2025- Pros and cons in general internal medicine and geriatrics

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Older people are often explicitly or implicitly excluded from research. As a result, study findings are often not applicable to this population, and older adults may not be offered effective treatments or technologies due to insufficient evidence. The complexity of the older patient, together with the processes surrounding care, requires consideration of multiple perspectives, including anatomical, physiological, pathological, mechanistic/kinetic, surgical, metabolomic, genetic, and radiological aspects, among others. This complexity calls for a holistic approach that prioritises the collection of patient data, employs appropriate mathematical modelling methods, and involves multidimensional assessment. The appropriateness of diagnostic, therapeutic, and follow-up instruments is frequently debated and may raise ethical concerns. Current evidence highlights the need for a multifaceted, large-scale change across education, guidelines, research, advocacy, and policy to improve the quality of care for older people and to make appropriateness a routine component of care for ageing generations. PROS & CONS aims to improve knowledge of the challenges involved in optimising interventions for older patients.

Diabetes in older adults

The impact of diabetes on healthcare in older adults represents a continuously growing global challenge due to the increasing number of individuals reaching advanced age. Diabetes alone has been shown to increase the risk of numerous complications, including ischemic heart disease, stroke, blindness, kidney failure, and neuropathies. In addition, the literature has widely highlighted that type 2 diabetes is associated with reduced functional status and sarcopenia, with an increased risk of falls and fractures. This risk is partly related to balance impairments caused by neuropathy, muscle atrophy, and hearing and visual deficits. Diabetes in older adults has also been shown to increase the risk of multi-infarct dementia and Alzheimer's disease. At the same time, the identification of appropriate glycemic targets in older adults with diabetes should be individualised, with the primary objective of minimising the risk of severe hypoglycemia. Moreover, older adults with diabetes often present with multiple comorbid conditions leading to geriatric syndromes that may interfere with their ability to perform self-care, thereby increasing the risk of poor glycemic control and adverse outcomes. The concurrent use of multiple medications (polypharmacy) represents another major concern in this population, due to the increased risk of drug interactions and side effects. Original articles, reviews, and clinical studies focusing on the impact of type 2 diabetes on patient care—particularly in relation to age-related comorbidities—may contribute to new findings on the effects of specific antidiabetic agents on clinical outcomes and help inform care strategies for older patients (1).

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Breathing difficulty predicts a sixfold increase in mortality risk among hospitalised patients

A simple nursing assessment of patient-reported breathlessness during hospitalisation can identify individuals at a markedly increased risk of death. Post-admission dyspnoea was associated with a sixfold increase in mortality compared with patients who reported no breathing difficulty. The investigation found that 18% of patients reported dyspnoea on admission, while an additional 10% developed breathing difficulty after admission. Most strikingly, patients who developed dyspnoea during their hospital stay experienced a 5.9% in-hospital mortality rate, compared with just 1% among those who never reported breathing difficulty. The predictive value of patient-reported dyspnoea extended well beyond the acute hospitalisation period. Patients who reported breathing difficulty at any point during admission had a 50% higher mortality rate over the subsequent two years compared with those without dyspnoea. This risk was even greater among patients who remained breathless at discharge, who faced a 2.6-fold increased hazard of death within two years. These findings suggest several potential clinical applications, including the use of dyspnoea as a trigger for rapid response team activation, a criterion for enhanced monitoring or telemetry, and an indicator to guide discharge planning and goals-of-care discussions. The researchers acknowledged limitations, including the single-centre design and potential inconsistencies in assessment methods. They suggested that electronic data collection using standardised questions could further strengthen the observed associations between dyspnoea and adverse outcomes (2).

