Supportive and palliative care for people with respiratory problems and pre-existing serious mental illness

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ABSTRACT

Purpose of review

People living with serious mental illness are at a higher risk of developing respiratory problems that can lead to increased morbidity and early mortality. This review aimed to identify recent advances in care provision for people with respiratory problems and pre-existing serious mental illness to ease symptom burden and reduce the risk of premature mortality.

Recent findings

Intervention-based studies in this area are scarce. The evidence reviewed originated from observational studies. Concluding comments from the synthesis suggest there are specific needs for proactive screening of respiratory function as part of routine physical health checks across care settings for people living with serious mental illness, more stringent monitoring of comorbid chronic lung conditions, and increased attention in reducing the frequency respiratory infections. Integrated services across care settings are needed to support people with serious mental illness to limit the impact of modifiable lifestyle factors known to be detrimental to respiratory health, such as smoking.

Summary

Key priorities are identified to improve accessibility and inclusivity of respiratory care pathways for people living with serious mental illness to support early detection and proactive monitoring of respiratory problems to help reduce the risk of early mortality.

Keywords

Mental illness, respiratory, integrated care, mortality

INTRODUCTION

People with serious mental illness (SMI) such as schizophrenia, bipolar disorder, and major depressive disorder are known to die prematurely [1*]. Excess mortality in people with SMI is largely attributable to common physical health conditions: deaths from respiratory diseases is one of the three main causes along with cardiovascular and metabolic-endocrine disease [2-5*]. Unmet supportive and palliative care needs for people with SMI have been identified [6, 7*-9*]. As health services aim to address growing complexities in care, adopting a person-centred approach to supportive and palliative care for people with SMI is needed to help detect and prevent avoidable health deterioration and relieve symptom burden [8**, 10-14]. Integrated care provision between service providers is required to facilitate more inclusive access to physical health management practices, enable new tailored interventions, and address inequities [6, 8**, 11**, 15, 16].

The aim of this review was to identify current evidence relating to supportive and palliative care of people with respiratory problems and pre-existing SMI. Database searches were conducted in MEDLINE and Embase (via OVID), CINAHL, PsycInfo, Web of Science, and SCOPUS. Medical subject headings for Palliative Care, Terminal Care, Mental Disorders, Respiration, and Respiratory Tract Diseases were combined with keyword searches (with term and spelling variants) for respiratory, lung, breathing, pulmonary '(serious or persistent or severe) mental illness', schizophrenia, bipolar, borderline personality, major depression. Results were restricted to peer-reviewed articles published in the English language from 2018 onwards describing primary research using experimental or observational designs.

RESULTS

Eight papers were eligible [17-21, 23-25*]: all reports used observational non-clinical designs. A summary of the papers is given in **Appendix 1**. Search results did not include any evidence relating to palliative or terminal care interventions specifically targeted at people with respiratory and SMI comorbidities. As such this review focuses on supportive needs at both the person level (e.g. smoking cessation strategies) and the system level (e.g. equitable access to care).

Burke et al, 2018 [17] reported a cross-sectional observational study involving a convenience sample of 82 adults with SMI admitted to an urban mental health unit in Australia over a 3-month period. The aim was to evaluate implementation of respiratory screening in a mental health unit and assess the feasibility and cost effectiveness of employing a mental health nurse to perform spirometry measures as part of a routine physical assessment. Ten of 57 patients screened using spirometry (18%) had results consistent with COPD; six of these did not have a COPD diagnosis, suggesting there is a significant number of people with SMI displaying signs of respiratory disease that are undiagnosed. Nurse-led questionnaire results indicated that n=33/75 (44%) reported breathlessness, n=29/77 (38%) wheezing, n=21/81 (26%) had diagnosed asthma, n=41/78 (52%) currently smoked tobacco, and n=11/77 (14%) reported using cannabis regularly. The study concluded: i) respiratory screening measures were feasible in a mental health unit, ii) an integrated treatment pathway between hospital, community-based mental health services, specialist units, and GPs is needed to identify currently hidden disease and enable earlier treatment and health promotion strategies.

