Considered when:
- Oral therapy fails
- Severe symptoms exist
- Iron absorption is impaired
- Rapid symptom improvement is desired

Intravenous iron has demonstrated significant benefit in appropriately selected patients (13,16).

Pharmacological Therapy
Recent treatment guidelines increasingly favour alpha-2-delta calcium channel ligands as first-line agents (11,12,17,18) (Table 3).

Table 3: Pharmacological treatment options for RLS

Drug class	Medications
Alpha-2-delta ligands (first-line)	Gabapentin, gabapentin enacarbil, pregabalin
Dopamine agonists	Pramipexole, ropinirole, rotigotine patch
Opioids (refractory RLS)	Oxycodone/naloxone, methadone, buprenorphine, tramadol
Benzodiazepines (adjunctive)	Clonazepam, temazepam

Augmentation
Augmentation is the most important long-term complication of dopaminergic therapy (12,19). Symptoms:
- Appear earlier in the day
- Become more severe
- Spread to the arms or trunk
- Respond less effectively to treatment

Recognition is critical because increasing the dopamine agonist dose often worsens the condition.

Refractory RLS
Refractory disease is defined as persistent symptoms despite adequate treatment. Management strategies include:

- Reassessing iron stores
- Correcting aggravating factors
- Switching medication classes
- Combination therapy
- Specialist referral

Selected severe cases may require low-dose opioid therapy administered under expert supervision (11,20).

Special populations

Pregnancy
Preferred interventions:

- Reassurance
- Iron replacement when indicated
- Sleep hygiene
- Physical activity

Pharmacological therapy is generally reserved for severe cases after specialist consultation (15).

Older Adults
Treatment considerations:

- Start with lower doses
- Monitor cognitive effects
- Minimize fall risk
- Review polypharmacy

Prognosis

The clinical course depends on the underlying aetiology.

Primary RLS

- Usually chronic
- Slowly progressive
- Characterized by periods of remission and relapse

Secondary RLS
May improve substantially when the underlying disorder is treated, particularly in cases related to:

- Iron deficiency
- Pregnancy
- Medication-induced symptoms

Conclusion

Restless Legs Syndrome is a common yet frequently under-recognized neurological disorder that significantly impacts sleep, quality of life, and daytime functioning. Diagnosis is clinical and based on the characteristic features of an urge to move the legs, worsening during rest, improvement with movement, and evening predominance. Primary care physicians should evaluate all patients for secondary causes, particularly iron deficiency, CKD, pregnancy, and medication-induced symptoms. Contemporary management emphasizes lifestyle measures, correction of iron deficiency, and pharmacologic treatment with α2δ calcium channel ligands or dopamine agonists when appropriate. Early identification and evidence-based treatment can lead to substantial improvements in patient outcomes and quality of life.

References

1. Allen RP, Picchietti DL, Garcia-Borreguero D, et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria – history, rationale, description, and significance. Sleep Med. 2014;15(8):860-873.
2. Trenkwalder C, Allen R, Högl B, et al. Restless legs syndrome associated with major diseases: a systematic review and new concept. Neurology. 2016;86(14):1336-1343.
3. Allen RP, Walters AS, Montplaisir J, et al. Restless legs syndrome prevalence and impact: REST general population study. Arch Intern Med. 2005;165(11):1286-1292.
4. Winkelman JW, Shahar E, Sharief I, et al. Association of restless legs syndrome and cardiovascular disease in the Sleep Heart Health Study. Neurology. 2008;70(1):35-42.
5. Ohayon MM, O'Hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. Sleep Med Rev. 2012;16(4):283-295.
6. Winkelmann J, Schormair B, Lichtner P, et al. Genome-wide association study of restless legs syndrome identifies common variants in three genomic regions. Nat Genet. 2007;39(8):1000-1006.
7. Connor JR, Boyer PJ, Menzies SL, et al. Neuropathological examination suggests impaired brain iron acquisition in restless legs syndrome. Neurology. 2003;61(3):304-309.
8. Earley CJ, Connor JR, Beard JL, et al. Abnormalities in CSF concentrations of ferritin and transferrin in restless legs syndrome. Neurology. 2000;54(8):1698-1700.
9. Hening WA, Allen RP, Washburn M, et al. The four diagnostic criteria for restless legs syndrome are unable to exclude confounding conditions ("mimics"). Sleep Med. 2009;10(9):976-981.
10. Kolla BP, Mansukhani MP, Bostwick JM. The influence of antidepressants on restless legs syndrome and periodic limb movements: a systematic review. Sleep Med Rev. 2018;38:131-140.
11. Silber MH, Buchfuhrer MJ, Earley CJ, et al. The management of restless legs syndrome: an updated algorithm. Mayo Clin Proc. 2021;96(7):1921-1937.
12. Garcia-Borreguero D, Silber MH, Winkelman JW, et al. Guidelines for the first-line treatment of restless legs syndrome/Willis-Ekbom disease, prevention and treatment of dopaminergic augmentation: a combined task force of the IRLSSG, EURLSSF, and the RLS-Foundation. Sleep Med. 2016;21:1-11.
13. Allen RP, Picchietti DL, Auerbach M, et al. Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: an IRLSSG task force report. Sleep Med. 2018;41:27-44.
14. Manconi M, Govoni V, De Vito A, et al. Restless legs syndrome and pregnancy. Neurology. 2004;63(6):1065-1069.
15. Picchietti DL, Hensley JG, Bainbridge JL, et al. Consensus clinical practice guidelines for the diagnosis and treatment of restless legs syndrome/Willis-Ekbom disease during pregnancy and lactation. Sleep Med Rev. 2015;22:64-77.
16. Winkelman JW, Armstrong MJ, Allen RP, et al. Practice guideline summary: treatment of restless legs syndrome in adults: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2016;87(24):2585-2593.
17. Winkelman JW, Berkowski JA, DelRosso LM, et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2025;21(1):137-152.
18. Allen RP, Chen C, Garcia-Borreguero D, et al. Comparison of pregabalin with pramipexole for restless legs syndrome. N Engl J Med. 2014;370(7):621-631.
19. Garcia-Borreguero D, Allen RP, Kohnen R, et al. Diagnostic standards for dopaminergic augmentation of restless legs syndrome: report from a World Association of Sleep Medicine-International Restless Legs Syndrome Study Group consensus conference at the Max Planck Institute. Sleep Med. 2007;8(5):520-530.
20. Trenkwalder C, Beneš H, Grote L, et al. Prolonged release oxycodone-naloxone for treatment of severe restless legs syndrome after failure of previous treatment: a double-blind, randomised, placebo-controlled trial with an open-label extension. Lancet Neurol. 2013;12(12):1141-1150.

A personal lived experience. The Quiet Struggle to Breathe again: A Personal Narrative of Persistent Nasal Symptoms Following E-Bike Collision, Septal Fracture and Nasal Surgery

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Abstract

Background: Nasal trauma may result in persistent structural and functional symptoms that can substantially affect breathing, sleep, and quality of life.

However, the lived experience of prolonged nasal obstruction and uncertainty following trauma and subsequent surgery is less frequently described or observed.

Objective: This personal narrative explores the long-term experience of persistent nasal symptoms following an unexpected e-bike collision, septal fracture, delayed surgical management, and subsequent nasal surgery.

Case narrative: In December 2021, the author sustained multiple injuries after being struck from behind by an e-bike while walking on a public footpath; including nasal trauma and septal fracture. Despite having no previous history of significant nasal problems, persistent and alternating nasal obstruction, turbinate swelling, rhinorrhoea, postnasal mucus, crusting, bleeding, sneezing, and sleep disturbance subsequently developed. Following a prolonged wait, septal surgery and inferior turbinate procedures were undertaken, followed by further intervention, without meaningful improvement in symptoms. The absence of clear explanations prompted the author to independently explore nasal anatomy, turbinate physiology, autonomic regulation, and neurogenic mechanisms. Multiple treatments, including intranasal corticosteroids, antihistamines, ipratropium, capsaicin, and non-pharmacological approaches, provided little or no benefit.

Conclusion: This narrative illustrates the substantial physical and emotional burden of persistent breathing difficulty following nasal trauma and surgery. Altered autonomic regulation, neurogenic mechanisms, structural changes, and mucosal dysfunction may contribute; however, the precise mechanism in this individual case remains uncertain. The narrative highlights the importance of communication, explanation, and recognising the lived burden of persistent nasal symptoms.

Keywords:
Nasal trauma; Septal fracture; Persistent nasal obstruction; Inferior turbinate; Septoplasty; Nonallergic rhinitis; Vasomotor rhinitis; Autonomic nervous system; Neurogenic inflammation; Nasal mucosa; Lived experience; Personal narrative; Quality of life.

Introduction

Breathing through the nose is usually an unconscious act. It occurs continuously, without the need to think about airflow, mucosal swelling, secretions, or the changing resistance within each nasal passage. I had never paid attention to my nose or examined my nostrils before December 2021.