New nextbrain atlas enables unprecedented granularity in human brain imaging analysis

Researchers at University College London have developed NextBrain, a probabilistic histological atlas of the entire human brain that enables automated segmentation of magnetic resonance imaging (MRI) scans into 333 distinct regions of interest. The atlas combines artificial intelligence–based registration techniques with Bayesian segmentation methods to provide unprecedented anatomical detail for neuroimaging studies. The NextBrain project addresses a fundamental limitation in neuroimaging: existing histological atlases either lack probabilistic labels across the whole brain or offer insufficient anatomical granularity for detailed regional analysis. An AI-driven registration method uses contrastive learning to achieve accurate alignment between MRI and histological modalities. In addition, a Bayesian refinement technique based on Lie algebra ensures three-dimensional smoothness across the reconstruction, even in the presence of outliers caused by tissue folding or tearing. The research team validated NextBrain through multiple experimental paradigms and has publicly released all components of the project. These include raw and aligned data, an online visualization tool, the probabilistic atlas, a Bayesian segmentation tool distributed with FreeSurfer, and ground-truth delineations for the high-resolution ex vivo hemisphere used in validation. “By enabling researchers worldwide to automatically analyse brain MRIs at a higher level of granularity, NextBrain holds promise for increasing the specificity of findings and accelerating our quest to understand the human brain in health and disease,” the authors conclude (3).

Implications for healthy longevity

Lifestyle and cardiovascular health (CVH) are key determinants of the biological ageing process, which is closely linked to healthy ageing and longevity. Multiple CVH factors may interact and exert combined effects on biological ageing. A cross-sectional study investigated the relative contributions of CVH-related behaviours (diet, sleep, nicotine avoidance, and physical activity) and clinical indicators (BMI, blood lipids, blood glucose, and blood pressure) to epigenetic age acceleration (EAA), as well as their collective associations. CVH was assessed using the American Heart Association’s Life’s Essential 8 and evaluated across five measures of EAA: intrinsic EAA (Horvath DNAmAge acceleration), extrinsic EAA (Hannum DNAmAge acceleration), PhenoAge acceleration, GrimAge2 acceleration, and the Dunedin Pace of

Ageing Calculated from the Epigenome (DunedinPACE). Better CVH was associated with lower EAA (ψ estimates of collective associations ranged from −4.29 to −0.79 across EAA measures). The CVH components contributing most to lower EAA varied by sex. In males, nicotine avoidance and better blood glucose control contributed most to lower EAA, accounting for 91% and 77% of the overall associations of CVH with lower GrimAge2 acceleration and DunedinPACE, respectively. Blood glucose alone accounted for 86% and 94% of these associations. In females, physical activity and better blood glucose or BMI were the greatest contributors to lower EAA. Physical activity accounted for 44% of the CVH–GrimAge2 association, while better blood glucose explained 54% and 50% of the associations with GrimAge2 acceleration and DunedinPACE, respectively. Better BMI contributed 46% to lower PhenoAge acceleration. In conclusion, simultaneous improvements in multiple CVH components are associated with lower EAA, with sex-specific differences in the most influential factors. Tailored health strategies—emphasizing smoking cessation and glucose control for males, and physical activity, glucose control, and weight management for females—may help slow biological ageing. These findings highlight the need for public health and clinical interventions that incorporate sex differences in health behaviours and the underlying biological mechanisms of ageing (4).

Dietary carbohydrate intake and cancer risk

Cancer is among the leading causes of death worldwide, and diet plays an important role in cancer risk. However, few studies have provided a comprehensive assessment of the associations between dietary carbohydrate intake and cancer risk. A large population-based prospective cohort study investigated this issue. Dietary information for each participant was collected using the Oxford WebQ, a web-based 24-hour dietary recall questionnaire. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between energy-adjusted carbohydrate intake and the incidence of overall cancer and 21 site-specific cancers. In conclusion, increased consumption of dietary fiber and non-free sugars is associated with a reduced risk of certain cancers (e.g., overall cancer, esophageal, colorectal, lung, and kidney cancers), potentially due to their anti-inflammatory effects, short-chain fatty acid production, and other protective mechanisms. In contrast, higher intakes of free sugars and sucrose are associated with an increased risk of certain cancers (e.g., lung and kidney cancer, and non-Hodgkin lymphoma), which may be attributed to inflammation and oxidative stress (5).