Sikjaer et al [18] conducted a national cohort study that identified distinct cohorts of people with SMI and COPD, tuberculosis, or lung cancer using the Danish National Patient Registry (1998-2009). People with pre-existing psychiatric morbidity who were diagnosed with one of the three pulmonary diseases were significantly older at diagnosis and had higher comorbidity index scores. Consistent with other studies, this was associated with reduced survival over the period of observation. Of those diagnosed with COPD who had psychiatric comorbidity, the majority died of cancer (most often lung cancer: n=4,464/18,942; 24%), whereas deaths from COPD accounted for n=583/18,942 (3%) within the sample. This was argued to emphasise the significance of early detection of respiratory disease, and the need to access intense treatment and comprehensive monitoring for people with psychiatric comorbidities.

Another large observational study using Danish national patient registries (2008-2013) was carried out by Jørgensen et al [19] who studied the association between quality of COPD care and clinical outcomes in people with schizophrenia. Adherence to a series of recommended process performance measures of outpatient COPD care was used to quantify quality including lung function assessment, nutrition status, dyspnea, smoking (status and cessation advice), offers of COPD rehabilitation, appropriate medication, and regularity of inhaler technique checks. COPD patients with a diagnosis of schizophrenia accounted for n=621/72,692 (0.9%) of the total cohort and were involved in n=1,502 hospital inpatient or outpatient contacts for COPD exacerbations during the observational period. People with schizophrenia and COPD were younger and more likely to be current smokers, admitted as an inpatient for an exacerbation, and have a higher Body Mass Index (BMI) than COPD patients without schizophrenia. Quality measures of COPD care were comparable overall between cases with and without schizophrenia, however, there were inequities of access to care. People with schizophrenia, particularly males, were less likely to receive long-acting muscarinic antagonists or long-acting β2-agonists maintenance treatment. Additionally, higher 30-day mortality following an admission for an exacerbation was recorded for those with COPD and schizophrenia. Authors concluded that further attention to this discrepancy is warranted, that systems of care must strive for parity of esteem for people with SMI, and physicians must ensure neither stigma and/or a lack of experience in treating people with SMI results in poorer clinical outcomes.

Arffman et al [20] performed an observational study using data derived over a 24 year period (1993-2013) from national patient registries in Finland. They identified cases of lung cancer-specific mortality in people with SMI: n=37,852 lung cancer cases were identified of which n=4,640 (12%) had a SMI diagnosis (n=3,629/27,557 (13%) men and n=1,011/10,295 (10%) women). Non-affective psychotic disorder was the most prevalent SMI diagnosis. Analyses identified excess cancer-specific mortality in people with lung cancer and SMI comorbidities. Potential reasons include differences in the cancer diagnostic process for people with SMI and potential adverse cancer treatment outcomes. Further studies are needed to discern the role of patient- and system-related factors such as treatment adherence and collaborative multidisciplinary working between care professionals. The study could not determine the influence of smoking and other lifestyle factors; however, the authors highlighted the need for smoking cessation interventions for this patient group.

A national observational study was conducted by Li et al [21] that included a nested case-control study to evaluate the incidence and risk factors for recurrent pneumonia in those with bipolar disorder (BD). A cohort of patients admitted between 1996-2012 (from Taiwan's National Health Insurance Research Database: NHIRD) included 830 cases with BD recorded to have had incident pneumonia after their first psychiatric admission during the observation period. There were 188 valid cases of recurrent pneumonia following a baseline episode of pneumonia who were linked to two controls matched for sex, age (±5 years), and year of first psychiatric admission. Average interval between baseline and subsequent pneumonia episodes was 727 days (SD=683, range=32-3441). Risk factors investigated were types of antipsychotic and mood stabilizing medications (including benzodiazepines) and comorbid physical illnesses. Analyses also estimated the effects of accumulative daily dose of the prescribed medications.

An excess incidence of recurrent pneumonia in people with BD was identified: six times higher than the incidence of initial pneumonia among people with BD without a history of pneumonia. Incidence of recurrent pneumonia increased with age. Nearly 10% of valid cases of recurrent pneumonia died within 30 days of admission. Comorbid physical illnesses that had an associated increased risk of a

recurrent pneumonia episode included asthma, cancer, hypertension, and diabetes. No association of increased risk of recurrent pneumonia was identified with current use of psychotropic medications. This result was notable for differing from previous findings of an increased risk associated with antipsychotics [22]. Authors concluded that physicians should monitor closely people with BD who have comorbid physical illnesses that could increase susceptibility to recurrent pneumonia. Strategies targeting prevention are needed to reduce the risk of recurrent pneumonia and mitigate the burden of respiratory illness for people with BD.