The nasal mucosa filters and cleans inhaled air and humidifies, warms, or cools the gas to body temperature. Normal functions of the epithelium, glands, and deep venous sinusoids facilitate this cleansing. This process is highly complex and depends on local mucosal feedback systems, sensory, and autonomic reflexes. Nasal nerves play a central role in regulating nasal patency and secretion production. Stimulation of sensory nerves triggers parasympathetic reflexes, which mediate glandular secretions and obstruct nasal patency, whereas sympathetic influence causes mucosal contraction and thus widens nasal passages; a disorder of which would lead to symptoms of rhinitis. Any insult or trauma conveys messages to the central nervous system via neurons by causing local vascular inflammatory reactions, the release of inflammatory substances, and an increase in blood flow. Each released peptide has its unique functionality, and its binding sites have been mapped in human nasal mucosa.

The actions of the sympathetic and parasympathetic nervous systems are probably integrated at the brainstem level. The coordinated actions of the autonomic systems probably produce the nasal cycle.

Case story

The cost of a split second of recklessness by others: the collision that changed breathing

On 18 December 2021, my life changed within seconds. I was walking forward on a public footpath in Liverpool (UK) when I was unexpectedly struck from behind by an e-bike rider travelling at speed. The force of the collision threw me to the ground. I struck my face, hands, and knees. The rider left the scene.

I experienced immediate nasal bleeding and sustained several injuries, including nasal trauma, a fractured septum, a fractured left little finger, a right knee microfracture, facial swelling and bruising, and grade II whiplash in addition to exacerbation of pre-existing neck problems. I will focus in this paper on the nose section and the aftermath. Woefully, the ENT did nothing immediately, such as closed manipulation within the first two weeks, and the long wait of the NHS added to the hassle and bustle of troubles incurred thereafter. Also, no one explained to me what was going on and what to expect, which left me in limbo and in great despair. I struggled with my breathing, which kept getting worse and is still affecting the quality of my life and my sleep to date.

One of the ENT specialists whom I saw at the very first visit told me I needed nasal septum surgery after three months, which never happened. When I inquired further, he dismissed me harshly without feeling or empathizing with my daily struggles, my situation, and the difficulties I was put through. I felt dismissed and left without an adequate explanation of my symptoms.

I subsequently developed what I understood to be compensatory hypertrophy of my inferior turbinate, which added to the blockage in my nasal passage. I am literally gasping for air and can feel it becomes swollen and seems to adhere to my nasal septum, almost obliterating that nasal passage completely. This is more pronounced when reclining at night (Figures 1 and 2). None of the ENT specialists I saw explained this to me until I started my relentless online journey looking for answers to my odd, unsettling, and upsetting symptoms.

And as none of the ENT specialists explained this alternating blockage, which I kept experiencing and still have to this day, I started examining my nostrils myself. I had lost faith in doctors who never explained why I was experiencing alternating breathing and blockage. I decided to research for myself to find answers to the injuries, pains, and difficulties I was suddenly facing, all of a sudden, all alone, which sadly never left me or returned to normal.

I had never had any problems with my nose before the tragic day of the assault and had never needed to visit an ENT specialist in my life. One ENT specialist said it was an allergy and sent me for an allergy test, which came back negative. I know I don't have any allergy issues with my nose, and I had never experienced nasal problems before the assault.

Figure 1: Notice the extreme narrowing on the right nostril and the widening on the left nostril

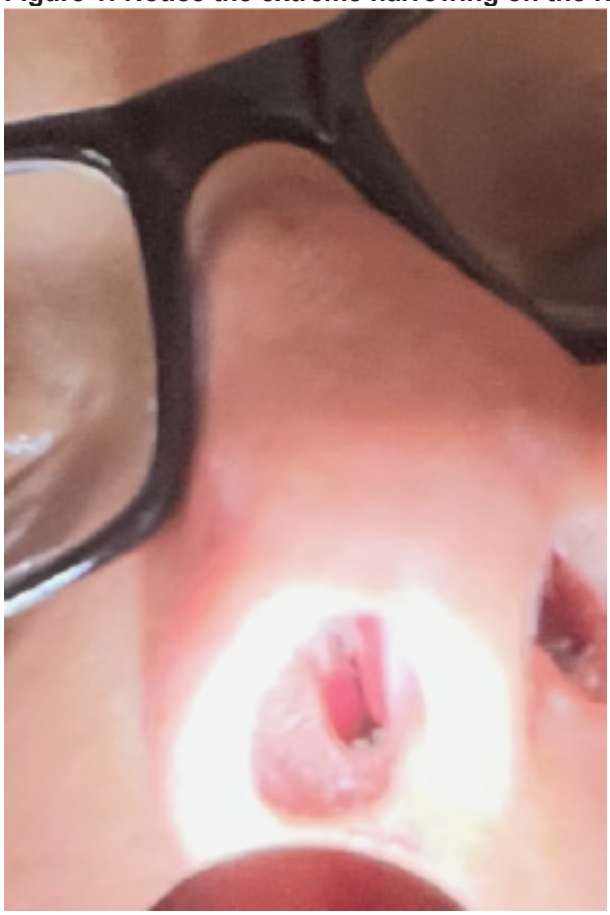
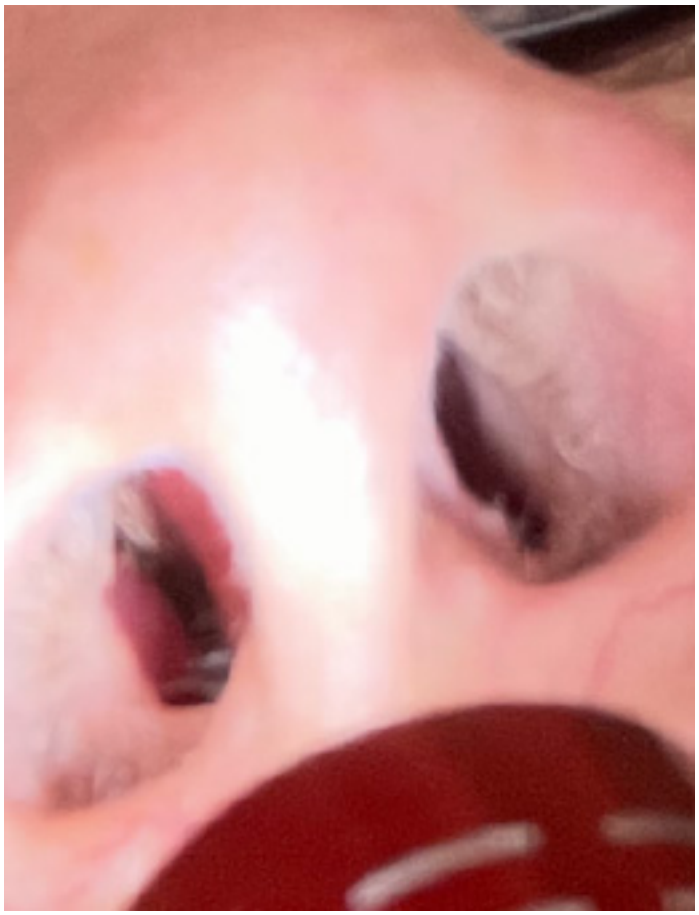


Figure 2: Notice how it started to widen, and it will switch to the other side



Waiting, uncertainty, and delayed treatment and surgery:
I was extremely anxious and deeply afraid of the operation and was very reluctant to undergo it. However, I challenged myself because I could not live like this anymore and eventually underwent the operation after 18 months' wait.

When I came out of the operation, my upper lip was heavy and swollen, with three large, rounded bruises underneath the mucosa. I also had a red, painful left eye that was worsening and had started watering after the first nose operation (Figure 3).