Diagnosis and management of musculoskeletal disorders

Bioelectrical impedance technology (EBI) offers a non-invasive, cost-effective method for body composition assessment and shows promise for diagnosing and managing musculoskeletal disorders, particularly osteoarthritis (OA). OA is a major global health concern among older adults, notably affecting the knee and hip joints. Conventional imaging techniques, such as X-rays and MRI, have limitations for early detection because they cannot detect microscopic changes in cartilage. Phase angle (PhA), a key EBI parameter, is widely used in the assessment of sarcopenia, tumors, and body fluid distribution and is gaining increasing relevance in OA research. PhA reflects cellular health through cell membrane impedance, and studies have shown that lower PhA values are associated with greater OA severity and can predict OA-related degeneration, supporting its potential role in early screening. Furthermore, EBI shows potential for monitoring OA progression and evaluating treatment effectiveness. This review summarises recent advances in OA diagnosis using EBI, with a particular focus on the applications of PhA and other bioimpedance parameters in screening, monitoring, and evaluation. Through a systematic analysis, this review provides theoretical support for the clinical application of EBI, highlighting its potential role in OA prevention, diagnosis, and intervention. With continued technological advancements, EBI is poised to become an important tool in OA management, especially for early diagnosis and personalised treatment (6).

Liberal fluid intake versus fluid restriction in chronic heart failure

Fluid restriction is frequently recommended for patients with chronic heart failure; however, randomised clinical trials assessing its effects remain scarce. In this multicenter, open-label trial, outpatients with chronic heart failure were randomised to receive advice for liberal fluid intake or advice for fluid restriction, limited to a maximum of 1,500 ml of fluid per day. The primary outcome of the trial was health status after 3 months; secondary outcomes included thirst distress and safety events. Among the 504 randomised patients (67.3% male), the KCCQ-OSS at 3 months was 74.0 in the liberal fluid intake group and 72.2 in the fluid restriction group, with a mean difference adjusted for baseline scores of 2.17 (95% confidence interval, −0.06 to 4.39; P = 0.06), indicating that the primary outcome was not met. Thirst distress was higher in the fluid restriction group, and no differences in safety events were observed between the two groups. These findings question the benefit of fluid restriction in patients with chronic heart failure (7).

Effectiveness and safety of respiratory syncytial virus vaccines for adults aged 60 years or older

Respiratory syncytial virus (RSV) is associated with significant morbidity and mortality among older adults. Characterising the safety and effectiveness of recently introduced RSV vaccines is therefore critical. This study aimed to evaluate the effectiveness of RSV vaccines among adults aged 60 years or older, including at-risk subgroups, and to assess the occurrence of major adverse events following vaccination. In this case-control study of 787,822 patients tested for RSV, vaccine effectiveness (VE) was approximately 75% among adults aged 60 years or older in preventing RSV-associated acute respiratory infection, urgent care or emergency department visits, or hospitalisation. Effectiveness was lower but remained substantial among immunocompromised patients. An estimated excess of 11.2 cases of Guillain–Barré syndrome (GBS) per 1,000,000 RSV vaccine doses administered was observed. The VE of the RSV protein subunit vaccine in this study was comparable to that reported in clinical trials (8). Vaccine effectiveness among immunocompromised patients was mildly reduced overall and moderately reduced among stem cell transplant recipients. The risk of immune thrombocytopenic purpura following vaccination was not increased. However, the risk of Guillain–Barré syndrome was statistically significantly elevated among recipients of the RSVPreF vaccine, but not among those who received the RSVPreF+AS01 vaccine, although the absolute risk remained small. These findings suggest that RSV vaccination in older adults is effective, including in most immunocompromised patients, but is associated with a small increase in Guillain–Barré syndrome. These observations should inform clinicians' vaccine selection and patient counselling.

In older adults with multimorbidity presenting with acute cholecystitis, does surgical management compared to non-surgical management result in better clinical outcomes?

Acute cholecystitis in older patients with multimorbidity is associated with a high risk of morbidity and mortality. There is ongoing debate as to whether operative or nonoperative treatment represents the most appropriate approach. In this comparative effectiveness research study including 32,527 older adults with multimorbidity and acute cholecystitis, operative treatment was associated with similar mortality rates but lower readmission rates, fewer emergency department revisit rates, and lower costs by 180 days after hospitalization compared with nonoperative treatment (9). The findings of this study suggest that risk-adjusted operative treatment in older patients with multimorbidity was associated with lower 30- and 90-day readmission rates and fewer emergency department revisits, as well as lower costs by 90 days. In older patients with multimorbidity for whom the management decision is in clinical equipoise, operative treatment should be considered. When uncertainty exists regarding the most appropriate treatment approach for this challenging population, strong consideration

should be given to operative management. In conclusion, in older patients with multimorbidity for whom the management decision is in clinical equipoise, operative treatment should be considered.