Staying with the theme of pneumonia, benzodiazepines are frequently prescribed to people with schizophrenia as an anxiolytic, and used frequently in palliative care drug regimens. As reported by Li et al [21], findings associating psychotropics with pneumonia among people with SMI are mixed. Cheng et al explored the relationship between benzodiazepine exposure and the risk of developing pneumonia for people with schizophrenia using a case-control design [23]. Data for this national cohort study were derived from the Psychiatric Inpatient Medical Claims database (subset of Taiwan's NHIRD). Medical records data from 1996-2010 for a cohort of n=34,929/187,117 (19%) people with schizophrenia were identified. Within the cohort were n=2,501 cases of pneumonia requiring a hospital admission. Controls were matched according to sex, age (±5 years), and year of baseline psychiatric admission using a 1:4 ratio. Results suggested that nearly all types of benzodiazepine used within 30 days of admission had a dose-dependent effect on pneumonia risk. A potential contributing factor is that hospitalised patients were sicker than outpatients with schizophrenia which may have influenced pneumonia risk. However, the authors concluded that use of benzodiazepines in people with schizophrenia is a clinical concern in need of further attention.

In another Taiwanese study, Shen et al [24] assessed the risk of people with schizophrenia developing pleural empyema through a nationwide propensity-matched cohort study using the Longitudinal Health Insurance Database 2000 (NHIRD subset containing data from a random selection of 1 million people). A cohort of n=55,888 cases diagnosed with schizophrenia indexed between 2000-2011 was identified and a 1:1 comparison cohort were selected matched for age,

sex, occupation, urban/rural location, year of diagnosis, and comorbid factors (e.g. asthma, COPD, obesity, tobacco/substance use, and cancer). Risk of pleural empyema for people with schizophrenia was 2.4-fold greater than the comparison cohort. Stratified results according to the propensity matched categories revealed significant hazard ratios for pleural empyema in all sub-groups. The pooled data indicated that the incidence was higher in men and increased with age for men and women. Although determining specific mechanisms that mediate risks were outside the scope of the study modifiable lifestyle factors such as smoking and substance abuse are viable contributors. Certain antipsychotic medications were also identified as warranting further research due to links with impaired swallowing, excessive salivation, and lowered white blood cell counts.

Finally, a UK cohort study used electronic health record data on secondary mental healthcare services (2013-2017) from the South London and Maudsley Foundation Trust [25*]. Kugathasan et al sought to identify associations between two or more physical comorbid health conditions with mortality in people with schizophrenia spectrum disorders (SSD). To establish associations for all-cause mortality statistical analyses used hazard ratios (HR) and population attributable fractions (PAFs): PAFs estimated the number of deaths that would not have occurred without the presence of the multiple comorbid disease combinations. Nearly two thirds of people with SSD also had two or more physical comorbidities (n=6,262/9,775: 64%); 12% (n=1,189/9,775) had six or more. The respiratory system was recorded as the third most prevalently affected physical comorbidity disease system in n=3,609/9,775 (37%) of cases, below neurologic n=4,859/9,775 (50%) and endocrine n=4,141/9,775 (42%). The order of prevalence of two-way disease system combinations with the respiratory system were neurologic (25%), endocrine (21%), viral infection (21%), cardiovascular (15%), musculoskeletal (15%), skin (13%), and digestive (11%). Nine per cent died during the observational period (n=880/9,775). The disease combinations with highest observed 5-year mortality were cardiovascular-respiratory diseases (HR: 2.23; 95% CI, 1.49 to 3.32), respiratory-skin (HR: 2.06; 95% CI, 1.31 to 3.24), and respiratory-digestive (HR: 1.88; 95% CI, 1.14 to 3.11). The top three highest PAFs for 5-year mortality associated with physical comorbid disease systems for

people with SSD were cardiovascular + respiratory (PAF 36%), neurologic + respiratory (PAF 33%) and respiratory + skin (PAF 30%).