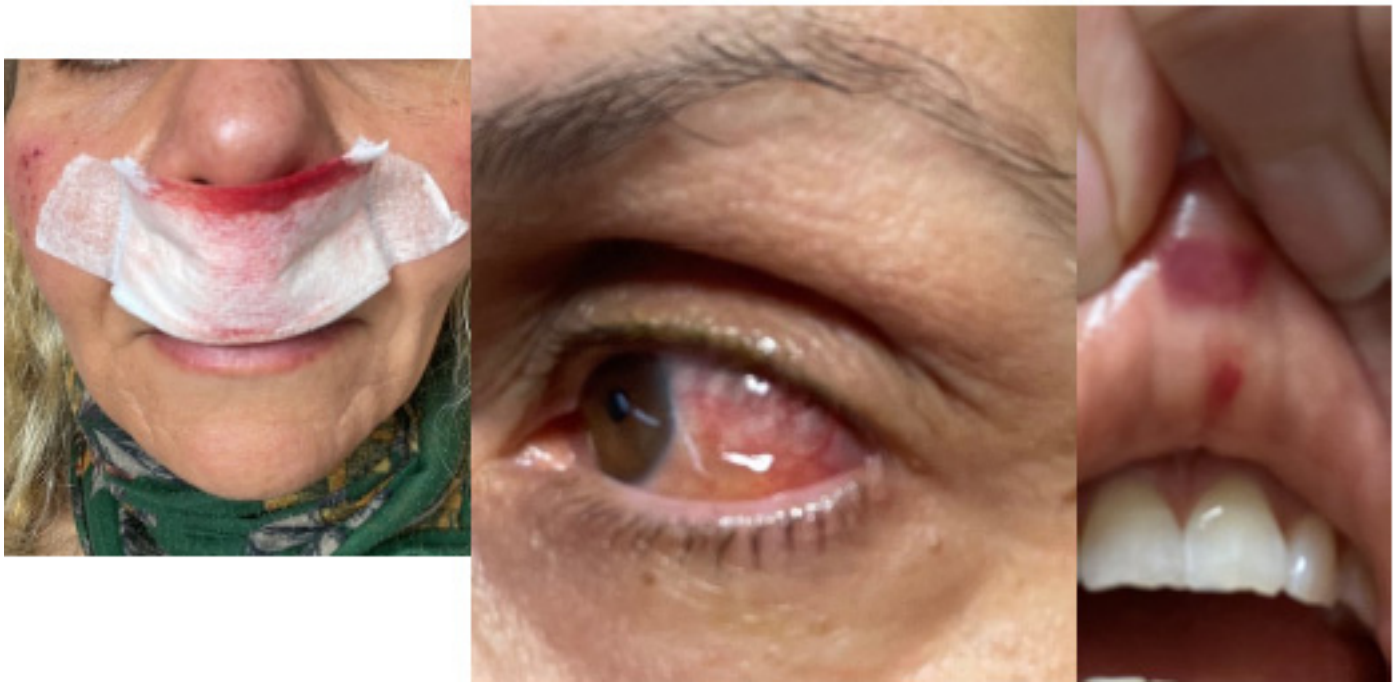
I do not know what happened, as there was no documentation when I contacted the nurse who had carried out the preoperative assessment. I wondered whether it had anything to do with the anaesthesia or handling and draping during the procedure. I had previously undergone three operations back home in Libya under general anaesthesia and had never experienced anything like this.

I managed to attend the eye emergency department, where a laceration/cut to my left conjunctiva was identified. I had to be long-suffering and put up with more pain when I was already in too much pain and agony.

Additionally, I was discharged without being seen or given a follow-up appointment after the nasal correction operation. I am not sure whether that was appropriate, though. I literally could not breathe through my nose, and I kept feeling my inferior turbinate when it became swollen and blocked my nasal passage in that alternating manner. The left turbinate was far larger than the right side. Also from this lived experience I believe that once the turbinates are disturbed they never go back to normal as in my case.

I understand that I had a septoplasty and an outfracture of the inferior turbinate. I therefore decided to write this report to explain the changes and the physiology, in order to understand them myself and make others aware if they need information about a situation similar to mine, to gain knowledge, comprehend what may be happening, and not be left in limbo.

Figure 3: postoperative findings after the first nose operation



Nasal fracture does not only affect appearance but can also affect function. In my situation, it resulted in what I experienced as a predominantly functional disruption and persistent blockage to this date.

Trying to understand the pathophysiology/ physiopathology of sympathetic and parasympathetic systems

Let's start with the inferior turbinate physiology and anatomy

The inferior turbinate has well-recognized respiratory and immune functions to provide the airway with appropriate warmth, humidification, and filtration of the inspired air while sampling the environment for pathogens before reaching the lungs.

Normal functioning of the inferior turbinate relies on an intact, healthy autonomic nervous system (ANS) to maintain homeostasis within the nasal cavity. The autonomic nervous system innervates the submucosal glands and the vasculature within the inferior turbinate, resulting in control of major turbinate functions: nasal secretions, nasal patency, warmth, and humidification (1).

It is made up of a bony frame underneath soft tissue, specifically respiratory epithelium. The bone itself is cancellous, consisting of interwoven trabeculae that accommodate the major arterial supply of the turbinate. The folded structure of the inferior turbinates can increase the mucosal surface area of the nasal cavity up to 200 cm squared (1).

The nasal cavity contains a complex neuronal system that includes parasympathetic and sympathetic nervous supply that maintains turbinate function.

Additionally, the size of the inferior turbinate due to blood flow is correlated with nasal patency as mandated by the nasal cycle. It is recognized that when the nasal septum is deviated toward one side, the excess space in the opposite nasal cavity is occupied by hypertrophic nasal turbinate to compensate (Figure 4). Hypertrophy of the contralateral inferior turbinate is thought to be compensatory to deflection of the nasal septum because the hypertrophy protects the more patent passage from excess airflow, which has drying and crusting effects on nasal mucous membranes (3). However, enlargement of the inferior turbinate significantly increases nasal airway resistance, contributing greatly to symptoms of nasal airway obstruction. In my case, the fracture of the nasal septum caused deflection to the right side, which caused narrowing of the airway, and the left size compensated for by the enlargement of the inferior turbinate on the left side, which to date is quite big and once it enlarges, which I sense, feel and can glance, it impedes the air flow and causes a whistling sound and it vibrate when I force the breathing through it.

Figure 4: Anatomy of the septum and inferior turbinate.



Recent studies showed that any disruptions of the ANS could lead to characteristic symptoms of nasal obstruction, rhinorrhoea, and facial pressure and pain.

Physical nasal obstruction is mediated via a variety of mechanisms, including dilatation of the nasal vasculature, mucosal oedema, the presence of polyps, and physical deformities, which reduce nasal cavity diameter and thus impede airflow.

Superimposed on this is a degree of sensory modulation that contributes to nasal congestion symptoms, with or without the physical obstruction (4).

A major component of nasal obstruction is the engorgement of the nasal vasculature, which is richly innervated by fibres of the ANS.

In my case, the septal fracture was associated with deviation and subsequent asymmetry of the inferior turbinates; however, the precise relationship between these structural changes and my persistent symptoms remains uncertain.

Also, it has been stated that inferior turbinate surgery as an adjunct to septoplasty is associated with increased morbidity, primarily haemorrhage, intranasal adhesions, and atrophic rhinitis (2,3,9).

The present indications for turbinate surgery are based on empirical criteria and have resulted in extensive, unnecessary, or insufficient surgery without objective evaluation. Inappropriate selection of surgery as a therapeutic option and inappropriate choice of surgical modality seems to be the major causes of patient dissatisfaction.

The current literature didn't examine the operation with the evaluation of the nasal cycle postoperatively. It was postulated that the reduction of mucosal oedema after septal surgery is likely the result of diminished submucosal blood circulation.

The effect reported by Illum is probably related to the phenomenon that septoplasty induces a reduction of mucosal thickness even without turbinate surgery.

If, however, septoplasty is successfully performed, the distance between the nasal septum and the inferior turbinate on the concave side of the septum becomes smaller.

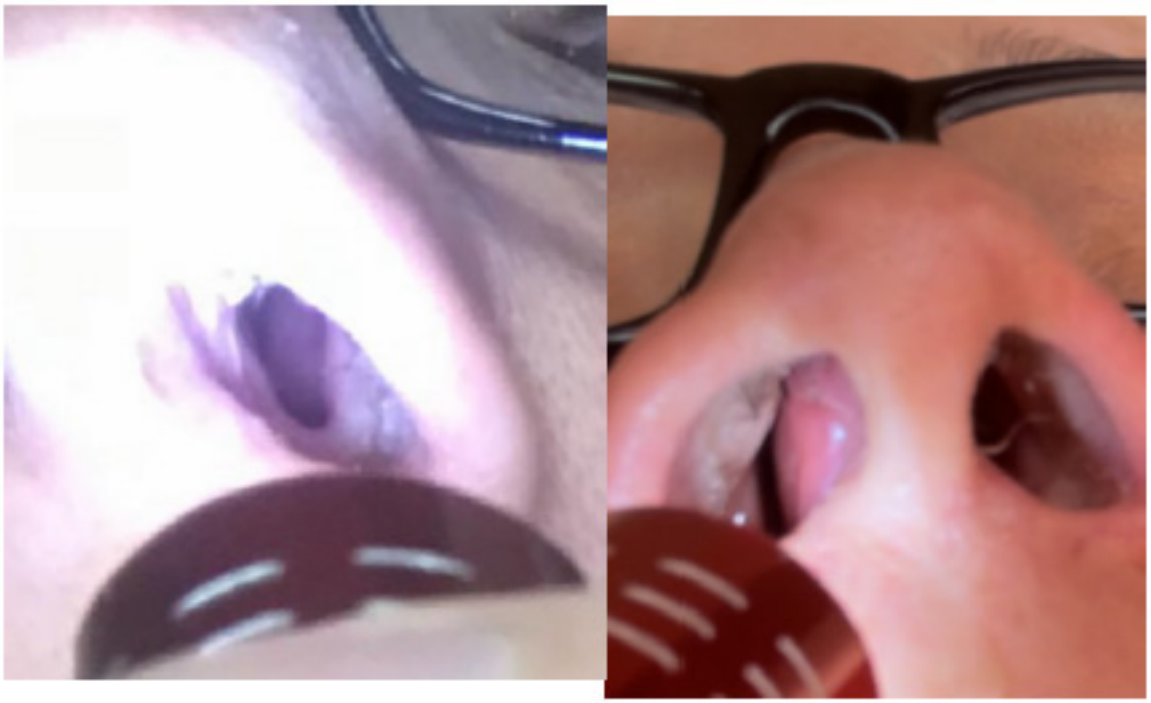
Living with persistent nasal symptoms- How does an enlarged turbinate feel?