New digital-based prehabilitation offers significant benefits for both patients and hospitals

There is increasing acceptance in the global clinical community that prehabilitation reduces postoperative complications, decreases unplanned readmissions, and improves patients' health-related quality of life. The "preoperative" period offers patients an opportunity to improve their fitness. When facing surgery, everyone wants a positive postoperative outcome and an early return to baseline health—or ideally, an even better state (10). However, face-to-face prehabilitation may exclude those who need it most, such as patients from lower socioeconomic backgrounds, because it imposes additional costs, including travel, childcare, and difficulty attending sessions during standard hours. Moreover, an increasing number of patients with frailty, sarcopenia, complex comorbidities, and advanced age are now being offered major surgical interventions. This leaves patients vulnerable to complications, which often translate into higher healthcare costs and increased utilisation, including total expenses, hospital costs, care transition costs, primary care use, dental care, emergency department visits, unplanned hospital readmissions, and hospitalisations. Fortunately, there is now a solution that can enhance theatre efficiency and improve population health, while simultaneously reducing pressure on clinicians and hospital staff. Digital prehabilitation (prehab) offers this potential. Prehab is a relatively new area of healthcare that focuses on improving patients' general health before surgery or treatment to support recovery and reduce the risk of complications. It is a multidisciplinary, personalised intervention centred around four key pillars: prescribed exercise, nutritional optimisation, tailored psychological support, and lifestyle modifications. Prehab programs should be tailored to each patient's perioperative journey. For example, some patients may need psychological support, while others may need assistance improving their physical fitness. The intervention must be delivered as an integrated whole, as each component complements the others. Among the four pillars, exercise is the most studied. It may include aerobic exercise, resistance/strength training, or both. The most critical element is personalisation—tailoring the program to the patient's clinical needs, planned surgical date, functional capacity, and available time. Nutritional optimisation primarily focuses on adequate protein intake, identifying deficiencies, and providing education. Psychological interventions range from talk therapies to cognitive behavioural therapy, addressing anxiety, depression, acceptance of diagnosis, and adherence to prescribed exercise. The fourth pillar, lifestyle modifications, provides active and empathetic support for smoking cessation and alcohol moderation, incorporating education and guidance (11). When delivered digitally, prehab is often significantly less costly than face-to-face services while maintaining comparable patient experience. Additional savings arise from improved health-related quality of life, leading to earlier return to work and reduced demand on social and primary care services.

A first-level cognitive assessment: TICS

This is an Italian study aimed at testing the convergence and deriving equating norms for the Telephone Interview for Cognitive Status (TICS), the Mini-Mental State Examination (MMSE), and the Montreal Cognitive Assessment (MoCA) (12).TICS and MoCA items were grouped as previously described: TICS-Orientation (range = 0–12), -Memory (range = 0–12), -Attention and Executive Functioning (range = 0–9) and -Language (range = 1–8); MoCA-Visuo-Spatial (range = 0–4), -Executive Functioning (range = 0–4), -Language (range = 0–5), -Attention (range = 0–6), -Memory (range = 0–5) and -Orientation (range = 0–6) [16; 20]. A Delayed Recall of the 10-word list was also administered as the final task of the TICS (TICS-Delayed Recall; range = 0–10), with the respective total score being also computed (TICS&DR; range = 1–51). The MMSE was instead subdivided as follows: MMSE-Orientation (including Spatial and Temporal Orientation items;