Discussion

Themes identified within and across the included papers therefore reflect known factors present in the literature: 1) Lifestyle factors, 2) Early detection and diagnosis, 3) Treatment access and Treatment uncertainty, 4) Poorer health outcomes and Elevated mortality, and 5) Service integration and Experience of care. The distribution of this thematic content within and across the papers is summarised in **Figure 1**. Potential reasons for inequalities may highlight the challenge of developing inter-disciplinary competencies in providing holistic care for people living with SMI. Psychiatrists and psychiatrically trained nurses may be benefit from palliative care training, and palliative care specialists may benefit from gaining competencies in caring for mentally ill patients [20, 26]. This may help reduce the chance of diagnostic overshadowing where physical signs of palliative care needs are misattributed to pre-existing mental health symptoms. A further reason for the inequities in accessing care is a known reluctance to engage in care planning conversations with people with SMI [27]. Current experiences for people with respiratory problems and SMI represent a perseverance of Tudor-Hart's Inverse Care Law [28]: an inverse relationship between the level of support needs people with SMI have and care and support they receive. In the current context of COVID-19, sectors of society facing structural vulnerabilities in accessing care have accentuated inequities in health service access. As health services move to adapt to an emerging and novel landscape there is opportunity to promote change collectively in previously neglected areas of care.

Future research

Future research should consider the influence of multiple disease systems. Two-way physical disease combinations increased the risk of 5-year mortality in people with SSD more than single physical diseases [25*]. Respiratory, neurologic, and cardiovascular disease combinations had the highest impact on mortality in people with SSD. This may suggest that managing disease burden of

one condition affects the development, management, and outcome of other comorbid illnesses and subsequent mortality. Modifiable lifestyle factors such as smoking or physical activity were identified as important contributing factors. The authors conclude that the aetiology of this elevated impact requires further study and a more proactive, coordinated approach to prevention and management of physical comorbidities is required [25*].