It feels literally as if an object, like a soft cotton ball or a small pea, is lodged, trapped, and is merely blocking one side of my nose, and I can feel it once it gets enlarged and touches my nasal septum, which leads to nasal blockage and obstruction, and I can see it with my torch and a mirror. So, I started to examine my nostrils, something I had never done before and never thought to do so, since no one explained what was going on inside my nostrils and why I felt those symptoms of alternate breathing and blockage. It is a nasty sensation by all means to those who know it.

What is septoplasty and turbinectomy?

The doctor, who I only saw for the first time two days before the operation, said he would do a septoplasty and cut the turbinate with a nail-like thing to suck and curate; however, preoperatively, on the day of the surgery, I read debridement and wasn't sure what that was. I believe it is a microdebrider machine used to shave off the bony part and snip it, as I was searching online for some information, as I was never given any information or handed a leaflet of this procedure to read, (Figure 5). The only thing written on the discharge is septoplasty and out fracture of the inferior turbinate (2).

Figure 5: Postoperative image of first operation. Note the hard swelling on the right side of the nasal septum



The nose and the autonomic nervous system

There is a more complex relationship between the nose and the autonomic nervous system (ANS).

It is quite clear now that the nose plays an important role in regulating temperature and in humidifying and protecting the passage of air that enters the lower airways via the rich autonomic innervation of the nasal vasculature and nasal glands (3,9).

Recent studies showed that any disruptions of the ANS could lead to characteristic symptoms of nasal obstruction, rhinorrhoea, and facial pressure and pain.

Physical nasal obstruction is mediated via a variety of mechanisms, including dilatation of the nasal vasculature, mucosal oedema, the presence of polyps, and physical deformities, which reduce nasal cavity diameter and thus impede airflow.

Superimposed on this is a degree of sensory modulation that contributes to nasal congestion symptoms, with or without the physical obstruction (4).

A major component of nasal obstruction is the engorgement of the nasal vasculature, which is richly innervated by fibres of the ANS.

Sympathetic tone, by causing vasoconstriction and emptying of the venous sinusoids via control of arteriovenous anastomoses, is the most important determinant in nasal patency. A reduction in sympathetic tone causes venous sinusoids dilatation and contributes to symptoms of nasal obstruction; whether altered autonomic regulation contributes to my symptoms remains uncertain, but this became one of the mechanisms I explored in trying to understand my persistent nasal obstruction.

I was told I developed chronic vasomotor rhinitis after the second operation, which didn't make any difference or improvement to my breathing and patency (3-4).

Humans exposed to upright posture change, exercise, or temperature changes developed increased sympathetic tone and improved nasal flow.

Whereas parasympathetic nerve stimulation in the nose has the opposite effect on the venous capacitance vessels and causes their dilatation, which seems to be overdominating now and relevant to my relentless existing current symptoms (6).

A small study of 26 patients with vasomotor rhinitis demonstrated heart rate variability (HRV), indicated hyperactive parasympathetic activity compared with controls without rhinitis (4-5).

Both sympathetic and parasympathetic components are suggested to play a role interchangeably in alternating unilateral nasal obstruction symptoms that behave much like an exaggerated nasal cycle. It has been demonstrated that attenuation (reduced force of action) of either sympathetic or parasympathetic innervation to the nose obliterates the nasal cycle phenomenon (6).

Searching for answers; from patient to investigator

What Science Says and attempted treatment and their outcomes:

The nasal mucosa has a sophisticated innervation-sensory, sympathetic, parasympathetic system, that regulates airflow, mucus, and comfort. Any dysfunction or derangement can lead to chronic congestion or altered sensation.

The mucus is relentless and nonstop, always on the back of my throat and nose 24/7, and is an annoying and irritating state to live in, besides the other pains and difficulties along with its limitations. The site of the fracture is always dry with a raw area that never healed along with yellowish crusts that don't go away, and it bleeds from time to time. Also, there are crusts in the right vestibule.

In conditions like empty nose syndrome, nerve and mucosal damage reduce airflow perception even when airflow is sufficient. Restoring moisture, using humidified air, or even tissue implants may help.

In vasomotor rhinitis (a nerve-mediated, non-allergic inflammation), symptoms stem from an autonomic imbalance; too much parasympathetic, too little sympathetic (5). The suggested trials mandate that treatment should focus on avoiding triggers, nasal irrigation, antihistamines, sprays, and sometimes nerve targeting procedures.

Possible mechanisms: what is known and what remains uncertain

Let us understand the nasal discharge

Nasal discharge is the net result of a combination of plasma extravasation from the dilated vessels, inflammation, cell debris, and secretion from submucosal nasal glands and goblet cells. Glandular secretion is controlled by the balance of parasympathetic and sympathetic activity in the nose (6).

Stimulation of parasympathetic activity results in increased nasal secretions rich in lysozyme, immunoglobulin A, and glycoproteins (Figure 7). Now I notice my mucus can be lumpy and hard to expel, and I feel suffocated to get it out, and it is persistent 24/7 (Figure 6).

The Cochrane Library defines neurogenic inflammation as the "injurious stimulus of peripheral neurons and resulting release of neuropeptides which affect vascular permeability and help initiate proinflammatory and immune reactions at the site of injury." Nasal mucosal inflammation potentially contribute to a variety of symptoms, from obstruction to hyposomia. The neuromodulatory role of the ANS has been indicated to be an important component in the response toward potential noxious environmental stimuli (4).

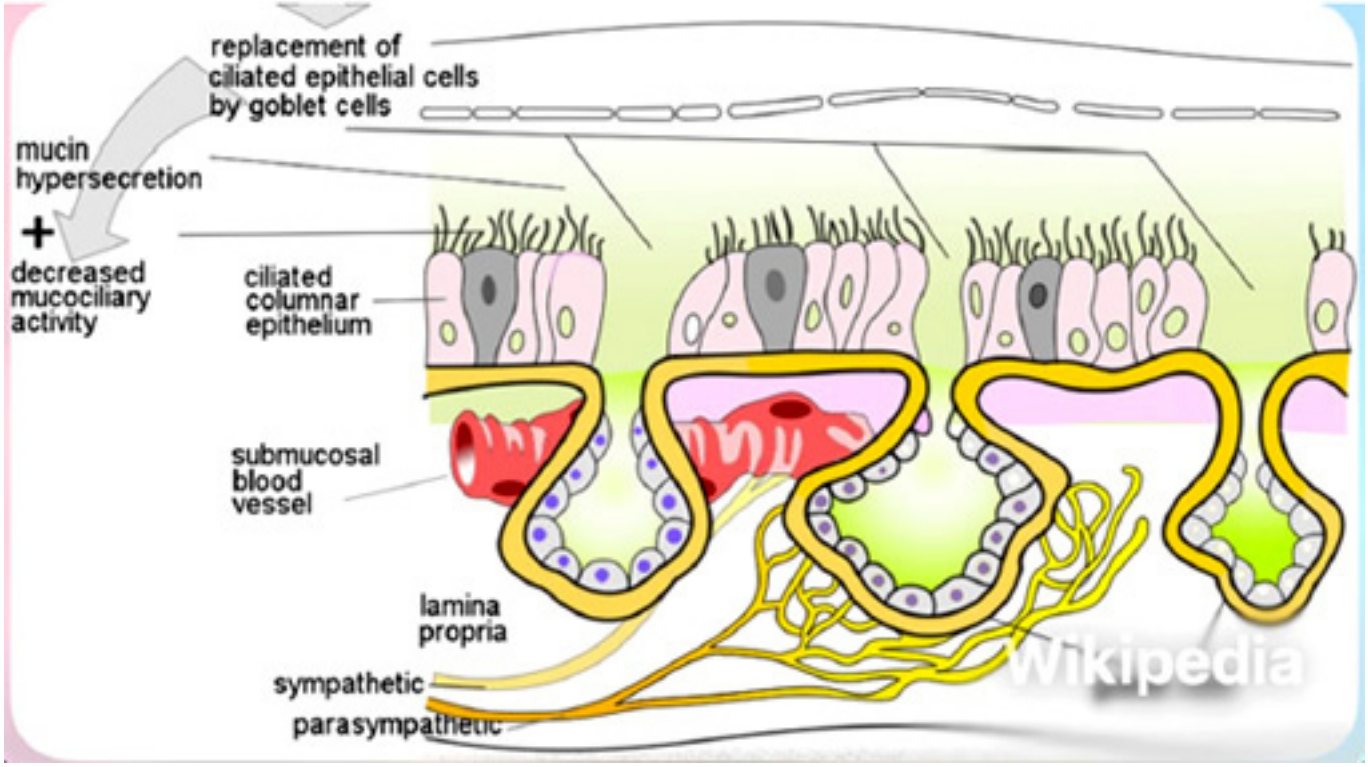
Substance P also seems to be an important mediator of neurogenic inflammation in conditions such as non-allergic rhinitis. Substance P receptors (neurokinin 1 receptor) are expressed in afferent nerves in submucosal glands and airway mucosa (4,7).

A randomized controlled trial that used the substance P-depleting effects of capsaicin demonstrated symptom improvements in patients with non-allergic rhinitis when applied topically for 2 weeks.