range = 0–10); MMSE-Attention (including the Serial subtraction/Backward spelling item; range = 0–5); MMSE-Memory (including Immediate Recall and Delayed Recall items; range = 0–6); MMSE-Language (including Naming, Repetition, Command, Reading and Writing items; range = 0–8). The Constructional Praxis item was forcedly left out of any of these groupings, and thus accounted for only within the MMSE global score.TICS scores converged with both MMSE (rs=0.34; p <.001) and MoCA scores (rs=0.42; p <.001)– the same being true for the TICS&DR (MMSE: rs=0.36; p <.001; MoCA: rs=0.42; p <.001).The Italian TICS validly captures examinees' cognitive efficiency as measured by MMSE or MoCA; derived crosswalks between the TICS and MMSE/MoCA allow for flexible use of in-person and telephone-based screeners. In conclusion, the Italian TICS validly captures examinees' cognitive efficiency as measured by the most used in-person screening tests, the MMSE and the MoCA. The flexibility of the current conversions could be further improved by the availability of Italian crosswalks between the MMSE and the MoCA, albeit with the understanding that a slightly different version of the MMSE was used in this study. The present report hence provides useful information that further supports the employment of the Italian TICS within both clinical settings– e.g., to offer a first-level cognitive assessment to patients that cannot access in-person services, as well as to monitor patients' trajectories over time by reducing the risk of loss-to-follow-up phenomena– and research scenarios– e.g., to facilitate the completion of large-scale, decentralised studies on cognition in both clinical and non-clinical populations.

Stepping down from standard care for stable asthma?

Standard care for stable asthma has been scheduled-dose inhaled corticosteroids (ICSs) plus as-needed fast-acting beta-agonists (FABAs). The efficacy and safety of stepping down from scheduled ICS plus an as-needed FABA compared with as-needed ICS/FABA are unclear. To evaluate the effectiveness and safety of stepping down from scheduled ICS plus as-needed FABA compared with as-needed ICS/FABA in patients with stable asthma, MEDLINE, EMBASE, Cochrane Central, and WHO ICTRP were screened for randomised controlled trials comparing outcomes between scheduled ICS plus as-needed FABA and stepping down to as-needed ICS/FABA for patients with stable asthma. Random-effects models-synthesised outcomes included severe exacerbations, asthma control, asthma quality of life, lung function (prebronchodilator FEV1% predicted), cumulative ICS dose (milligrams per year), and severe adverse events. The Grading of Recommendations, Assessment, Development, and Evaluations approach informed certainty of evidence assessments. Meta-analysis showed little to no difference between the scheduled and as-needed ICS groups for severe exacerbations (risk ratio, 0.88; 95% CI, 0.67 to 1.17), asthma quality of life (mean difference [MD], -0.11; 95% CI, -0.28 to 0.07), lung function (MD, -1.24; 95% CI, -3.09 to 0.61), and severe adverse events rate (risk ratio, 1.13; 95% CI, 0.43 to 2.95). Asthma control scores favoured scheduled ICS (MD, 0.13; 95% CI, 0.04 to 0.22), though the effect was trivial. Cumulative ICS dose was lower with as-needed ICS (MD, -105.36 mg/y; 95% CI, -120.85 to -89.88). In the Grading of Recommendations, Assessment, Development, and Evaluation, all outcomes were rated as having moderate certainty of evidence. In conclusion, in patients with stable asthma on scheduled ICS and as-needed FABA, stepping down to as-needed ICS/FABA resulted in noninferior asthma control and asthma quality of life with reduced cumulative ICS exposure. And these findings can reduce drug use, also in old patients (13). Really, evolutionary imaging technology addresses clinical challenges: this is the future of care in any field of medicine, and in any comprehensive programme designed to accelerate clinical development by providing biopharma and medical device companies with streamlined access to de-identified clinical data, artificial intelligence tools, and international research networks. Traditional barriers in clinical development should be withdrawn by consolidating access to real-world clinical data, biospecimens, multi-omics profiling capabilities, and physician-scientist expertise. There are critical phases of therapeutic development: discovery through real-world clinical data and

biospecimens; validation, particularly in older multimorbid patients, via rigorous testing of AI models and digital solutions; and deployment through scalable infrastructure, to develop and validate AI models for early disease detection, identify patient populations, including geriatric patients, for targeted therapies, and enhance clinical trial recruitment strategies. Development of multimodal AI models for disease detection, creation of precision patient identification tools, diversification of clinical trial recruitment, and deployment of validated digital health solutions are needed to support incoming clinical development programmes across multiple therapeutic areas, including internal medicine and geriatrics.

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