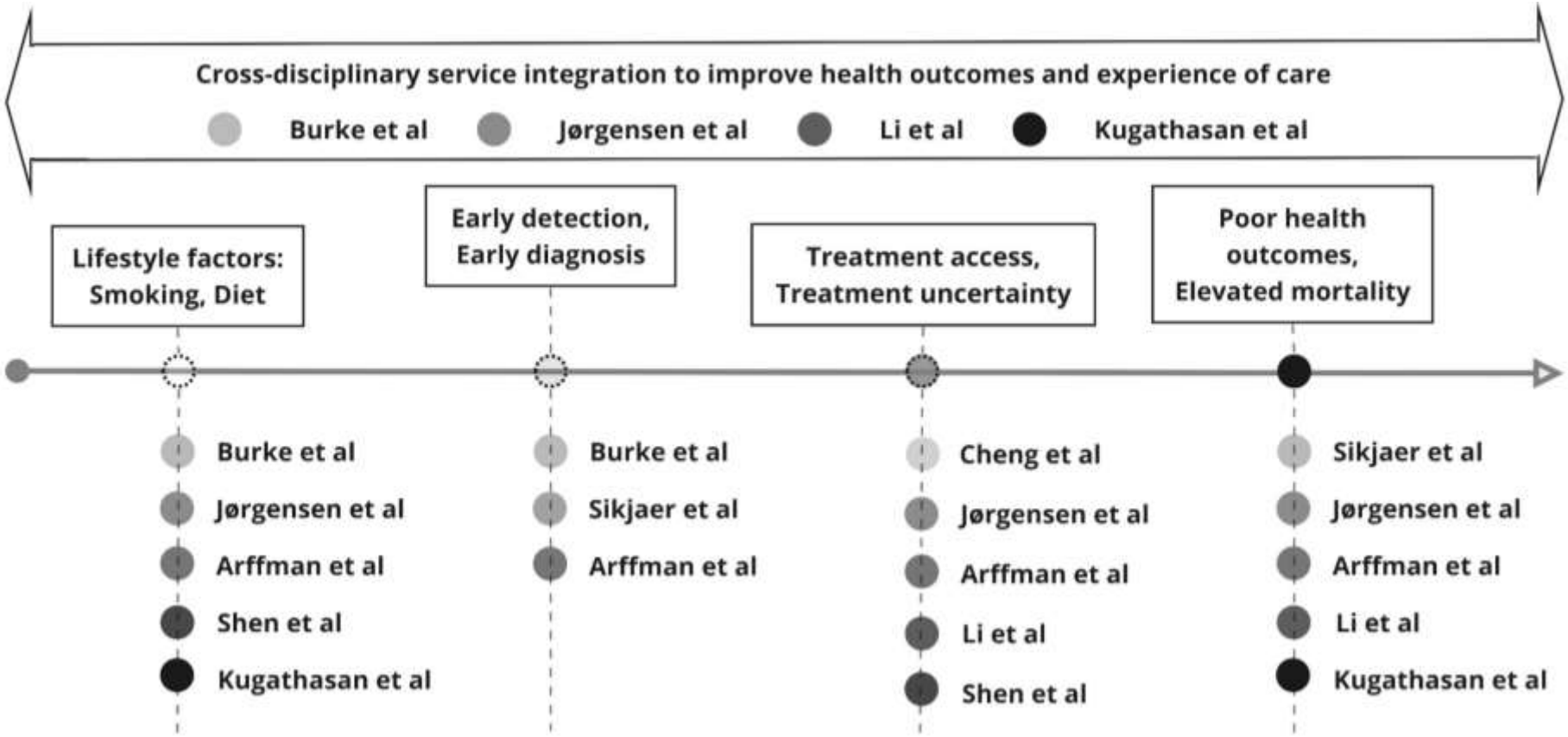

Figure 1: Themes derived from the synthesis of papers highlight the need for increased attention in bridging service delivery gaps to enable equitable access to supportive care involving person-centred approaches focused on prevention, early detection, comprehensive monitoring, and responsive to trajectories of health deterioration for people with mental and respiratory comorbidities.

CONCLUSION

The review authors' interpretation of the synthesis suggest developments are needed in three key areas to improve supportive, palliative, and end of life care for people with respiratory problems and SMI.

1) At a service level, integrated and coordinated care across sectors is needed to align care priorities to ease the burden of comorbid diseases and reduce the prevalence of early mortality in people with SMI experiencing respiratory problems [6, 12, 13, 15, 26]. Proactive detection of respiratory illness and stringent monitoring of respiratory function as part of periodic physical health checks for people with SMI across care settings is required [5*, 17, 29]. Promising examples of integrated services that bridge respiratory and palliative care may provide a model for wider consideration [30**]. Interdisciplinary training and practice development needs to challenge stigma that may limit people with SMI taking an active role in discussing preferences for the type and place of care in the period approaching the end of life [12, 14, 16, 30**, 31*-33]. To advance evidence-based practice, pragmatic effectiveness studies of novel approaches to integrate services across care settings are needed [8**].

2) There is currently clinical uncertainty and prescribing dilemmas for people with respiratory problems and SMI. There is evidence of respiratory infections and serious adverse effects associated with antipsychotics, anxiolytics, and polypharmacy for people with SMI [23, 34, 35]. Clinical opinion is divided on appropriate use of palliative agents such as opiates for people with comorbid SMI and respiratory problems due to increased risk of respiratory depression [36, 37]. Some antipsychotic medications have known associations with QT prolongation (seen on an electrocardiogram) and using additional pain medications such as methadone may increase this risk [38]. Due to heterogeneity and prevalence of metabolic side effects from antipsychotic medication further research is needed to address potential determinants for serious adverse drug interactions and individual tolerability for palliative care medications [39**].

3) A clear priority for rigorous non-pharmacological research to support people with respiratory problems and SMI are behavioural interventions to modify lifestyle [40, 41], especially smoking cessation strategies. There are indications that smoking cessation interventions are feasible for people with SMI and more research is needed to evaluate implementation strategies across settings in pragmatic effectiveness studies [42-44].

Key points

Identified supportive care needs for people with respiratory problems and SMI:

- Interventions to promote healthy behaviours to reduce harm from unhealthy lifestyle practices (e.g. smoking) that may prevent further morbidity and earlier mortality;
- Periodic respiratory health risk assessment, early detection and early diagnosis to allow early intervention and reduce the number of people with SMI and chronic respiratory conditions;
- Proactive and comprehensive monitoring to allow timely response to mediate and ameliorate signs of deterioration in chronic respiratory diseases, prevent the incidence and recurrence of respiratory infections, and respond to changing priorities of care;
- Equitable access to the best available treatments to mitigate the burden of comorbid diseases and promote wellbeing.

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Conflicts of Interest

There are no conflicts of interest

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