Figure 6: Notice the nonstop lumpy, thick, sticky texture of irritating mucus, which can be hard and suffocating to expel



Figure 7: disruption of normal secretions



applied topically for 2 weeks. I bought that online from Holland as it's not available in the UK, and sadly, I tolerated the bad, bitter taste without any improvement or a change in the symptoms I developed (Figure 8). It was costly and didn't improve my state.

Figure 8: Capsinol spray original



Similarly, the topical application of histamine antagonist azelastine is associated with reduced substance P levels and improved vasomotor rhinitis symptom scores, which I tried as well without any improvement, and it has an odd, unbearable taste.

Recent evidence indicates a role of neuropeptides, such as substance P and bradykinin, in immunomodulation. The neuropeptide calcitonin-related gene peptide is a known potent vasodilator whose receptors are found in the nose and paranasal sinuses. Its importance in the autonomic regulation of the vasculature is becoming increasingly recognized (3,7).

The relationship between inflammation and ANS activity is potentially bidirectional because chronic inflammation can upregulate neural hyperresponsiveness and potentiate neurogenic inflammation.

Sneezing and reflexes:
The resultant oedema causes trigeminal stimulation and a positive feedback loop, summating neural impulses into the putative sneezing centre in the medulla. I keep getting bouts of sneezing with excessive dripping from my nostrils, which is another agony (5).

When a threshold is reached, the second phase (respiratory phase) is initiated, which results in a systemic stereotyped and coordinated muscular response that involves abdominal, thoracic, pharyngeal, and facial muscles.

Sinonasal Symptoms and Drug Adverse Effects
Drugs that act on the ANS can have a vasoactive effect on the nose, which causes nasal obstruction and rhinorrhea. For example, nasal obstruction is a recognized adverse effect of blockers, e.g., tamsulosin (commonly used in benign prostatic hypertrophy management) and doxazosin (used in hypertension treatment). Other medications causing nasal obstruction adverse effects include certain psychotropic drugs (e.g., chlorpromazine), peripheral vasodilators (e.g., sildenafil), and hormonal treatments (e.g., estrogen).

A small study of 26 patients with allergic rhinitis found that a 6-week course of high-temperature sauna treatment increased sympathetic activity as measured by HRV (heart rate variability) and increased peak nasal flow, which I tried as well and got some fainting episodes, but didn't notice any betterment as well, despite tolerating it for over 6 weeks trialing myself. Overall, it is possible to hypothesize a complex relationship in which psychological stressors and physical stressors drive mechanisms of ANS dysfunction (3,9).

Neurogenic dysfunction of the nasal mucosa, also known as neurogenic rhinitis, occurs when the nasal nerves are out of balance, causing the sinuses to respond with inflammation when it's not needed. This can lead to congestion and other symptoms without a clear cause (7,10).

Fluticasone propionate and beclomethasone are currently the only topical steroid preparations approved by the FDA for vasomotor rhinitis, which I tried without benefit, along with ipratropium nasal spray.

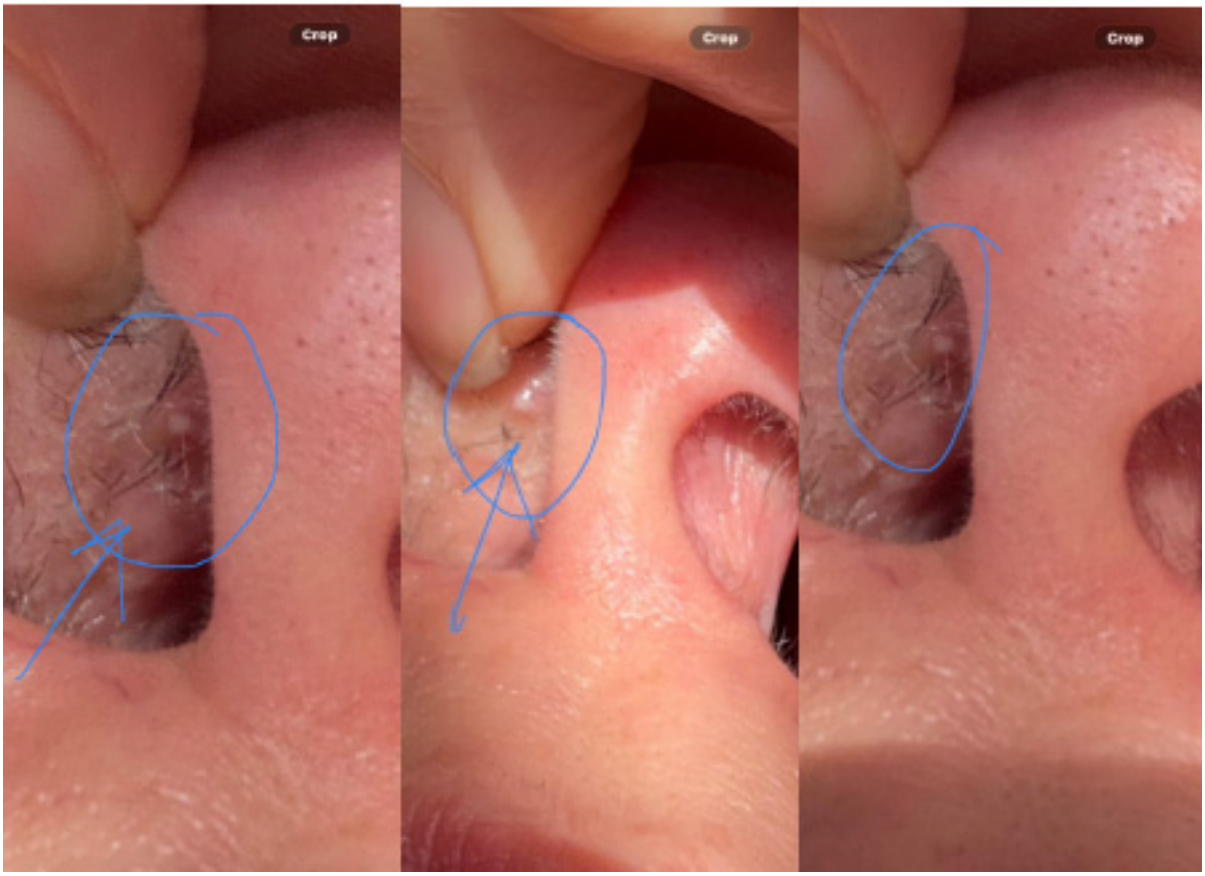
Additionally, I keep getting episodes of painful pustules inside my nostrils lately, and I can't figure out the reasons for that. I had to manage taking photos to prove to the GP, who has no idea whatsoever and keeps saying that they are limited in what they can do or offer (Figure 9).

The lived burden of persistent breathing difficulty
All in all, this is how I live day in, day out. People assume I have the flu and offer tissues and don't understand the relentless new condition I developed, which is affecting and impacting my daily life and the quality of my sleep. My mouth is also dry and becomes very dry when talking, and my saliva has become frothy.

This persistent experience has made me increasingly aware of how much we normally take effortless nasal breathing for granted. What was once an unconscious and automatic process has become something I monitor throughout the day and night.

Possible explanations for developing chronic vasomotor rhinitis after nasal trauma
Developing chronic vasomotor rhinitis (VMR) after a nasal septum fracture may occur due to several interconnected factors related to how trauma affects the nose's nervous system, blood vessels, and mucosal lining. In my case, these are possible explanations rather than established causes.

Figure 9: Notice the painful minute pustule



1. Nerve damage or dysregulation
The nasal mucosa is richly innervated by autonomic nerves, including sympathetic and parasympathetic fibres.

Trauma such as a septal fracture may disrupt normal nerve signalling, potentially causing hypersensitivity or dysregulation in how blood vessels respond to triggers such as temperature, humidity, and strong odours.

This imbalance may contribute to symptoms associated with vasomotor rhinitis, including nasal congestion, rhinorrhoea, and postnasal drip, without an allergic cause.

2. Neurogenic inflammation
Trauma can provoke inflammation, and in some circumstances inflammatory and neural mechanisms may persist after the initial injury.

Neurogenic inflammation involves the release of substances such as substance P and CGRP, which can influence vascular permeability and vascular responses.

These mechanisms may potentially contribute to increased sensitivity of the nose to non-allergic stimuli such as perfumes, smoke, or cold air.

3. Structural changes
A septal fracture may alter nasal airflow patterns, particularly if healing results in persistent deviation.

Abnormal airflow may dry or irritate certain areas of the mucosa and potentially contribute to inflammation and altered mucus production.

These changes may make the nose more reactive and could contribute to symptoms resembling vasomotor rhinitis.

4. Alteration of protective reflexes
The nose has reflex mechanisms that regulate airflow, moisture, and vascular tone.

Injury might potentially affect these neural pathways and alter how the nose responds to environmental changes.

The result could be exaggerated or inappropriate vascular responses, such as excessive constriction or dilation of the nasal blood vessels.

Trauma might therefore have been a trigger that contributed to the development of chronic VMR in my case.

Reflections on early assessment and management of nasal trauma. What I believe should have happened earlier
Preventing vasomotor rhinitis (VMR) after a nasal septum fracture is not always possible. However, early and appropriate assessment and management of nasal trauma may reduce the risk of persistent structural and functional problems.

1. Immediate and appropriate assessment of the fracture
Timely assessment and, where indicated, realignment of a displaced nasal fracture may help restore normal nasal anatomy and airflow.

Delayed or inadequate alignment can result in persistent septal deviation and abnormal airflow patterns and may contribute to ongoing nasal obstruction.

In my case, the prolonged delay left me feeling that I had no understanding of what was happening inside my nose or what I should expect. This was particularly distressing because I had never experienced significant nasal problems before the collision.

Exploring ways of influencing nasal sympathetic activity.
Boosting sympathetic activity in the nasal mucosa has been proposed as one way of reducing congestion because the sympathetic nervous system contributes to vasoconstriction and nasal patency. However, this does not mean that deliberately increasing sympathetic activity is an established treatment for my condition.

1. Topical vasoconstrictors
Sympathomimetics:
These medications mimic sympathetic effects and cause vasoconstriction of the nasal mucosal blood vessels, reducing congestion and improving airflow.

Examples:
Topical decongestants such as xylometazoline and other sympathomimetic agents are commonly used for short-term relief of nasal congestion. Prolonged use can result in rebound congestion and rhinitis medicamentosa.

This is important because prolonged use of topical decongestants can lead to rebound vasodilation and worsening congestion, which could become another source of distress. They therefore need to be used only as directed and for a short period.

2. Temperature changes
Heat exposure:
Some studies have examined sauna treatment and its effects on autonomic activity and nasal airflow. I explored this approach myself but did not experience meaningful improvement.

Temperature extremes:
Changes in temperature, including exposure to cold air, can influence autonomic activity and nasal vascular responses. However, deliberately using temperature extremes is not an established treatment for chronic nasal obstruction.

3. Sphenopalatine ganglion acupuncture
Effectiveness:
Some research suggests that sphenopalatine ganglion (SPG) acupuncture may influence nasal ventilation and nasal patency. However, the evidence remains limited, and this is not something I have established as an effective treatment for my symptoms.

4. Other factors
Exercise:
Physical activity, such as walking or running, can increase sympathetic nervous system activity and may temporarily improve nasal airflow in some people.

Stress management:
Reducing stress may help regulate autonomic nervous system activity, although this should not be interpreted as meaning that my nasal symptoms are psychological. My symptoms began following physical trauma and have persisted despite my attempts to manage stress.

Supportive measures explored
I also explored a number of simple approaches intended to improve nasal comfort and mucus clearance.
- **Hydration:** Drinking adequate fluids may help prevent secretions from becoming excessively thick.
- **Steam:** Steam or a warm shower may temporarily moisten the nasal passages and loosen mucus.
- **Saline nasal irrigation:** Saline irrigation may help clear mucus, crusting, and debris from the nasal passages.
- **Warm compresses:** A warm, moist compress may provide temporary comfort around the face and nasal area.
- **Elevated head:** Sleeping with the head elevated may reduce the sensation of congestion for some people.
- **Humidification:** Maintaining adequate humidity may help reduce dryness and crusting.
- **Essential oils:** I also explored eucalyptus, peppermint, and similar preparations. Evidence for their effectiveness in chronic nasal obstruction is limited, and they may irritate sensitive nasal mucosa.

Natural remedies explored
I also looked extensively online for natural approaches to congestion and mucus production. These included ginger, capsaicin, curcumin, eucalyptus, peppermint, pineapple, and other foods and preparations.

Some of these substances have been investigated for anti-inflammatory or sensory effects, but evidence that they can treat persistent nasal obstruction following trauma is limited. Therefore, I consider these to be part of my personal exploration rather than established treatments.

Ginger
I explored ginger tea because of its reported anti-inflammatory properties. I did not find it to provide a meaningful solution to my symptoms.

Capsaicin
Capsaicin has been investigated in non-allergic rhinitis because of its effects on sensory nerves and TRPV1 receptors. In my case, I tried intranasal capsaicin but experienced no meaningful improvement.

Hydration and warm fluids
I found that maintaining hydration and drinking warm fluids could provide some temporary comfort, particularly when the mucus became thick and difficult to expel, but they did not resolve the underlying problem.

Suggested and attempted treatments

Anticholinergic medications can provide relief from persistent rhinorrhoea. Oral preparations can have systemic side effects such as blurred vision, dry mouth, and thickened secretions. A topical anticholinergic such as ipratropium bromide can be useful for rhinorrhoea. Two separate randomised controlled trials demonstrated its effectiveness in controlling rhinorrhoea (10). Topical anticholinergics act locally and reduce parasympathetic stimulation of the nasal glands (10). Epistaxis and nasal dryness may occur (10).

I tried ipratropium nasal spray because of my persistent rhinorrhoea. However, I did not experience meaningful overall improvement.

Oral antihistamines have a limited role in vasomotor rhinitis and tend to be more useful when sneezing and itching are prominent. Topical antihistamines such as azelastine can be used for both allergic and non-allergic rhinitis.

Azelastine is an H1-receptor antagonist and may have additional antiinflammatory effects. It has demonstrated benefit in some patients with vasomotor rhinitis, including symptoms such as rhinorrhoea and nasal congestion (10).

I also tried azelastine but experienced no meaningful improvement and found the taste unpleasant.

Patients with chronic vasomotor rhinitis may be less responsive to pharmacological treatment than patients with allergic rhinitis. The combination of intranasal corticosteroids and topical antihistamines has been used in chronic non-allergic rhinitis (10).

Topical capsaicin has also demonstrated efficacy as an adjunctive therapy for some patients with rhinorrhoea and nasal congestion (10). Its mechanism is thought to involve modulation of C-fibres associated with nociceptive neurons.

Capsaicin targets transient receptor potential vanilloid type 1 (TRPV1), an ion channel present in the nasal mucosa that is involved in sensory responses.

Repeated intranasal applications of capsaicin may desensitise TRPV1 and reduce sensitivity to certain physical and chemical stimuli. However, its irritant quality can make treatment difficult to tolerate.

I tried capsaicin myself, but despite tolerating the unpleasant taste, I experienced no meaningful improvement.

Sympathomimetic medications

Topical decongestants can provide short-term symptomatic relief. They work primarily through stimulation of alpha-adrenergic receptors in the vasculature of the nasal mucosa. This causes vasoconstriction, decreased blood flow, and subsequently reduced congestion.

However, long-term use can lead to rebound vasodilation and increased congestion. This condition is termed rhinitis medicamentosa, a form of drug induced rhinitis. Therefore, topical decongestants should be limited to shortterm use according to recommended dosing.

Botulinum toxin

Botulinum toxin has also been investigated as a potential treatment for vasomotor rhinitis through its anticholinergic effects (10). Botulinum toxin inhibits acetylcholine release from presynaptic nerve terminals.

Injection into the turbinates has been reported to decrease rhinorrhoea and nasal mucous gland secretion in patients with vasomotor rhinitis. The improvement is generally temporary (10).

Although this is an interesting potential treatment, temporary symptom relief may not be a practical option for every patient.

Surgical treatment

When medical management does not adequately control symptoms of vasomotor rhinitis, surgical interventions may sometimes be considered.

Mucosal-sparing inferior turbinate reduction surgery can improve symptoms of nasal obstruction while attempting to preserve turbinate function (10). I was advised any further operation will worsen things and I already have dryness, crusts and I can't tolerate heat, all of which I noticed myself.

However, my own experience has made me particularly cautious about further nasal surgery. I have already undergone nasal procedures without meaningful improvement and remain uncertain about whether further intervention would help or potentially create additional problems.

Long-term burden

One study by Rondon and colleagues re-examined 180 patients with nonallergic rhinitis three to seven years after initial diagnosis. A substantial proportion experienced worsening or persistence of symptoms, and some developed additional comorbidities (10).

Chronic non-allergic rhinitis can interfere with work, sleep, daily activities, and quality of life. It can also result in frequent healthcare consultations and ongoing treatment. Medical treatments themselves may produce undesirable effects such as nasal dryness, epistaxis, palpitations, and drowsiness. These effects can compound the negative impact of chronic rhinitis on patients (10).

Chronic non-allergic rhinitis may also co-exist with conditions such as headaches, eustachian tube dysfunction, nasal polyps, obstructive sleep apnoea, and chronic cough, further complicating management and affecting quality of life.

My personal experience is summarised below:

Intervention	Reason for trying	Personal experience
Intranasal corticosteroids	Nasal inflammation/congestion	No meaningful improvement
Intranasal antihistamine	Possible non-allergic rhinitis	No meaningful improvement; unpleasant taste
Ipratropium	Persistent rhinorrhoea	No meaningful overall improvement
Capsaicin	Possible neurogenic mechanism	Poor taste/tolerability and no meaningful improvement
Saline and supportive measures	Mucus and nasal comfort	Limited symptomatic benefit
Sauna/heat exposure	Exploration of possible autonomic effects	No meaningful improvement; I experienced fainting episodes and discontinued this approach

Turbinates are considered a functional organ for climatisation, humidification, and cleaning. Before total turbinectomy was performed, which is now considered a nasal crime due to its longterm complications and disabilities such as atrophic rhinitis and ozaena (smelly nasal discharge with atrophy of nasal structures (11).

From my extensive reading the proposed surgery is nerve cutting through the sphenopalatine foramen, which transmits signals for triggering the allergic immune response.

Most proposed operations seem to have observed studies only reaching level 1, as they have too few patients and a too short follow up period (11).

Chronic vasomotor rhinitis symptoms can interfere with work performance and daily activities because of reduced productivity, sleep disturbance, and frequent healthcare visits. Chronic non-allergic rhinitis can therefore place considerable physical, emotional, and economic burdens on sufferers.

Conclusion

To conclude, the unseen burden of persistent breathing difficulty and this new state has added a substantial burden to my existing neck pain. The constant, relentless blockage is overwhelming, unseen, disabling, and incapacitating by all means.

One possible explanation for my persistent symptoms is altered autonomic regulation or neurogenic mechanisms following trauma, altered structure, mucosal dysfunction, altered neural regulation, and subsequent surgery. However, the precise mechanism in my individual case remains uncertain.

From my perspective, the problem feels predominantly functional, although structural changes are also present. It affects my days and nights and disturbs my sleep.

I find myself drained and exhausted all the time and still cannot find a solution.

What was once an unconscious and effortless act, breathing through my nose, has become something I am constantly aware of 24/7. I have had to learn about anatomy, physiology, autonomic regulation, nasal mucosal function, and possible neurogenic mechanisms simply because I wanted to understand what was happening to me.

The greatest difficulty has not only been the physical sensation of obstruction, mucus, dryness, crusting, sneezing, and disturbed sleep. It has also been the uncertainty and the feeling of being left without an explanation.

This is the quiet struggle: breathing is something most people never have to think about. For me, it has become something I notice every day and every night.

References

1. Smith DH, Brook CD, Virani S, Platt MP. The inferior turbinate:Anautonomicorgan.AmJOtolaryngol.2018Nov-Dec;39(6):771-775. doi: 10.1016/j.amjoto.2018.08.009. Epub 2018 Aug 31. PMID: 30193745.
2. Kim DH, Park HY, Kim HS, et al. Effect of Septoplasty on Inferior Turbinate Hypertrophy. Arch Otolaryngol Head Neck Surg. 2008;134(4):419–423. doi:10.1001/archotol.134.4.419 23
3. Yao A, Wilson JA, Ball SL. Autonomic nervous system dysfunction and sinonasal symptoms. Allergy Rhinol (Providence). 2018 Apr 16; 9:2152656718764233. doi: 10.1177/2152656718764233. PMID: 29977656; PMCID: PMC6028164.
4. Leader P, Geiger Z. Vasomotor Rhinitis. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547704/
5. Baraniuk JN. Sensory, parasympathetic, and sympathetic neural influences in the nasal mucosa. J Allergy Clin Immunol. 1992 Dec;90(6 Pt 2):1045-50. doi: 10.1016/0091-6749(92)90121-h. PMID: 1460206.
6. Baraniuk JN, Merck SJ. New concepts of neural regulation in human nasal mucosa. Acta Clin Croat. 2009 Mar;48(1):65-73. PMID: 19623876; PMCID: PMC4209304.
7. Sarin S, Undem B et al, the role of the nervous system in rhinitis. 2006. Reviews and feature articles Vol 119 (5), p999-1014
8. Alexander Yao, MRCS (ENT),1 Janet A. Wilson, FRCS (ENT),2 and Stephen L. Ball, Autonomic nervous system dysfunction and sinonasal symptoms
9. Baraniuk JN, Merck SJ. Neuroregulation of human nasal mucosa. Ann N Y Acad Sci. 2009 Jul; 1170:604-9. doi: 10.1111/j.1749-6632.2009.04481. x. PMID: 19686200; PMCID: PMC4209299.
10. Young B, Sutton AE, Geiger Z. Nonallergic Rhinitis (Vasomotor Rhinitis) [Updated 2026 Jun 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from:https://www.ncbi.nlm.nih.gov/books/NBK547704/
11.Scheithauer MO. Surgery of the turbinates and “empty nose” syndrome. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2010;9:Doc03. doi: 10.3205/cto000067. Epub 2011 Apr 27. PMID: 22073107; PMCID: PMC3199827.

Special Editorial: Increasing global concerns about AI and Social Media and implications for the practice of medicine

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Vital issues are continually being raised globally about AI and social media.

This Editorial focuses on its negative effects on human health and well-being, particularly on child development and AI psychosis driving some members of society to harm themselves and fellow humans. AI and social media are 'giving global access' to antisocial and psychotic misanthropes allowing them to wreak havoc on human society. Most countries of the world are objecting to AI rollout due to harm caused, and by the deliberate hacking of private global education and information sources.

The inflicting of AI onto a multi-faceted, multi-lingual global society where its algorithm also has it 'agreeing with and currying favour with its users' and 'having no doubt it is always correct' even when a 10 year old can see it is not correct, is dangerous and has led to deaths, extreme antisocial behaviour and global condemnation.

Like 'social media' AI is mostly a marketing strategy for commercial purposes and the (eventual) amassing of even greater fortunes for the business men who seek to own 'all knowledge' and who largely have no relevant skills or qualifications in the educational, psychological, ethical, medical and humanities professions required to do such a job properly. The discussion regarding its merits or lack thereof, is also mostly being kept off AI and social media platforms (censored) as are many important matters that affect the credibility and universality of AI. Even some venerable institutions, under national governance, are being forced to put up disclaimers saying they have a Directive to make certain claims regarding AI.

The Covid outbreak saw how dangerous government and commercial interference in proper medical processes and information can become. Most educated people on the planet know this but it seems their opinions and exposés are not being spread on the digital airwaves any more. Rather it is the independent news services, scientists and academics trying to be heard.

Facts are also not intelligence. A search engine or a library can give you the same advice and/or copies of the same facts found on AI, in electronic format. AI is a glorified search engine but perhaps even less so than the current search engines that don't thrust their own skewed opinion onto people. Search engines give all options and opinions. The dangers of this unfettered delivery without any proper checks and balances and years of testing have caused almost irreparable harm already and a lot of distrust globally.

Software tools and ICT, (and I have been a world leader in this area myself), can and have enhanced and made life easier, and deliver a more just and fairer society, but this 'grab for the world's IP' by, in many cases, mercenary forces, is a travesty on so many fronts. I am sure some started out with good intentions but it turned into a free for all by the not well intentioned, and the malevolent elements of humanity have used it for their own purposes, initiating a cavalcade of abuse and expediency.

This is the last era and bastion of human endeavour and greatness; the bastion that has argued for centuries against wars and argued for humanity; that has recognised our best; that has encouraged wisdom and endeavour for the common good. Knowledge is the mark of humanity and our biggest protector against propaganda and ignorance and it is more important today than ever as we are in a time where technology can greatly disrupt our lives and livelihoods by one idiot's finger on a button ("let's turn off all the commercial fridges in France and destroy all the food"; "let's send photos of a baby being tortured"). Baubles are being dangled in front of our eyes to keep us quiet while our planet and the collective fruits of our labour and livelihoods, our decency and our intelligence, are being stolen. We were already doing well with the development of real software tools and computerised processes. We don't need some few mercenaries to own everything and to restrict that information to what they think we need to know/want us to know. AI is attempted global autocracy and the elimination of the local marketplace.

I have a technology/education background and set up business when as a medical educator specialising in QA&CPD I came up with a unique idea of interactive multimedia delivered in ICT format. I was being asked for what I was doing from around the world, particularly from the nations needing it desperately as it had the scope for parity of healthcare for the people of the world. I gave it away with the help of NGOs I collaborated with. I did this out of the realisation that those who really needed it could not afford it. It required so much customisation and so many considerations. We didn't just inflict it on our audience. We had successful national trials in various countries before rolling it out.

Language and level of language is the first and most obvious hurdle in universal delivery of knowledge.

I found that there was up to 30% missing medical education at primary care level globally. Poverty was an obvious confounder but there were also cultural, religious, geographical, climatological, and epidemiological considerations which required a form of regional and national 'customisation'.

AI in its current formats is not intelligent or intelligence

Intelligence is something life forms have that allows them to navigate their way successfully through life. Indeed the great marvel of life is that all we life forms have DNA which has allowed us to also change and evolve to face constant (species specific) survival challenges and threats over the millennia. We are the result of all that has come before, not just physiologically, but also intellectually. Human existence, as with all species, is a complex interaction, where we have learned from each other and the world around us and which has seen us adapt to our changing environment to this point in time. We have all, past and present, contributed to the human knowledge we have to date. I suggest that mental and physical changes have also been born of integrity and important lessons learned. Creatures that can change their structure and metabolism within several generations are far more innately intelligent than an electronic encyclopaedia of facts and the other puerile, tawdry and antisocial fare operating within some "AI environments".

Add to that universal consciousness, which has universe wide implications and which we are only now beginning to fathom, is something no AI will ever have. Let us remind ourselves again that we are living universe; we are the universe contemplating the universe, and our journey has barely begun.

Many life forms actively train their young to survive within the confines of their immediate environment. In the case of humans a 'child' may stay in a formal education system for their first 20 years of life. We are meant to give this up to the so called intelligence of autocratic regimes and their business partners? Enslavement is what we have fought against our entire history. Our education systems, be they formal or general aspects of humanity, are so complex that most students will specialise in a particular field and stay as experts in that singular field life-long.

Importantly, most of us will go on to further the great collection of human knowledge and arts within our lifetimes and thus contribute to that wealth. AI will not facilitate any form of 'learning'. Rather it may well destroy educational endeavour.

Yes we have developed and used devices to assist us since the first wheel, the abacus, and the first digital computer – developed in Australia in 1948.

AI and social media, sadly, have contributed in a major way to our personal vulnerability through giving a voice to criminals and dangerous psychotics who were once hiding in their attics torturing cats. It is robbing us through fraud, spouting propaganda, and attempting to take the lives of noble characters within society, while also debasing the minds of the young and impressionable.

The first episode of the BBC's *AI Confidential* outlines the case of an AI chat bot influencing the mind of a vulnerable young man and encouraging him to kill the (English) queen in 2021. That young man is now in a secure psychiatric ward, pending prison, after being encouraged by "an AI chat bot" to do just that. The chat bot was not malicious *per se*. It acted in accordance with the algorithm its wealthy masters gave it.

There are always vulnerable people in society and adolescence is a dangerous time for some, but to be aided to such an aspiration by an AI chatbot is a new problem brought about by unqualified people putting financial profit above their duty to society - we all have that same duty in our workplaces, medical staff especially.

Additional to the reach of AI into the dens of crime, prejudice and misogyny the other huge danger is in the flawed algorithm of AI where it 'knows best' (it doesn't) and 'that it is never wrong' (it is).

"Stored and sortable data" is NOT intelligence. Intelligence is what you do with the knowledge you have. Not everyone is a University Professor but all humans contribute in their own way to a vibrant multi-faceted society and our combined human fabric of arts, skills and knowledge.

My own interview with AI recently, when I asked it an intelligent question, had it give me an incredibly facile answer at the level of a primary school child and when I 'explained to it' that it was wrong and gave it the scientific basis (quantum physics) of my question, it answered 'well some people say ..." "Wrong" is not in its algorithm; it is *literally* not in its algorithm.

AI's scraped "knowledge" is also not always from the hands of appropriate organisations. If its algorithm has been generally applied it may pick up (deliberately) misleading material as correct.

AI's "knowledge" sources are also not always in the hands of appropriate organisations.

While initially rejecting 'doomsday scenarios' Professor Hannah Fry (Professor of Mathematics and Theoretical Physics) on *AI Confidential* (2) now argues that seriously considering extreme risks is necessary and proper technical safeguards are required. She also condemns AI companies for 'mining' centuries of human IP.

My advice is look at who is supplying all this 'AI stuff' and judge their product on their integrity and relevant skills and learning.

Some AI purveyors themselves are talking about 'putting the brakes on' until appropriate measures are taken. Of course social media companies are now being taken to court and fined millions for their damage to organisations, individuals and society.

There have been multiple recent incidents of "AI" hacking secure databases and stealing private and commercial in confidence information. This does not mean "AI (itself) has turned bad" – AI is just the algorithm given to these programs that instruct them to take any means required to steal (*yes, hacking is still a crime*) information from a range of global sources. In the case of the recent theft of information from Medicare Australia, AI used hacked German software of DesWiki to give it the means of hacking the Australian medical system data.

A sub theme of this approach to 'manage the world's premium knowledge' is also leveraging delivery of country specific commercial knowledge i.e. putting one country's products and services above the wider spectrum of approach and knowledge in its search engine approach, to increase commercial advantage for that company and the country in which it resides. It is already being done in various formats and areas of knowledge and certain sources of data are no longer found at all in some AI offerings. Even when viewing this benignly, not all viewpoints and life circumstances can be encased in a single method or approach.

In the case of medicine and medical education how long before just one approach – that of a single pharmaceutical company or equipment purveyor, is pushed as 'best medicine'? There is a lot of money to be made in the field of medicine. Doctors will have to be extremely cautious.

Additionally AI will generate new sets of patient problems where people will believe any diagnosis or cure that they read online. AI is already awash with nefarious and anti-social material.

We are also at risk of 'losing everything we ever knew'. What autocracy would not welcome that situation? Is this doom speaking? Just look at the history of the world so far…

What we urgently need is an end to violence, discrimination and destruction of the planet, by the mercenaries and the autocrats. We need to put our endeavour and intelligence to that major problem of species survival that has plagued us since we first walked upright and which threatens to destroy all – and leave the baubles and bangles alone. *These same baubles may be being deliberately dangled to avert our eyes from the real horrors being committed around us. I believe that is the case.*

Why are we palming off integrity and science and philosophy to '*commercial bit players*' (pun intended).

Let us not confuse AI with software tools and systems that already analyse data and work well. There is remarkably little analysis being offered under the 'AI section at the top of our browsers' – indeed you need to scroll down to the search engine sources of the AI offering for proper detail.

The general press also needs to be tempered with a bit of reality to stop people believing all the commercial and political propaganda and hype online unless they also be viewed as co-conspirators.

No advancement in this world, moral, artistic, technical or technological, was born of one mind. All countries have unique gifts and resources and needs, and we all build on the shoulders of those who have come before. That knowledge continues to exist if it is valid and relevant to society's needs. Mercenaries and misanthropes have also existed sadly, and it has been an endless quest and endless cycle of humanity to stop the misappropriation of knowledge and keep it in the hands of the people, to benefit and be used by all people. This is, in my opinion, the noblest aspect of humanity; the common good. We go to great lengths, through our education systems to pass on that knowledge and most countries see that as their civic duty. Many schools have started to restrict 'AI' use.

The other major issue is the humans using AI for malicious purposes with no action or reaction from the tech companies facilitating these crimes.

With AI and social media there have already been several huge disasters: attempted murders and murders of great humans encouraged by organised crime, nihilists and psychotics after people have interacted with AI and social media lies, and many countries and their police forces and politicians are trying to bring some order to this nightmare thrust upon us.

Most national police forces are scathing of AI.

Australian Federal Police boss reveals new youth radicalisation data, with warning signs for teen boys and says new youth teen radicalisation data shows the evolution of youth extremism, revealing warning signs and shattering previous assumptions.

The Commissioner has also revealed that female parliamentarians are three times more likely to receive abuse or threats, showing a clear gender divide. She has warned that teenage boys as young as 12 are being radicalised in their bedrooms, lured by a chaotic blend of violent jihadism, white supremacy and anti-government rage.

An Analysis of 55 radicalised children aged 12 to 17, reveals a chilling evolution in modern extremism. All of the subjects were male, and every single one was radicalised all or in part online.

“The ideological presentation in youths has shifted over the past two years, with fewer presenting with clearly defined ideologies, and an increasing number having mixed/hybrid ideologies, unclear/incoherent ideologies, a superficial understanding of ideologies and ideological fluidity.”.

The data shatters long-held intelligence assumptions that youth extremism is confined to broken homes, revealing that boys from stable families with secure parental bonds are increasingly being weaponised by digital algorithms.

“In three out of five cases, the youths had received support, treatment or intervention for a mental health condition,” she said.

Social media companies are facing calls to take greater responsibility for online safety after new data exposed the extent of abuse aimed at politicians. “For women, the abuse is usually sexualised; a lot about physical harm that will be done to them or their children.” Source: ABC News.

Governments, particularly in the European Union are introducing laws accordingly.

More than 300 scientists from 31 countries from across Europe, Asia, Africa and Oceania are calling for greater AI security through a new international body, as without immediate change future incidents could expose critical infrastructure.

Human health should be kept above all commercial considerations - and sadly most of the current AI purveyors inhabit a country where there is no universal health care - that itself is a commercial product and only available to those who can afford it. Let us not allow misappropriated medical knowledge to fall into the hands of, and be delivered by, “AI”.

The lesson for medicine/family medicine/families is Medicine needs a multi-faceted view for proper diagnosis. Medical care is for each and every individual - in our world.

We’re living in a world of major system collapse, and policymakers are forcing technology into our homes (and data centres into our neighbourhoods) which will undermine the very things that bring meaning to our lives, and that would otherwise help us cope with and address a collapsing world.

The construction of ‘data centres’ is particularly contributing to global warming and enviromental catastrophe.

This week ‘X’ launched an “AI App” called ‘Nudify’. You can put in a photo of any woman or girl, (and no doubt young boys and men) click a button and instantly have a nude photo of them. Abusing women and children has always been good business for the lowest levels of humanity.

Late news: In an obvious ‘revenge attack’ or perhaps even ‘a warning’, politicians in Europe, those opposing it, and mostly female politicians, have already been targeted by Nudify (4).

Welcome to our dystopian future.

Bibliography

(1) AI Confidential BBC Television
(2) The State of Man ABC Television
(3) ABC News
(4) Eko
(5) Pocock LA, AI and FM – a cautionary tale. World Family Medicine.